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## **ORIGINAL RESEARCH ARTICLES**

### **Risk factors associated with the histological grade of canine mast cell tumor based on Kiupel's two-tier classification of malignancy**

*Factores de riesgo asociados al grado histológico del mastocitoma canino basado en la clasificación de malignidad de dos niveles de Kiupel*

*Fatores de risco associados ao grau histológico do tumor de mastócitos canino com base na classificação de malignidade de dois níveis de Kiupel*

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**Abstract**

**Background:** mast cell tumor (MCT) is one of the most common neoplasms in dogs, and histological grading is critical for its prognosis. However, there is limited local information on the influence of factors such as sex, age, breed, and anatomic location of the lesion on the malignant grade of this neoplasm. These factors are important for risk assessment and understanding the biological behavior of the tumor. **Objective:** to evaluate the association between risk factors (sex, age, breed, anatomical location) and histological grade of MCTs diagnosed at the Laboratorio de Patología Animal of the Universidad de Antioquia between 2019 and 2023. **Methods:** this is a retrospective study based on histopathology reports, 3468 canine biopsies were identified, of which 363 cases were diagnosed by cutaneous MCTs. Data on the year of the report and tumor classification were included. Statistical analysis included relative frequencies, and the risk of developing low-grade (LG) or high-grade (HG) MCT was estimated using univariable analysis with the Fisher exact test to determine odds ratios (ORs) with 95% confidence intervals (CI). **Results:** In all canine MCT reports, 74.7% were LG and 25.3% were HG. Males and females presented with equal frequency of tumor regardless of grade (round up to 50.0%). Patients aged 5-8 years had a higher risk for LG-MCT (OR = 2.16, CI 1.32, 3.52), while those aged 9-12 years had a higher risk for HG-MCT (OR = 2.10, CI 1.30, 3.39). The French Bulldog breed had an increased risk for HG-MCT (OR = 5.77, CI 1.96, 16.96). Pitbull, Mixed, and Pug breeds were most frequently diagnosed with the neoplasm, with no risk for a specific histologic grade. The most common location was the trunk, with 23.9% of HG and 21.4% of LG cases, with no statistical differences. **Conclusions:** the findings allowed to identify the risk associated with age and breed with the development of more aggressive forms of the tumor; other variables such as sex did not have an influence. This information may be relevant for clinical management and early risk prediction.

**Keywords:** *age; breed; canine; histologic grade; Kiupel's classification; mast cell tumor; prognosis; risk factors; sex; skin.*

## Resumen

**Antecedentes:** el mastocitoma (MCT) es una de las neoplasias más comunes en caninos, y la gradificación histológica es crucial para su pronóstico. Sin embargo, existe poca información local sobre la influencia de factores como el sexo, la edad, la raza y la localización anatómica de la lesión sobre el grado de malignidad de esta neoplasia. Estos factores son importantes para evaluar los riesgos y entender el comportamiento biológico del tumor. **Objetivo:** evaluar la asociación entre los factores de riesgo (sexo, edad, raza, localización anatómica) y el grado histológico de los MCTs diagnosticados en el Laboratorio de Patología Animal de la Universidad de Antioquia entre 2019 y 2023. **Métodos:** estudio retrospectivo basado en informes histopatológicos, se identificaron 3468 biopsias caninas, 363 tuvieron diagnóstico de MCT cutáneo. Se incluyeron datos sobre el año del informe, el perro y la clasificación del tumor. El análisis estadístico incluyó frecuencias relativas, y el riesgo de desarrollar MCT de bajo grado (LG) o alto grado (HG) se estimó mediante análisis univariable con la prueba exacta de Fisher para determinar odds ratios (OR) con intervalos de confianza (IC) del 95%. **Resultados:** de todos los informes de MCT, el 74.7% fueron de LG y 25.3% de HG. Machos y hembras presentaron la misma frecuencia de tumor independientemente del grado (alrededor del 50,0%). Pacientes de 5 – 8 años mostraron mayor riesgo para LG-MCT (OR = 2.16, CI 1.32, 3.52), mientras que, de 9 – 12 años a HG-MCT (OR = 2.10, CI 1.30, 3.39). La raza Bulldog Francés tuvo un mayor riesgo para el HG-MCT (OR = 5.77, CI 1.96, 16.96) y las razas Pitbull, Mestizo y Pug, fueron las más frecuentemente diagnosticadas con la neoplasia, sin riesgo por un grado histológico específico. La localización más común fue el tronco, con 23.9% de casos de HG y 21.4% de LG, sin diferencias estadísticas. **Conclusiones:** los hallazgos permitieron identificar el riesgo asociado a la edad y a la raza con el desarrollo de formas más agresivas del tumor, otras variables como el sexo no tienen influencia. Esta información puede ser relevante para el manejo clínico y la predicción temprana del riesgo.

**Palabras clave:** *canino; clasificación de Kiupel; edad; factores de riesgo; grado histológico; mastocitoma; piel; pronóstico; raza; sexo.*

## Resumo

**Antecedentes:** o tumor de mastócitos (MCT) é uma das neoplasias mais comuns em caninos, e a classificação histológica é crucial para seu prognóstico. No entanto, há poucas informações locais

sobre a influência de fatores como sexo, idade, raça e localização anatômica da lesão no grau de malignidade dessa neoplasia. Esses fatores são importantes para a avaliação de risco e para a compreensão do comportamento biológico do tumor. **Objetivo:** avaliar a associação entre os fatores de risco (sexo, idade, raça, localização anatômica) e o grau histológico dos MCTs diagnosticados no Laboratório de Patología Animal da Universidad de Antioquia entre 2019 e 2023. **Métodos:** estudo retrospectivo baseado em relatórios histopatológicos, foram identificadas 3.468 biópsias caninas, sendo que 363 foram diagnosticadas com MCT cutâneo. Foram incluídos dados sobre o ano do laudo, o cão e a classificação do tumor. A análise estatística incluiu frequências relativas, e o risco de desenvolvimento de MCT de baixo grau (LG) ou alto grau (HG) foi estimado por análise univariada usando o teste exato de Fisher para determinar as razões de chances (OR) com intervalos de confiança (IC) de 95%. **Resultados:** de todos os relatos de MCT, 74,7% eram LG e 25,3% HG. Machos e fêmeas apresentaram a mesma frequência de tumores, independentemente do grau (cerca de 50,0%). Pacientes com idade entre 5 e 8 anos apresentaram maior risco de LG-MCT (OR = 2,16, IC 1,32, 3,52), enquanto os pacientes com idade entre 9 e 12 anos apresentaram HG-MCT (OR = 2,10, IC 1,30, 3,39). A raça Bulldog Francês teve um risco aumentado de HG-MCT (OR = 5,77, IC 1,96, 16,96) e as raças Pitbull, Mestiço e Pug foram as mais frequentemente diagnosticadas com a neoplasia, sem risco para um grau histológico específico. A localização mais comum foi o tronco, com 23,9% dos casos de HG e 21,4% de LG, sem diferenças estatísticas. **Conclusões:** os achados permitiram identificar o risco associado à idade e à raça para o desenvolvimento de formas mais agressivas do tumor; outras variáveis, como o sexo, não têm influência. Essas informações podem ser relevantes para o gerenciamento clínico e a previsão de risco precoce.

**Palavras-chave:** *canino; classificação de Kiupel; fatores de risco; grau histológico; idade; tumor de mastócitos; pele; prognóstico; raça; sexo.*

## **Introduction**

Mast cell tumor (MCT) is a neoplastic skin disease caused by mast cells, round connective tissue cells histologically characterized as ovoid with a central nucleus and grayish cytoplasm with abundant intracytoplasmic granules (Meuten, 2017). Although the cause of this neoplasm is

unknown, a mutation in the c-kit gene, a proto-oncogene signaling cell proliferation, has been postulated as particularly relevant (Vicario *et al.*, 2018).

MCT is the most frequently diagnosed malignant round cell tumor in the skin of dogs (Vicario *et al.*, 2018). According to Kiupel *et al.* (2011), this condition accounts for 7-21% of cases. There are reports that associate the presentation and development of the neoplasm with variables such as sex, age, and breed, although the results are not always consistent. For instance, one study indicated a higher proportion of MCT in females (O'Connell *et al.*, 2013), while another showed no sex association (Shoop *et al.*, 2015). Several authors have reported greater susceptibility between the ages of 7 and 10 years (Shoop *et al.*, 2015; Torres *et al.*, 2006; Millán, 2021). The breeds with the highest incidence are Boxer, Pug, Weimaraner (Lozano *et al.*, 2016), and Golden Retriever (Millán, 2021). The most frequently reported anatomical locations were the trunk and extremities, with a lower prevalence in the head (Rojas, 2017).

Although there is no definitive parameter to predict the biological behavior of a tumor, histopathological analysis is essential to confirm its tissue origin and to assign a malignancy grade. In MCT, the grade depends on factors such as the number of mitoses, the presence of multinucleated cells, and karyomegaly (Kiupel *et al.*, 2011). High-power field (HPF) mitotic count has been shown to predict the biological behavior and prognosis of canine MCT in 90-95% of cases (Meuten, 2017). There are several grading systems, one of which is widely used by Kiupel. Consequently, low-grade MCT (LG-MCT) has minimal recurrence and an estimated survival of 3-4 years (Meuten, 2017; Lozano *et al.*, 2016), whereas high-grade cases (HG-MCT) show survival of less than 4 months (Lozano *et al.*, 2016). The main causes of euthanasia are recurrence, lymph node metastasis, and the development of mastocytosis (Meuten, 2017).

The lack of precise data in local veterinary practice regarding the correlation between risk factors and histological grade highlights the need for further investigation. To date, no studies have been conducted in this area. This study evaluated the association between sex, age, breed, anatomical location, and histological grade based on Kiupel's two-stage malignancy classification (Kiupel *et al.*, 2011) using cases previously examined at the Laboratorio de Patología Animal of the Universidad de Antioquia (2019–2023).

## **Materials and Methods**

### *Ethical considerations*

The study involved the analysis of information obtained during routine histopathological examination in the Laboratorio de Patología Animal of the Universidad de Antioquia with prior authorization from the laboratory's Technical Direction. Approval from an ethical committee on animal experimentation was not necessary.

### *Study population and data collection*

Inclusion criteria were MCT cases diagnosed within the study period, with data extracted on the year of the case report, sex, age, breed, and tumor characteristics (including location and histologic grade). Histological grading was based solely on Kiupel's 2-tier system, which classifies MCTs as HG-MCT if they have any of the following features: mitotic count  $>7$  per 10 high-power fields (HPF),  $>3$  multinucleated cells per 10 HPF,  $>3$  bizarre nuclei per 10 HPF, or marked karyomegaly. Tumors lacking these criteria are classified as LG-MCT (Kiupel et al., 2011). This histologic classification system has been shown to be more consistent and less ambiguous than others in predicting the biological behavior of MCT (Kiupel et al., 2011). Reports presented in a different grading system and variable categories with fewer than five cases were not included in the analysis.

### *Statistical analysis*

Data from the reports were entered into Excel worksheets (Microsoft Corp., Redmond, WA, USA). A reference group was defined for each respective analysis. To compare the overall risk of developing MCT, all canine histopathologic biopsy reports for various causes during the study period were considered. To evaluate the grading in contrast to the variable sex, age, breed, and anatomical localization, the reference group was the reports with a specific MCT diagnosis. Descriptive statistics are reported as absolute and relative frequencies. The risk of MCT, HG-MCT, and LG-MCT were assessed by the odds ratio (OR). Univariate analysis with the Fisher's exact test was used to calculate the OR with 95% confidence intervals (CI). For each variable, ORs were calculated by comparing the incidence in the analyzed category with the number of reports in the corresponding reference group. An OR was considered statistically significant if the 95% CI excluded the value 1. All analyses were performed using Infostat/L® software, version 2020.

## Results

During the years included in the study, 3468 canine cases were received, of which 363 biopsy reports were diagnosed as MCT. Of these, 25.3% (92/363) were classified as high grade (HG), and 74.7% (271/363) were classified as low grade (LG). Samples were submitted by several veterinary institutions located in the region of Valle de Aburrá (Antioquia, Colombia) and surrounding areas. Detailed data are presented in Table 1.

**Table 1.** Distribution of MCT cases according to histological grade at the Laboratorio de Patología Animal of the Universidad de Antioquia during the analyzed period, 2019-2023.

Year	No. of consultations 2019-2023	No. of MCTS	High grade	% High grade	Low grade	% Low grade
2019	684	73	18	19.6	55	20.3
2020	487	49	17	18.5	32	11.8
2021	639	60	19	20.7	41	15.1
2022	816	89	21	22.8	68	25.1
2023	842	92	17	18.5	75	27.7
Total	3468	363	92	25.3	271	74.7

### *Sex and histologic grade*

The diagnosis of MCTs was distributed almost equally between males and females, representing 11.5% (184/1,598) and 9.6% (179/1,870) of the total cases for each sex, respectively (Table 2).

**Table 2.** Distribution of MCT cases according to sex in canine patients diagnosed at the Laboratorio de Patología Animal of the Universidad de Antioquia (2019 - 2023).

Sex / Grade	No. of consultations 2019-2023	No. of MCTS	% MCTS	OR MCTS	CI 95%
Males	1598	184	11.5	1.36	1.04, 1.69
Females	1870	179	9.6	0.92	0.74, 1.14
Total	3468	363			

OR: Odds Ratio; CI: Confidence Interval; % MCTS: percentage of MCTS within the total number of consultations by each sex during the study period (e.g., Males:  $184 \times 100 / 1598 = 11.5\%$ ).

Considering the total number of cases by histological grade, 50.0% (46/92) of the HG-MCT cases were reported in males, with an equal percentage observed in females (50.0%, 46/92). For LG-MCT, 50.9% (138/271) of cases occurred in males and 49.1% (133/271) in females. When analyzing the total number of cases by sex, males were slightly more affected by LG-MCT, with 138 of 184 cases (75.0%), followed by females with 133 of 179 cases (74.3%). Conversely, females had a slightly higher frequency of HG-MCT, with 46 of 179 cases (25.7%), compared to males with 46 of 184 cases (25.0%). No statistical difference was observed between sex and histological grade (Table 2.1).

**Table 2.1.** Distribution of high- and low-grade MCT cases by sex in canine patients diagnosed at the Laboratorio de Patología Animal of the Universidad de Antioquia (2019 - 2023), n = 363.

Sex/Grade	High grade	% High grade	% High grade MCTs per sex	OR High grade	CI 95%	Low grade	% Low grade	% Low grade MCTs per sex	OR Low grade	CI 95%
Males	46	50.0	25.0	0.96	0.60, 1.54	138	50.9	75.0	1.04	0.65, 1.66
Females	46	50.0	25.7	1.04	0.65, 1.66	133	49.1	74.3	0.96	0.60, 1.54
Total	92	100				271	100			

OR: Odds Ratio; CI: Confidence Intervals; % High-grade and % Low-grade: percentage of each sex among all HG and LG-MCT cases, respectively (e.g., Males:  $46 \times 100 / 92 = 50.0\%$  and  $138 \times 100 / 271 = 50.9\%$ ); % High-grade and % Low-grade MCTs per sex: percentage of HG and LG-MCTs within the total number of MCT cases for each sex (e.g., Males:  $46 \times 100 / 184 = 25.0\%$  and  $138 \times 100 / 184 = 75.0\%$ ).

### *Age range and histologic grade*

The variable age was evaluated considering the ranges 1 - 4, 5 - 8, 9-12 and 13-16 years. The diagnosis of MCT was 8.2% (31/378), 13.6% (177/1306), 9.2% (130/1410) and 6.7% (25/374) within each of these ranges, respectively. A higher risk of MCT presentation was observed in patients aged 5-8 years, with a statistical difference (OR = 1.82, CI 1.47, 2.27) with respect to the total number of animals diagnosed with the neoplasm in the other age categories (Table 3).

**Table 3.** Distribution of MCT cases according to age range in canine patients diagnosed at the Laboratorio de Patología Animal of the Universidad de Antioquia (2019 - 2023).

Age / Grade	No. of consultations 2019-2023	No. of MCTs	% MCTs	OR MCTs	CI 95%
1 - 4	378	31	8.2	0.83	0.57, 1.22
5 - 8	1306	177	13.6	<b>1.82</b>	<b>1.47, 2.27</b>
9 - 12	1410	130	9.2	0.90	0.72, 1.12
13 - 16	374	25	6.7	0.66	0.43, 1.00
Total	3468	363			

OR: Odds Ratio; CI: Confidence Intervals; Bold: Statistical difference; % MCTs: percentage of MCTs among the total number of consultations by age group during the study period (e.g., age 1–4 years:  $31 \times 100 / 378 = 8.2\%$ ).

Regarding histological grade, the highest frequency of HG-MCT cases was observed in patients aged 9–12 years (48.9%, 45/92), followed by those aged 5–8 years (34.8%, 32/92), 13–16 years (9.8%, 9/92), and 1–4 years (6.5%, 6/92). LG-MCT cases were most common in the 5 – 8-year age group (53.5%, 145/271), followed by 9–12 years (31.4%, 85/271), 1–4 years (9.2%, 25/271), and 13–16 years (5.9%, 16/271). A detailed analysis by age is presented in Table 3.1. Statistical difference was observed between age range and histologic grade, showing that patients aged 5–8 years had a lower risk of developing HG-MCT (OR = 0.46, CI 0.28, 0.76) and a higher risk of LG-MCT (OR = 2.16, CI 1.32, 3.52), while those aged 9–12 years had a higher risk of HG-MCT (OR = 2.10, CI 1.30, 3.39) and a lower risk of LG-MCT (OR = 0.48, CI 0.30, 0.77).

**Table 3.1.** Distribution of high- and low-grade MCT cases according to age range in canine patients diagnosed at the Laboratorio de Patología Animal of the Universidad de Antioquia (2019 - 2023), n = 363.

Age/Grade	High grade	% High grade	% High grade MCTs per age range	OR High grade	CI 95%	Low grade	% Low grade	% Low grade MCTs per age range	OR Low grade	CI 95%
1-4	6	6.5	19.4	0.69	0.28, 1.68	25	9.2	80,6	1.46	0.59, 3.57
5-8	32	34.8	18.1	<b>0.46</b>	<b>0.28, 0.76</b>	145	53.5	81,9	<b>2.16</b>	<b>1.32, 3.52</b>
9-12	45	48.9	34.6	<b>2.10</b>	<b>1.30, 3.39</b>	85	31.4	65,4	<b>0.48</b>	<b>0.30, 0.77</b>
13-16	9	9.8	36.0	1.73	0.75, 3.99	16	5.9	64,0	0.58	0.25, 1.33
Total	92					271				

OR: Odds Ratio; CI: Confidence Intervals; Bold: Statistical difference; % High-grade and % Low-grade: percentage of each age group within the total number of HG and LG-MCT cases, respectively (e.g., age 1–4:  $6 \times 100 / 92 = 6.5\%$  and  $25 \times 100 / 271 = 9.2\%$ ); % High-grade and % Low-grade MCTs per age group: percentage of HG and LG-MCTs within the total number of MCTs for each age group, respectively (e.g., age 1–4:  $6 \times 100 / 31 = 19.4\%$  and  $25 \times 100 / 31 = 80.6\%$ ).

### *Breed and histologic grade*

The risk associated with this variable was calculated by breed. Note that the breeds were not equally represented in the total number of cases evaluated. The breeds with the highest frequency of MCT presentation were Pug (35.5%, 43/121), Boston Terrier (23.0%, 17/74), Pitbull (22.2%, 97/437) and Weimaraner (21.7%, 5/23), whereas breeds with a lower frequency of MCT presentation were Mixed Breeds (6.8%, 78/1142), Cocker Spaniel (5.6%, 6/107), Poodle (3.8%, 6/160) and Beagle (3.5%, 7/202). The Pug (OR = 5.77, CI 3.91, 8.50), Boston Terrier (OR = 2.93, CI 1.69, 5.05), Pitbull (OR = 3.25, CI 2.51, 4.21), and Weimaraner (OR = 2.67, CI 1.03, 6.97) breeds showed statistical differences suggesting a higher risk of developing MCT, whereas Mixed-breeds (OR = 0.60, CI 0.46, 0.78), Cocker Spaniel (OR = 0.36, CI 0.16, 0.80), Poodle (OR = 0.36, CI 0.16, 0.80), and Beagle (OR = 0.33, CI 0.16, 0.69) had a lower risk (Table 4).

The Pitbull, Mixed-breed, and Pug had the highest frequency of MCTs, accounting for 58.8% of HG-MCT and 60.5% of LG-MCT cases. The remaining pure breeds accounted for 41.2% of HG-MCT and 39.5% of LG-MCT cases. When considering the number of cases per breed, the Boston Terrier was the breed most affected by LG-MCT. 15 out of 17 cases (88.2%) were diagnosed with this condition. This was followed by Springer Spaniel with 6 of 7 cases (85.7%), Poodle with 5 of 6 cases (83.3%), Labrador Retriever with 23 of 27 cases (81.5%), and Golden Retriever with 16 of 20 cases (80.0%) diagnosed with LG-MCT. In contrast, the breed most affected by HG-MCT was the French Bulldog, with 9 of 14 cases (64.3%) classified as HG-MCT. The Bulldog also showed a notable frequency, with 4 of 7 cases (57.1%) diagnosed with HG-MCT. A statistical difference between breed and histological grade was observed in the French Bulldog breed, which had a higher risk of developing HG-MCT (OR = 5.77, CI 1.96, 16.96) and a lower risk of LG-MCT (OR = 0.17, CI 0.06, 0.51) (Table 4.1).

**Table 4.** Distribution of MCT cases according to breed in canine patients diagnosed at the Laboratorio de Patología Animal of the Universidad de Antioquia (2019 - 2023).

Breed / Grade	No. Consultations 2019-2023	No. of MCTs	% MCTs	OR MCTs	CI 95%
Pitbull	437	97	22.2	<b>3.25</b>	<b>2.51, 4.21</b>
Mix-breed	1142	78	6.8	<b>0.60</b>	<b>0.46, 0.78</b>
Pug	121	43	35.5	<b>5.77</b>	<b>3.91, 8.50</b>
Labrador	244	27	11.1	1.19	0.79, 1.80
Golden Retriever	201	20	10.0	1.05	0.66, 1.68
Boston Terrier	74	17	23.0	<b>2.93</b>	<b>1.69, 5.05</b>
French Bulldog	156	14	9.0	0.94	0.54, 1.62
Schnauzer	229	14	6.1	0.60	0.35, 1.04
Pinscher	137	10	7.3	0.74	0.39, 1.41
Beagle	202	7	3.5	<b>0.33</b>	<b>0.16, 0.69</b>
Bulldog	130	7	5.4	0.53	0.25, 1.12
Springer Spaniel	43	7	16.3	1.87	0.85, 4.14
Poodle	160	6	3.8	<b>0.36</b>	<b>0.16, 0.80</b>
Cocker Spaniel	107	6	5.6	<b>0.36</b>	<b>0.16, 0.80</b>
Fox Terrier	62	5	8.1	0.83	0.35, 2.02
Weimaraner	23	5	21.7	<b>2.67</b>	<b>1.03, 6.97</b>
Total	3468	363			

OR: Odds Ratio; CI: Confidence Intervals; Bold: Statistical difference; % MCTs: percentage of MCTs within the total number of consultations per breed during the study period (e.g., Pitbull:  $97 \times 100 / 437 = 22.2\%$ ).

**Table 4.1.** Distribution of high- and low-grade MCT cases according to breed in canine patients diagnosed at the Laboratorio de Patología Animal of the Universidad de Antioquia (2019 - 2023), n = 363.

Breed / Grade	High grade MCTs	% High grade MCTs	% High grade MCTs per breed	OR High grade	CI 95%	Low grade MCTs	% Low grade MCTs	% Low grade MCTs per breed	OR Low grade	CI 95%
Pitbull	26	28.3	26.8	0.90	0.53, 1.52	71	26.2	73.2	1.11	0.66, 1.88
Mix-breed	18	19.6	23.1	0.86	0.48, 1.53	60	22.1	76.9	1.17	0.65, 2.10
Pug	10	10.9	23.3	1.14	0.54, 2.38	33	12.2	76.7	0.88	0.42, 1.84
Labrador	5	5.4	18.5	0.65	0.25, 1.70	22	8.1	81.5	1.54	0.59, 4.03
Golden Retriever	4	4.3	20.0	0.72	0.25, 2.11	16	5.9	80.0	1.38	0.47, 4.02
Boston Terrier	2	2.2	11.8	0.38	0.10, 1.47	15	5.5	88.2	2.64	0.68, 10.24
French Bulldog	9	9.8	64.3	<b>5.77</b>	<b>1.96, 16.96</b>	5	1.8	35.7	<b>0.17</b>	<b>0.06, 0.51</b>
Schnauzer	3	3.3	21.4	1.26	0.37, 4.25	11	4.1	78.6	0.80	0.24, 2.70
Pinscher	3	3.3	30.0	0.79	0.22, 2.86	7	2.6	70.0	1.27	0.35, 4.62
Beagle	2	2.2	28.6	1.18	0.26, 5.37	5	1.8	71.4	0.85	0.19, 3.84
Bulldog	4	4.3	57.1	4.06	0.98, 16.76	3	1.1	42.9	0.25	0.06, 1.02
Springer Spaniel	1	1.1	14.3	2.06	0.34, 12.36	6	2.2	85.7	0.49	0.08, 2.91
Poodle	1	1.1	16.7	1.71	0.28, 10.57	5	1.8	83.3	0.58	0.09, 3.61
Cocker Spaniel	2	2.2	33.3	1.48	0.31, 7.09	4	1.5	66.7	0.67	0.14, 3.22
Fox Terrier	1	1.1	20.0	0.73	0.11, 4.73	4	1.5	80.0	1.36	0.21, 8.78
Weimaraner	1	1.1	20.0	0.73	0.11, 4.73	4	1.5	80.0	1.36	0.21, 8.78
Total	92	100				271	100			

OR: Odds Ratio; CI: Confidence Intervals; Bold: Statistical difference; % High-grade and % Low-grade: percentage of each breed within the total number of HG and LG-MCT cases, respectively (e.g., Pitbull:  $26 \times 100 / 92 = 28.3\%$  and  $71 \times 100 / 271 = 26.2\%$ ); % High-grade and % Low-grade MCTs per breed: percentage of HG and LG-MCTs within the total number of MCTs for each breed, respectively (e.g., Pitbull:  $26 \times 100 / 97 = 26.8\%$  and  $71 \times 100 / 97 = 73.2\%$ ).

### *Anatomical localization and histologic grade*

During the study period, the anatomical location of the MCT was not specified in 16.1% of cases (200/1242). In cases where the anatomical location was known, the distribution of MCTs was as follows: limbs 15.6% (56/360), trunk 6.8% (80/1185), and head 4.0% (27/681). Statistical differences were observed, with higher risk of neoplasia in the trunk (OR = 1.71, CI 1.32, 2.22), limbs (OR = 1.86, CI 1.37, 2.54), or non-specified anatomical location (OR = 2.62, CI 2.11, 3.26), and lower risk in the head (OR = 0.34, CI 0.23, 0.51) (Table 5).

**Table 5.** Distribution of MCT cases according to anatomical localization in canine patients diagnosed at the Laboratorio de Patología Animal of the Universidad de Antioquia (2019 - 2023).

<b>Anatomical localization / Grade</b>	<b>No. of consultations 2019-2023</b>	<b>No. of MCTs</b>	<b>% MCTs</b>	<b>OR MCTs</b>	<b>CI 95%</b>
Head	681	27	4.0	<b>0.34</b>	<b>0.23, 0.51</b>
Trunk	1185	80	6.8	<b>1.71</b>	<b>1.32, 2.22</b>
Limbs	360	56	15.6	<b>1.86</b>	<b>1.37, 2.54</b>
No specified	1242	200	16.1	<b>2.62</b>	<b>2.11, 3.26</b>
Total	3468	363			

OR: Odds Ratio; CI: Confidence Intervals; Bold: Statistical difference; % MCTs: percentage of MCTs within the total number of consultations by anatomical localization during the study period, e.g., Head:  $27 \times 100 / 681 = 4.0\%$ .

In terms of histological grade, cases in which the anatomic location was not specified had the highest frequency of both HG and LG lesions: 57.6% (53/92) for HG-MCT and 54.2% (147/271) for LG-MCT. HG-MCTs were also frequently observed in the trunk (23.9%, 22/92), extremities (10.9%, 10/92), and head (7.6%, 7/92). Similarly, LG-MCT was spread over the trunk (21.4%, 58/271), extremities (17.0%, 46/271), and head (7.4%, 20/271). No statistical differences were found between the anatomic location and histological grade (Table 5.1).

**Table 5.1.** Distribution of high- and low-grade MCT cases according to anatomical localization in canine patients diagnosed at the Laboratorio de Patología Animal of the Universidad de Antioquia (2019 - 2023), n = 363.

Anatomical localization/ Grade	High grade	% High grade				Low grade	% Low-grade			
		% High grade	MCTs per anat. loc.	OR High grade	CI 95%		% Low grade	MCTs per anat. loc.	OR Low grade	CI 95%
Head	7	7.6	25.9	1.03	0.34, 2.47	20	7.4	74.1	0.97	0.40, 2.31
Trunk	22	23.9	27.5	0.87	0.50, 1.51	58	21.4	72.5	1.15	0.66, 2.01
Limbs	10	10.9	17.9	0.60	0.29, 1.22	46	17.0	82.1	1.68	0.82, 3.43
No specified	53	57.6	26.5	0.87	0.54, 1.40	147	54.2	73.5	1.15	0.71, 1.84
Total	92					271				

OR: Odds Ratio; CI: Confidence Intervals; % High and % Low grade: percentage that each anatomical localization represents within the total number of HG and LG-MCT cases, respectively, e.g., Head:  $7 \times 100 / 92 = 7.6\%$  and  $20 \times 100 / 271 = 7.4\%$ ; % high and % Low grade MCTs per anatomical localization: percentage of HG and LG-MCTs within the total number of MCTs for that specific anatomical localization, respectively, e.g., Head:  $7 \times 100 / 27 = 25.9\%$  and  $20 \times 100 / 27 = 74.1\%$ .

## Discussion

Cutaneous neoplasms are common in dogs, accounting for approximately 30 – 40% of neoplastic diseases in the species (Medina, 2015). Round up to nearly 60% of these tumors are histologically malignant (Meirelles *et al.*, 2010; Medina *et al.*, 2017) and proliferate from epithelial, mesenchymal, and round cells (Cubillos *et al.*, 2021). Cutaneous round cell neoplasms represent 61.15% of all neoplasms in dogs (Torres *et al.*, 2017), and MCT is the most common, accounting for up to 21% of all skin tumors (Meuten, 2017; Kiupel *et al.*, 2011) and 47.1% of all round cell neoplasms (Cano-Botero *et al.*, 2024). Understanding the biological behavior of this tumor is critical for an accurate diagnosis and prognosis. This study evaluated the context of the local area, as local characterizations are essential for understanding how specific epidemiological and environmental factors influence the presentation of pathologies. It is important to note that not all information from the existing literature can be directly applied to other contexts.

In this study, 3468 canine cases were received during the study period, of which 363 were diagnosed as MCT, representing 10.5% of all biopsy reports. Of these, 74.7% were classified as LG-MCT and 25.3% as HG-MCT. These proportions are consistent with other studies reporting that according to Kiupel's 2-tier malignancy classification (Kiupel *et al.*, 2011), it is estimated that 80-90% of MCTs are LG and 20-10% are HG (Meuten, 2017). This supports the validity and utility of Kiupel's MCT classification system. Furthermore, although LG-MCTs are more common, the significant proportion of HG cases highlights the importance of accurate assessment for optimal management.

#### *Sex and histological grade*

No statistical difference was observed to suggest a sex-related risk in the presentation of a particular histologic grade of MCT. Total reports by histologic grade, both males and females each represented round up to 50% of both HG-MCT and LG-MCT cases. These findings are consistent with previous studies that found no sex-related predisposition (Torres *et al.*, 2006; Lozano *et al.*, 2016). Similar findings have been reported by authors such as Martins *et al.* (2021). However, contrasting results have been reported in some previous studies. Śmiech *et al.* (2018) observed a higher risk of MCTs in females, especially for LG tumors, while Jaramillo (2019) reported a higher risk of developing HG neoplasms. In addition, O'Connell *et al.* (2013) found that multiple MCTs were more common in females, and White *et al.* (2011) suggested that spayed females were four times more likely to develop MCTs than non-spayed females. In contrast, Mochizuki *et al.* (2017) found that non-neutered males were more likely to develop HG MCTs, while neutered dogs were less likely to develop HG tumors. The lack of statistical difference suggests that sex is not a primary determinant of MCT grade, and further research is needed on other biological and genetic elements that may influence the malignant grade of the tumor.

#### *Age range and histological grade*

A statistical difference was observed between the age groups. Patients aged 5-8 years had a higher risk (OR = 1.82, CI 1.47, 2.27) of developing MCT. Most studies have previously reported a higher prevalence of MCTs in dogs of a similar age range (London *et al.*, 2003; Hahn *et al.*, 2008; Kiupel *et al.*, 2011). On the other hand, this study also observed a relationship between the age at presentation of the neoplasm and its histological grade, suggesting an age-related risk in terms of

biological behavior. Younger dogs, especially those aged 5–8 years, were more prone to LG-MCT, whereas dogs aged 9–12 years were more prone to HG-MCT. In the 9–12-year group, 48.9% (45/92) of cases were HG and had the second highest percentage of LG-MCTs (31.4%, 85/271), LG-MCTs were most common in dogs aged 5–8 years (53.5%, 145/271) and had the second highest percentage of HG-MCTs (34.8%, 32/92). Previously, Śmiech *et al.* (2018) found that the risk of LG-MCT was highest in dogs aged 4–6 years, while the risk of HG-MCT increased with age, peaking in dogs aged 11–16 years. Another study also showed an increased risk of HG with age (Mochizuki *et al.*, 2017). Jaramillo (2019) observed that geriatric dogs (over 9.1 years of age) have a higher risk of developing HG-MCTs compared with younger and adult dogs, which are more likely to develop LG-MCTs. However, Martins *et al.* (2021) found a decreased risk of LG-MCTs in all age groups studied (0–3, 4–6, 7–10 years).

#### *Breed and histological grade*

Statistical difference was found between breed and histologic grade. We observed that breed is a significant factor in the incidence and histologic grade of MCTs, with French Bulldogs showing a higher risk (OR = 5.77, CI 1.96, 16.96) for the development of HG-MCT, and the Bulldog as the second breed most affected by the same MCT grade. Similarly, previous studies have reported that Bulldogs are highly affected by MCTs (Meuten, 2017), and that French Bulldogs have an increased risk of HG-MCTs (Martins *et al.*, 2021; Jaramillo, 2019). Mochizuki *et al.* (2017) found that bulldogs were more likely to develop HG-MCT when scored by the Patnaik system (Patnaik *et al.*, 1984), although this significance decreased when scored by the Kiupel system (Kiupel *et al.*, 2011). However, other studies have shown that French Bulldogs have an increased risk of developing LG-MCT (Śmiech *et al.*, 2018; Śmiech *et al.*, 2019). Nevertheless, these discrepancies may be due to breed-specific variations in MCT behavior. Genetic factors such as mutations in mast cells or immune response may contribute to this predisposition, including mutations in mitochondrial DNA (Śmiech *et al.*, 2016) or the c-kit gene (Vicario *et al.*, 2018). Bulldog-related breeds have a common ancestor in their phylogenetic development and show elevated risks for developing MCTs of all different histologic grades (Śmiech *et al.*, 2018). More effective clinical management will be facilitated by further investigation to elucidate the genetic basis of breed predisposition to HG tumor development.

According to histological-grade cases, Pitbulls, Mixed-breeds, and Pugs were most frequently associated with both HG and LG-MCT, with slight differences in proportions. Pitbulls had a prevalence of 28.3% HG and 26.2% LG, and Pugs had a prevalence of 12.2% LG and 10.9% HG, which is consistent with other studies noting that Pitbulls are predisposed to developing HG-MCT, whereas Pugs usually have LG lesions (Martins *et al.*, 2021). Śmiech *et al.* (2018) and Mochizuki *et al.* (2017) also reported that Pugs are more susceptible to LG-MCT. In addition, Mixed-breeds showed a distribution of 22.1% LG and 19.6% HG-MCT. Martins *et al.* (2021) reported that Mixed-breeds were the second most common breed to develop HG and LG-MCT, and Śmiech *et al.* (2018) found that Mixed-breeds are often associated with both HG and LG-MCT, with a higher propensity for LG-MCT. Looking at cases by histological grade within each breed, the breeds most affected by LG-MCT were the Boston Terrier (88.2%), Springer Spaniel (85.7%), Poodle (83.3%), Labrador (81.5%), and Golden Retriever (80.0%). Martins *et al.* (2021) reported similar data for the Poodle, Labrador, and Golden Retriever breeds, with 66.7%, 78.6%, and 75.0% of LG-MCT cases, respectively. Śmiech *et al.* (2018) noted a high frequency of LG-MCT cases in Labrador (81.6%) and Golden Retriever (84.2%) and mentioned that Boston Terriers are more susceptible to MCT development. Simpson *et al.* (2004) also mentioned Labrador and Boston Terrier as breeds more susceptible to MCT development, without histological-grade specificity. In contrast, a reduced risk is reported in Springer Spaniels (Warland *et al.*, 2013), but no information about the risk by histologic grade could be found. The other purebred dogs showed no discernible risk of any grade of MCT.

The present analysis also found that the Pug, Boston Terrier, Pitbull and Weimaraner breeds exhibit a higher risk of developing MCT, while the Mixed-breeds, Cocker Spaniel, Poodle and Beagle have a lower risk. This is partially consistent with previous studies (Shoop *et al.*, 2015; Mochizuki *et al.*, 2017; Śmiech *et al.*, 2018).

#### *Anatomical localization and histological grade*

A higher risk of occurrence of this neoplasm was observed on the trunk (OR = 1.71, CI 1.32, 2.22), limbs (OR = 1.86, CI 1.37, 2.54), or an non-specified anatomical localization (OR = 2.62, CI 2.11, 3.26), whereas a lower risk was associated with the head (OR = 0.34, CI 0.23, 0.51). North *et al.* (2009) reported that most cutaneous MCTs occur on the trunk and extremities and less frequently

on the head and neck. No association between anatomic location and histological grade was observed. However, a significant proportion of both HG and LG-MCT cases lacked information, with 57.6% (53/92) and 54.2% (147/271) of HG and LG-MCT cases, respectively. This could reflect how the referring physicians documented the case, highlighting the need for improved consistency with clinical documentation.

The anatomical location of the MCT may be a significant prognostic factor (Kiupel et al., 2005). For both HG (23.9%) and LG-MCT (21.4%), the trunk was the most common location reported. Veterinary literature offers several perspectives to consider. Previous studies have reported an increased risk of HG-MCT in the genital and inguinal areas (Jaramillo, 2019; Reynolds et al., 2019). North et al. (2009) reported that 50-60% of HG-MCT occurs in the trunk and perineal region. Śmiech et al. (2018) found that LG tumors most commonly develop in the trunk (80.2%), while HG tumors are concentrated in the axillary and inguinal regions (73.3%), particularly the scrotum, which they identified as the site with the highest risk of MCT development of all cutaneous tumor sites. Martins et al (2021) also reported a high risk of HG lesions in the perigenital area and trunk. The limbs were the second most common site for MCTs with 17.0% of LG and 10.9% of HG cases. Jaramillo (2019) and North et al. (2009) state that the limbs are a site with increased risk of HG-MCT. Martins et al. (2021) mention that the limbs are more prone to grade II tumors (Patnaik et al., 1984) and LG tumors (Kiupel et al., 2011). Lesions in the head were less common. In the head, 7.6% were HG and 7.4% were LG. According to Reynolds et al. (2019), the head has an increased likelihood of HG-MCT. However, in this study, the lower frequency in the head may indicate a lower predisposition to these regions or may be related to the proportion of unspecified anatomic localization reports.

In conclusion, the results of this study demonstrated that, in canines, age and breed were risk factors associated with the development and histological grade of MCT, with sex and anatomic localization of the lesion demonstrating no such influence. However, the lack of significance for location may be influenced by the incomplete data in the clinical remissions. Dogs aged 5 – 8 years had a higher risk of developing LG-MCT, whereas those aged 9 – 12 years had a higher risk of developing HG-MCT. In addition, breeds such as the French Bulldog showed an increased risk of developing HG-MCT. Although several prognostic determinants have been suggested, the histological grade of the tumor seems to be the most important to predict the biological behavior of the tumor; therefore,

this information is relevant to the clinical assessment of the risk associated with this neoplasm in the local context, allowing for more effective patient management.

## **Declarations**

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### *Conflicts of interest*

The authors declare that they have no conflicts of interest concerning the work presented in this report.

### *Author contributions*

The study was designed by ACB. Data was collected by ACB. Statistical analyses were performed by both authors. The manuscript was written by ACB and reviewed by JZC. Both authors performed a critical reading and editing of the manuscript and approved the final version of it.

### *Use of artificial intelligence (AI)*

No AI or AI-assisted technologies were used during the preparation of this work.

### *Data availability*

The data sets used in the current study are available from the corresponding author on request.

## **References**

Cano-Botero A, Zapata-Cardona J, Agudelo-Quintero J, Quintana-Diosa LE. Morfología, Fisiología y Patología: Frecuencia de mastocitomas caninos diagnosticados mediante histopatología en el Laboratorio de Patología Animal de la Universidad de Antioquia - UdeA. Rev

<https://revistas.udea.edu.co/index.php/rccp/article/view/356631/20813740>

Cubillos García PA, Gutiérrez Moreno TM. Algunas generalidades sobre tumores de células redondas en perros [trabajo de grado pregrado]. Villavicencio: Universidad Cooperativa de Colombia, Facultad de Ciencias de la Salud, Medicina Veterinaria y Zootecnia; 2021.

<https://repository.ucc.edu.co/entities/publication/0055f93a-99bf-464e-8f4d-74b4b9283bc0>

Hahn K, Ogilvie G, Rusk T, Devauchelle P, Leblanc A, Legendre A et al. Masitinib is safe and effective for treating canine mast cell tumors. J Vet Intern Med. 2008;22(6):1301-1309.<https://doi.org/10.1111/j.1939-1676.2008.0190.x>

Jaramillo Burneo MJ. Estudio Retrospectivo de Mastocitoma Cutáneo en Perros (Canis lupus familiaris) Diagnosticado por Histopatología en el Período 2014-2018 [Tesis de maestría]. Cuenca: Universidad de Cuenca; 2019. <https://dspace.ucuenca.edu.ec/items/a29e5f61-55b5-4833-a0fb-37311889a1b4>

Kiupel M, Webster JD, Bailey KL, Best S, DeLay J, Detrisac CJ, et al. Proposal of a 2-tier histologic grading system for canine cutaneous mast cell tumors to more accurately predict biological behavior. Vet Pathol. 2011;48(1):147–55. <https://doi.org/10.1177/0300985810386469>

Kiupel M, Webster JD, Miller RA, Kaneene JB. Impact of tumor depth, tumor location and multiple synchronous masses on the prognosis of canine cutaneous mast cell tumours. J Vet Med A Physiol Pathol Clin Med. 2005;52(6):280–286. <https://doi.org/10.1111/j.1439-0442.2005.00726.x>

London CA, Hannah AL, Zadovoskaya R, Chien MB, Kollias-Baker C, Rosenberg M et al. Phase I dose-escalating study of SU11654, a small molecule receptor tyrosine kinase inhibitor, in dogs with spontaneous malignancies. Clin Cancer Res. 2003;9(7):2755–2768. <https://aacrjournals.org/clincancerres/article/9/7/2755/203586/Phase-I-Dose-Escalating-Study-of-SU11654-a-Small>

Lozano D, Murcia S, Mayorga S. Frecuencia de Neoplasias de piel en caninos Remitidos a un Laboratorio de Patología Veterinaria de Bogotá: Estudio retrospectivo en el período 2015 – 2016 [trabajo de grado pregrado]. Bogotá: Universidad de Ciencias Aplicadas y Ambientales – UDCA;

2016. <https://repository.udca.edu.co/entities/publication/2d0f4b29-6dc5-46dd-af70-100fae709014>

Martins AL, Carvalho FF, Mesquita JR, Gärtner F, Amorim I. Analysis of risk factors for canine mast cell tumors based on the kiupel and patnaik grading system among dogs with skin tumors. *Open Vet J.* 2021;11(4):619–34. <https://doi.org/10.5455/ovj.2021.v11.i4.12>

Medina I, Puicón V, Sandoval N. Frecuencia de Tumores en Piel de Caninos Diagnosticados Histopatológicamente en el Laboratorio de Patología Veterinaria de la Universidad Nacional Mayor de San Marcos (1999–2012). *Rev Inv Vet Perú.* 2017;28(2):448–454. <https://doi.org/10.15381/rivep.v28i2.13065>

Medina I. Frecuencia de tumores en piel de caninos diagnosticados histopatológicamente en el Laboratorio de Histología, Embriología y Patología Veterinaria de la UNMSM durante el periodo 1999- 2012 [Tesis]. Perú: Universidad Nacional Mayor De San Marcos; 2015. <https://core.ac.uk/download/pdf/323345754.pdf>

Meirelles AEWB, Oliveira EC, Rodrigues BA, Costa GR, Sonne L, Tesser ES, et al. Prevalência de neoplasmas cutâneos em cães da Região Metropolitana de Porto Alegre, RS: 1.017 casos (2002-2007). *Pesq Vet Bras.* 2010;30(11):968–973. <https://doi.org/10.1590/S0100-736X2010001100011>

Meuten DJ. *Tumors in Domestic Animals.* 5th Ed. Wiley-Blackwell; 2017. <https://doi.org/10.1002/9781119181200>

Millán Sepúlveda LF. Presentación de mastocitoma canino y neoplasias múltiples en un Golden Retriever. Un reporte de caso [Trabajo de grado]. Caldas: Corporación Universitaria Lasallista; 2021. <https://repository.unilasallista.edu.co/items/81bdfdd4-7837-4662-9922-9eb80a5ccb35>

Mochizuki H, Motsinger-Reif A, Bettini C, Moroff S, Breen M. Association of breed and histopathological grade in canine mast cell tumors. *Vet Comp Oncol.* 2017;15(3):829–839. <https://doi.org/10.1111/vco.12225>

North SM, Banks TA. Mast cell tumours. In: *Small Animal Oncology: An Introduction.* Elsevier; 2009. p. 183–196. <https://doi.org/10.1016/B978-0-7020-2800-7.00023-6>

O’Connell K, Thomson M. Evaluation of prognostic indicators in dogs with multiple, simultaneously occurring cutaneous mast cell tumors: 63 cases. *Vet Comp Oncol.* 2013;11(1):51–

62. <https://doi.org/10.1111/j.1476-5829.2011.00301.x>

Patnaik AK, Ehler WJ, MacEwen EG. Canine Cutaneous Mast Cell Tumor: Morphologic Grading and Survival Time in 83 Dogs. *Vet Pathol.* 1984;21(5):469–474. <https://doi.org/10.1177/030098588402100503>

Reynolds BD, Thomson MJ, O’Connell K, Morgan EJ, Gummow B. Patient and tumor factors influencing canine mast cell tumor histological grade and mitotic index. *Vet Comp Oncol.* 2019;17(3):338–344. <https://doi.org/10.1111/vco.12477>

Rojas Parada DF. Revisión bibliográfica de mastocitoma en caninos [monografía de grado]. Villavicencio: Universidad de los Llanos, Facultad de Ciencias Agropecuarias y Recursos Naturales, Escuela de Ciencias Animales, Programa de Medicina Veterinaria; 2017. <https://core.ac.uk/download/pdf/287326796.pdf>

Shoop SJ, Marlow S, Church DB, English K, McGreevy PD, Stell AJ, et al. Prevalence and risk factors for mast cell tumours in dogs in England. *Canine Genet Epidemiol.* 2015;2:1-10. <https://doi.org/10.1186/2052-6687-2-1>

Simpson AM, Ludwig LL, Newman SJ, Bergman PJ, Hottinger HA & Patnaik AK. Evaluation of surgical margins required for complete excision of cutaneous mast cell tumors in dogs. *JAVMA.* 2004;224(2):236–240. <https://doi.org/10.2460/javma.2004.224.236>

Śmiech A, Łopuszyński W, Ślaska B, Bulak K, Jasik A. Occurrence and distribution of canine cutaneous mast cell tumour characteristics among predisposed breeds. *J Vet Res.* 2019;63(1):141–148. <https://doi.org/10.2478/jvetres-2019-0002>

Śmiech A, Ślaska B, Łopuszyński W, Jasik A, Bochyńska D, Da,browski R. Epidemiological assessment of the risk of canine mast cell tumours based on the Kiupel two-grade malignancy classification. *Acta Vet Scand.* 2018;60(70):1–9. <https://doi.org/10.1186/s13028-018-0424-2>

Śmiech A, Ślaska B, Surdyka M, Grzybowska-Szatowska L, Łopuszyński W, Różańska D. Identification of additional mitochondrial DNA mutations in canine mast cell tumours. *Acta Vet Scand.* 2016;58(28):1-6. <https://doi.org/10.1186/s13028-016-0210-y>

Torres González-Chávez M, Fabré Rodríguez Y, Rodríguez Aurecochea JC, Calaña Seone L.

Frecuencia de presentación de tumores cutáneos en caninos de la provincia La Habana entre 2009-2013. Rev Electron Vet. 2017;18(3):1-19. <http://www.redalyc.org/articulo.oa?id=63651263004>

Torres Vidales G, Eslava Mocha P. Mastocitoma canino. Orinoquia. 2006;10(2):45–51. <https://www.redalyc.org/articulo.oa?id=89610206>

Vicario C, Freixa N. Factores clínicos y patológicos importantes en el pronóstico del mastocitoma canino. Clin Vet Peq Anim. 2018;38(4):235–240. <https://www.clinvetpeqanim.com/img/pdf/1534109958.pdf>

Warland J & Dobson J. Breed predispositions in canine mast cell tumour: A single centre experience in the United Kingdom. The Veterinary Journal. 2013;197(2):496–498. <http://dx.doi.org/10.1016/j.tvjl.2013.02.017>

White CR, Hohenhaus AE, Kelsey J, Procter-Gray E. Cutaneous MCTs: Associations with Spay/Neuter Status, Breed, Body Size, and Phylogenetic Cluster. J Am Anim Hosp Assoc. 2011;47(3):210–216. <https://doi.org/10.5326/jaaha-ms-5621>