

## A RETROSPECTIVE ANALYSIS OF CANINE SKIN ADNEXAL TUMORS OVER A FIVE-YEAR PERIOD

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This research provides a retrospective analysis of skin adnexal tumors (SATs) in canines, diagnosed between 2019 and 2023. The objective was to assess the prevalence, classification, and localization of these tumors. Tissue samples from 3886 dogs collected during a five-year period were examined at the Laboratory of Pathology of the Faculty of Veterinary Medicine, University of Belgrade, Serbia. Diagnoses were classified based on the criteria set by the World Health Organization. Statistical analysis included data on breed, sex, age, and tumor location. A total of 511 SATs were diagnosed, accounting for 13.15 % of all diagnoses obtained after the examination of canine tissue over five years and 31.43 % of all canine skin tumors. Of these, 56.75 % were benign and 43.25 % malignant. The most frequently observed types were sebaceous and modified sebaceous gland tumors (55.38 %), followed by follicular tumors (37.96 %). Male dogs (56.36 %) exhibited a higher incidence of SATs compared to females (41.10 %). The most frequently affected were mixed-breed dogs (17.61 %), bichons (11.55 %), and poodles (6.26 %). The mean age of dogs with SATs was 9.1 years, with tumors predominantly found on the head (26.61 %) and in the perianal region (24.07 %). This study offers valuable insights into the prevalence and characteristics of canine SATs, emphasizing the predominance of sebaceous gland tumors and the notable occurrence of malignancy. These findings underscore the importance of early diagnosis and highlight the need for further research into breed predispositions and prognostic factors.

**Keywords:** benign tumors, dogs, malignant tumors, skin adnexal tumors

## INTRODUCTION

Skin adnexal tumors (SATs) encompass a broad spectrum of benign and malignant neoplasms originating from various skin structures, such as hair follicles, sebaceous glands, apocrine glands, and eccrine glands. According to the World Health Organization

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(WHO), these neoplasms are divided into six categories based on their histogenetic origin: hair follicle tumors, nailbed tumors, sebaceous and modified sebaceous gland tumors, apocrine and modified apocrine gland tumors, eccrine gland tumors, and undifferentiated SATs [1]. These tumors are commonly diagnosed in dogs, whereas their occurrence is less frequent in other animal species and humans [2]. Most SATs are benign, with limited impact on prognosis. However, malignant forms, though rare, must be carefully differentiated from cutaneous metastases [1,3].

*Follicular tumors* – Follicular stem cells, located mainly in the distal compartment of the bulge region within the isthmus, and are believed to play a key role in the development of certain SATs in animals [4, 5]. The WHO categorizes canine follicular tumors into five distinct types, each defined by the type of follicular epithelium involved: infundibular keratinizing acanthoma (IKA), tricholemmoma, trichoepithelioma, pilomatricoma, and trichoblastoma [1].

IKA is a rare benign tumor in dogs that originates from the squamous epithelium of the follicular isthmus and infundibulum. This tumor typically features a central pore filled with keratin. Histologically, the pore is surrounded by multilayered squamous epithelium with keratinization with minimal pleomorphism and low mitotic activity [6,7]. Tricholemmomas, also rare in dogs, are classified into two types: the inferior type, derived from the outer root sheath of the hair bulb, and the isthmus type, which resembles the follicular isthmus. Inferior type tricholemmomas consist of glycogen-rich keratinocytes that keratinize poorly and lack keratohyalin granules. Isthmus-type tricholemmomas form aggregates of epithelial cells with tricholemmal keratinization in their centers [6,8]. Isthmus-type tricholemmomas lack central cysts and exhibit tricholemmal keratinization, unlike IKA [7]. Trichoepitheliomas show differentiation from all three segments of the hair follicle and can present as cystic variants. This tumor usually comprises a mixture of squamous and matrical epithelial cells, occasionally accompanied by ghost cells. Pilomatricomas originate from the hair bulb's matrix and are characterized by multiple cystic formations lined with basaloid cells that resemble those present during the anagen phase of the hair cycle. [6,7].

Although most hair follicle tumors are benign, trichoepitheliomas and pilomatricomas can occasionally become malignant with the potential to spread to other organs [1,3,9].

*Nailbed tumors* – Primary tumors of the nailbed are rare in dogs. Among these, squamous cell carcinoma is the most frequently encountered subungual tumor [10,11]. It is described that these tumors occur more often on the fingers of the forelimbs. Subungual squamous cell carcinoma is a malignant neoplasm originating from the nailbed epithelium. Neoplastic squamous cells organize into islands, cords, and trabeculae that infiltrate the dermis and subcutaneous tissues. Keratin production varies, influencing tumor differentiation [7].

*Sebaceous and modified sebaceous gland tumors* – Tumors of sebaceous glands represent the third most common type of skin neoplasm in dogs [12,13]. Modified sebaceous glands are found in certain areas of the dog's body, such as the meibomian glands (in

the eyelids), perianal glands, and hepatoid glands. Both sebaceous and meibomian glands are composed of two primary components: a glandular section containing undifferentiated peripheral cells and mature sebocytes at the center, and a duct lined with flattened, keratinizing epithelium that connects to the infundibulum of the hair follicle [7, 14]. Tumors of sebaceous and modified sebaceous glands include benign and malignant tumors. Prognosis is excellent for benign tumors after surgical removal, while the prognosis for malignant tumors like sebaceous carcinoma or perianal gland carcinoma depends on the extent of local invasion and metastasis at the time of diagnosis [6,7].

*Apocrine and modified apocrine gland tumors* – Apocrine glands secrete via decapitation, where the apical portion of the cells is released into the lumen. Both apocrine and modified apocrine glands (such as ceruminous and anal sac glands) contain secretory and ductal components from which tumors can develop [6,7].

*Eccrine gland tumors* – Eccrine gland neoplasms, showing differentiation toward eccrine secretory epithelium, can be benign or malignant and are very rare in domestic animals. In dogs and cats, eccrine glands are confined to the footpads, making this the only site for these tumors, with metastatic pulmonary carcinoma being the primary differential diagnosis in cats. Distinguishing eccrine from apocrine gland tumors is difficult, even with immunohistochemistry, so anatomical distribution and the presence of decapitation secretion are considered the most important parameters [7,15].

*Undifferentiated SATs* – Clear cell adnexal carcinoma is a rare, poorly differentiated SAT characterized by the presence of “clear cells.” The prognosis is moderate after surgical excision, though occasional recurrence and metastasis to local lymph nodes have been reported in tumors with high mitotic index [16].

## MATERIAL AND METHODS

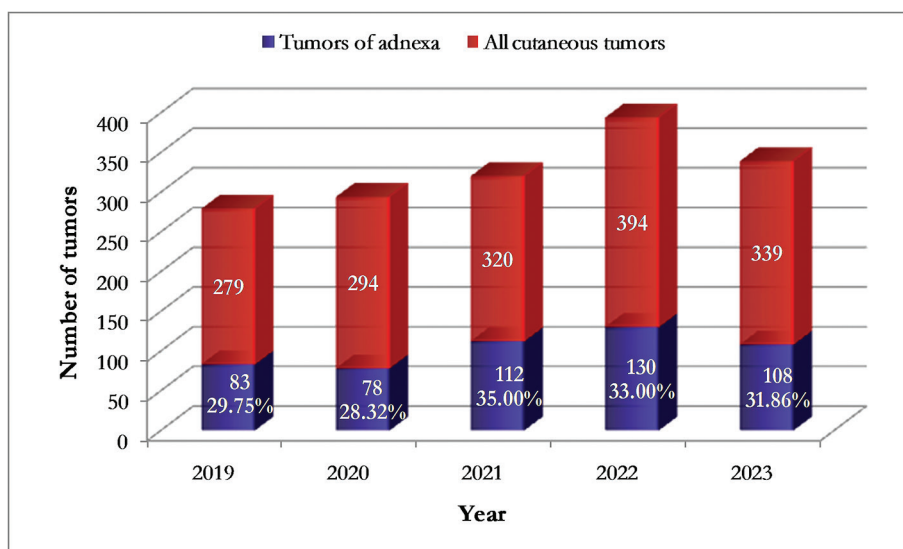
Tissue samples were collected from 3886 dogs exhibiting masses suggestive of tumors through surgical biopsy performed at various veterinary clinics across Serbia between January 2019 and December 2023. These samples were subsequently submitted to the Laboratory of Pathology within the Department of Pathology at the Faculty of Veterinary Medicine, University of Belgrade. Following excision, the obtained tissue samples were promptly fixed in 10 % buffered formalin and transported to the laboratory. Each sample was submitted with a referral containing details about the dog, including breed, sex, age, tumor location (e.g., head, neck, back, chest, abdomen, forelimbs, hind limbs, anus, eyelid, ear, tail), and the macroscopic features of the lesions. The tissue samples were processed using an automatic tissue processor, embedded in paraffin, and sectioned into slices 3–5  $\mu\text{m}$  thick. These sections were routinely stained with hematoxylin and eosin for histopathological examination.

Tumor diagnosis and classification were conducted according to the criteria established by the World Health Organization [1].

Statistical analysis was performed using descriptive measures, including the arithmetic mean, as well as minimum and maximum values. The relative frequency of each tumor type was calculated by dividing the number of cases with the same diagnosis by the total number of analyzed samples. Cases lacking data for the selected parameters were excluded from the analysis. Statistical analyses were performed using Microsoft Excel 2016 software.

## RESULTS

During the period from 2019 to 2023, 511 SATs were diagnosed, accounting for 13.15 % of all diagnoses obtained after the examining dog tissue (3886 cases), or approximately one-third (31.43 %) of all diagnosed skin tumors (1626 tumors) in dogs. Of this number, 290 (56.75 %) were benign, and 221 (43.25 %) were malignant. The number of SATs by years is shown in Figure 1.



**Figure 1.** Distribution of adnexal tumors in dogs over five-year period (2019-2023)

SATs were diagnosed in 288 (56.36 %) males and 210 (41.10 %) females, while sex data were missing for 13 (2.54 %) dogs. SATs were found in a total of 85 breeds, with mixed breeds being the most common (90 dogs, 17.61 %), followed by Bichons (59 dogs, 11.55 %), Poodles (32 dogs, 6.26 %), Maltese Poodles (26 dogs, 5.09 %), and Golden Retrievers (20 dogs, 3.91 %). For 12 dogs (2.35 %), no breed data were available. The average age of dogs with adnexal tumors was 9.1 years (the youngest dog was 9 months old, and the oldest was 16.5 years), while age information was unavailable for 27 dogs.

The majority of SATs were localized on the head (136 cases, 26.61 %), followed by the perianal region (123 cases, 24.07 %), the neck (92 cases, 18.00 %), the extremities (49 cases, 9.59 %), the back (46 cases, 9.00 %), the abdominal area (21 cases, 4.11 %), the chest (16 cases, 3.13 %), and the tail (15 cases, 2.94 %). Localization data were missing for 13 dogs (2.54 %).

More than half of the adnexal tumors were sebaceous and modified sebaceous gland tumors, accounting for 283 cases (55.38 %). Of these, 177 (62.54 %) were malignant, and 106 (37.46 %) were benign (Table 1).

**Table 1.** SAT prevalence in dogs

Tumor type	Number	%
<b>Sebaceous and modified sebaceous gland tumors</b>	<b>283</b>	<b>55,38</b>
Hepatoid epithelioma	54	10,57
Hepatoid adenoma	50	9,78
Sebaceous adenoma	47	9,20
Sebaceous adenocarcinoma	34	6,65
Meibomian gland epithelioma	32	6,26
Sebaceous epithelioma	27	5,28
Hepatoid adenocarcinoma	16	3,13
Meibomian gland adenocarcinoma	14	2,74
Meibomian gland adenoma	8	1,57
Sebaceous ductal adenoma	1	0,20
<b>Follicular tumors</b>	<b>194</b>	<b>37,96</b>
Trichoblastoma	78	15,26
Pilomatricoma	46	9,00
Trichoepithelioma	41	8,02
Malignant pilomatricoma	11	2,15
Tricholemmoma	10	1,96
Malignant trichoepithelioma	6	1,17
Infundibular keratinizing acanthoma	2	0,39
<b>Apocrine and modified apocrine gland tumors</b>	<b>30</b>	<b>5,87</b>
Apocrine adenocarcinoma	17	3,33
Apocrine adenoma	4	0,78
Apocrine ductal adenocarcinoma	3	0,59
Anal sac adenocarcinoma	2	0,39
Ceruminous adenocarcinoma	2	0,39
Ceruminous adenoma	2	0,39
<b>Eccrine gland tumors</b>	<b>4</b>	<b>0,78</b>
Eccrine gland adenocarcinoma	3	0,59
Eccrine gland adenoma	1	0,20

The average age of dogs with these tumors was 9.9 years (ranging from 9 months to 16.5 years), with age data unavailable for 15 dogs. Tumors of sebaceous and modified sebaceous glands were twice as common in males (188 dogs, 66.43 %) compared to females (90 dogs, 31.80 %), with gender data unavailable for 5 dogs (1.77 %). These tumors were most frequently diagnosed in mixed-breed dogs (50 cases, 17.67 %), followed by Bichons and Poodles, each with 17 cases (6.01 %), Golden Retrievers (14 cases, 4.95 %), and Maltese Poodles (13 cases, 4.59 %). The majority were localized in the perianal region (114 cases, 40.28 %), followed by the head (88 cases, 31.09 %), with 58 of these (20.49 %) occurring on the eyelids. Other localizations included the neck (24 cases, 8.48 %), the extremities (21 cases, 7.42 %), the back (11 cases, 3.89 %), the tail (9 cases, 3.18 %), the abdomen (7 cases, 2.47 %), and the thorax (2 cases, 0.71 %). Localization data were unavailable for 7 dogs (2.47 %).

Follicular tumors were present in 194 dogs, representing 37.96 % of dogs with SATs. Benign tumors were nearly ten times more common (177 cases, 91.24 %) compared to malignant ones (17 cases, 8.76 %). The distribution of specific types of follicular tumors is shown in Table 1. The average age of dogs with follicular tumors was 7.8 years (ranging from two to 15 years), with age data unavailable for 9 dogs. Follicular tumors were more common in females (105 dogs, 54.12 %) than in males (82 dogs, 42.27 %), with gender data unavailable for 7 dogs (3.61 %). The highest prevalence of follicular tumors was observed in Bichons (38 cases, 19.59 %), followed by mixed-breed dogs (33 cases, 17.01 %), Poodles (12 cases, 6.19 %), and Maltese Poodles (10 cases, 5.15 %). About one-third of tumors in this group were found in the neck region (63 cases, 32.47 %), followed by the head (41 cases, 21.14 %), back (31 cases, 15.98 %), extremities (21 cases, 10.82 %), thorax (12 cases, 6.19 %), abdominal skin (11 cases, 5.67 %), perianal region (7 cases, 3.61 %), and tail (6 cases, 3.09 %). Localization data were unavailable for two dogs (1.03 %).

Tumors of apocrine and modified apocrine glands were diagnosed in a total of 30 dogs, accounting for 5.87 % of all SATs (Table 1). The tumors in this group were predominantly malignant, with 24 cases (80.00 %) classified as malignant, while the remaining 6 cases (20.00 %) were benign. The average age of dogs with apocrine and modified apocrine gland tumors was 9.72 years, with the youngest dog being 3 years old and the oldest 14 years old. Age data were unavailable for three dogs.

Dogs with tumors from this group were almost evenly distributed between males (16 dogs, 53.33 %) and females (13 dogs, 43.33 %), with one case (3.33 %) lacking gender information. These tumors were most commonly diagnosed in mixed breed dogs (7 cases, 23.33 %), followed by Poodles (3 cases, 10.00 %). Two cases (6.67 %) each were observed in Labrador Retrievers and Maltese Poodles, while the remaining 16 breeds each had one case (3.33 %).

Of the total number of dogs with adnexal tumors, the fewest cases (4 tumors, 0.78 %) belonged to the group of eccrine gland tumors (Table 1), with one case (25 %) being benign and the remaining three (75 %) malignant. The average age of dogs with this

tumor type was 8.75 years (ranging from 6 to 12 years). Eccrine gland tumors were equally diagnosed in males and females, with 2 cases each. They were observed in a Maltese Poodle, a German Hunting Terrier, a Bullmastiff, and a Black Russian Terrier. Eccrine gland tumors were most commonly located on the skin of the extremities (2 cases, 50 %) and the skin of the back (1 case, 25 %), with localization data unavailable for one dog (25 %). No nail bed tumors or undifferentiated SATs were identified in the examined material.

## DISCUSSION

Due to their high visibility to owners, tumors originating from adnexal structures are frequently excised and submitted for histopathological analysis. Skin tumors constitute a significant proportion of all diagnosed neoplasms and are the most common tumors found in dogs [17,18] followed by mammary gland tumors as the second most prevalent type [19]. Among these, SATs are frequently observed, accounting for nearly one-third of all diagnosed skin tumors and 13.15 % of the total number of diagnoses obtained over the five-year period. Similarly, Sharif et al. [17] found that SATs comprised approximately one-third of the examined skin tumors. The most frequently identified tumors were those of the sebaceous and modified sebaceous glands, which represented more than half (55.38 %) of all adnexal tumors, followed by follicular tumors (37.96 %). Some studies have reported that sebaceous gland tumors are the third most common type of skin tumor, comprising 21–35 % of all cutaneous epithelial tumors in dogs [13,14], while Vail et Withrow, [10] state that sebaceous gland tumors account for 6.8 % to 7.9 % of all skin tumors, placing them among the most common skin tumors in dogs. Beck et al. [8] concluded that follicular tumors are rare in canine patients, while Wiener [9] reports that follicular tumors account for approximately 10 % of all tumors.

In this study, 511 SATs were identified in dogs between 2019 and 2023, demonstrating a higher prevalence of benign tumors (56.75 %) compared to malignant ones (43.25 %). More than half of the tumors were classified as sebaceous and modified sebaceous gland tumors, with a notable occurrence of malignancy (62.54 %), while follicular tumors show predominance of benign forms (91.24 %). This pattern is consistent with previous research, which has reported varying proportions of benign and malignant SATs, often highlighting the predominance of benign lesions [20]. Within specific subgroups of SATs, follicular tumors are predominantly benign [8], whereas sebaceous gland tumors occur in nearly equal proportions of benign (adenomas) and malignant forms (epitheliomas and adenocarcinomas) [21].

Statistical analysis of the data from this study revealed a higher incidence of SATs in male dogs (56.36 %) compared to females (41.10 %). Although the literature does not provide detailed data on the sex-related occurrence of adnexal tumors in dogs, it is generally recognized that skin tumors are more common in male dogs [22,18]. However, some studies have found that females had an increased likelihood of

developing skin tumors compared to males [23]. For follicular tumors, males showed a slightly higher incidence [9], while female dogs were more often affected by multiple follicular tumors [24]. Sebaceous tumors are more frequently observed in females, accounting for approximately 60 % of cases [14]. Conversely, other studies have found that benign sebaceous tumors are more commonly seen in males [21], while some researchers suggest there is no sex-related predisposition for these tumors [7].

Based on our findings, the most commonly affected breeds were mixed breeds, followed by Bichons and Poodles. In the studies of other authors, it is difficult to clearly identify the breeds most affected by SATs, as the occurrence of these tumors varies greatly depending on the specific type of tumor being considered.

The average age of dogs diagnosed with SATs in this study was 9.1 years, aligning with previous reports that these tumors predominantly occur in older dogs [21,18]. The detection of tumors in dogs as young as 9 months emphasizes the need for routine examinations, even in younger populations. This is especially relevant since other studies have also documented the occurrence of various tumors in younger dogs [25].

The tumors were predominantly localized on the head (26.61 %) and in the perianal region (24.07 %), likely due to the abundance of sebaceous glands in these areas. Literature supports these findings, with reports indicating that sebaceous tumors are most commonly found on the head [7,21,14]. A significant number of tumors were located on the eyelids (20.49 % of head tumors), a finding also reported by other authors [10], which is particularly relevant as eyelid tumors are frequently observed in canine dermatopathology [6,26]. Benign hair follicle tumors were often found on the head, back, and neck according to Kok et al. [21], or on the head, neck, and hind legs according to Beck et al. [8].

Eccrine gland tumors were sporadic in this study, accounting for only 0.78 % of the total cases, with similarly low occurrences reported in other studies [6,26]. The rarity of these tumors underscores the need for heightened awareness among veterinary practitioners when diagnosing cutaneous masses.

## **CONCLUSION**

Overall, the results of this study contribute to the understanding of adnexal tumors in dogs, providing insight into their prevalence, demographic distribution, and localization. Future studies with larger sample size and a broader range of breeds may enhance the understanding of these tumors. Additionally, highlighting potential areas for future research, such as improving diagnostic tools or understanding genetic predispositions in certain breeds, could strengthen this section.

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### Authors' contributions

IV participated in the study design, sample preparation, performed the histopathological examination, and wrote and translated the manuscript. VK participated in the histopathological examination, conducted the statistical analysis, and prepared the graphs. SN participated in the sample preparation and histopathological examination. MA participated in the sample preparation and histopathological examination. BD participated in the analysis of the results and technically edited the manuscript. DM participated in the histopathological examination. SAK participated in the planning and coordination of the study and contributed to writing the manuscript. All authors read and approved the final version of the manuscript.

### Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Statement of Informed Consent

The owner understood procedure and agrees that results related to investigation or treatment of their companion animals, could be published in Scientific Journal Acta Veterinaria-Beograd.

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## **RETROSPEKTIVNA ANALIZA TUMORA ADNEKS STRUKTURA KOŽE PASA TOKOM PETOGODIŠNJEG PERIODA**

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Ova studija predstavlja retrospektivnu analizu tumora adneks struktura kože kod pasa dijagnostikovanih u periodu od 2019. do 2023. godine. Cilj istraživanja bio je da se odredi prevalenca, tip i lokalizacija ovih tumora. Uzorci tkiva od ukupno 3886 pasa prikupljeni tokom petogodišnjeg perioda ispitivani su u Laboratoriji za patologiju Fakulteta veterinarske medicine Univerziteta u Beogradu, Srbija. Dijagnostikovani tumori klasifikovani su prema kriterijumima Svetske zdravstvene organizacije. Statistički su analizirani podaci o rasi, polu, starosti i lokalizaciji tumora. Ukupno je dijagnostikovano 511 adneksalnih tumora kože, što predstavlja 13,15 % svih dijagnoza dobijenih nakon analize uzoraka tkiva pasa u petogodišnjem periodu i 31,43 % svih tumora kože kod pasa. Od ukupnog broja, 56,75 % tumora bilo je benigno, dok je 43,25 % bilo maligno. Najčešće dijagnostikovani tumori bili su tumori lojne žlezde i modifikovanih lojnih žlezda (55,38 %), a zatim folikularni tumori (37,96 %). Učestalost adneksalnih tumora kože bila je veća kod mužjaka (56,36 %) nego kod ženki (41,10 %). Najčešće pogođeni bili su psi mešanci (17,61 %), bišoni (11,55 %) i pudle (6,26 %). Prosečna starost pasa sa tumorima adneks struktura kože iznosila je 9,1 godina, dok su tumori najčešće lokalizovani na glavi (26,61 %) i u perianalnoj regiji (24,07 %). Ova studija pruža dragocene uvide u prevalencu i karakteristike tumora adneks struktura kože kod pasa, naglašavajući dominaciju tumora lojnih žlezda i značajnu učestalost maligniteta. Nalazi ističu važnost rane dijagnoze i potrebu za daljim istraživanjima predispozicija po rasi, kao i prognostičkih faktora.