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Abstracts of the *II Encontro de Patologia Mamária Diagnóstico, Prognóstico e Tratamento das Neoplasias Mamárias da Cadela*

Introduction

The abstracts published in this section have been presented at the *II Encontro de Patologia Mamária: Diagnóstico, Prognóstico e Tratamento das Neoplasias Mamárias da Cadela* [II Mammary Pathology Meeting: Diagnosis, Prognosis, and Treatment of Canine Mammary Neoplasia]. These abstracts reflect the efforts of professionals from several Brazilian institutions aiming to develop better protocols for diagnosing and classifying as well as for treating canine mammary neoplasia. These abstracts supported the establishment of the new consensus that is being published in this issue of the Brazilian Journal of Veterinary Pathology, which represents an advance on the previous consensus published in 2010.

Renato de Lima Santos
Editor

Scientific Committee

Alessandra Estrela-Lima

Departamento de Patologia e Clínicas, Escola de Medicina Veterinária, Universidade Federal da Bahia, Salvador, BA, Brazil.

Enio Ferreira

Departamento de Patologia Geral, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil.

Renata Sobral

Onco Cane Clínica Veterinária Ltda, São Paulo, SP, Brazil.

Clinical Pathological Study of Mammary Tumors in Female Dogs at CenterVet Animal

Juliana Emerick Reis Delecrodi*, Willian Delecrodi Gomes, Enio Ferreira

CenterVet Hospital Veterinário – Contagem – MG.

* **Corresponding author:** Rua Juscelino Kubitschek, 539, Industrial, Contagem/MG, Brasil, 32230-090. E-mail: juliana@centervet.com.br

Mammary tumors are the most common neoplasms in female dogs, and due to increased survival time of the dogs, cancer calls, particularly regarding mammary neoplasms, have increased every year. Therefore technical knowledge about mammary neoplasia and their standardization in the diagnosis, prognosis and treatment, becomes most relevant in order to reduce tumor recurrence rates and improve survival time of patients. This study aims to characterize epidemiological and pathological data related to clinical evaluation of female dogs with mammary lesions cared for at CenterVet Veterinary Hospital from 2010 to 2012. The protocol was based on the Consensus for the Diagnosis, Prognosis and Treatment of Canine Mammary Tumors (2010).

Material and Methods

From 2010 to 2012, a survey of anatomopathological and clinical lesions of 10 tumors in female dogs was conducted. They were diagnosed at CenterVet Veterinary Hospital by filling in the oncological file regarding mammary neoplasia, by observing, and comparing mainly the reproductive aspect of these female dogs, date of commencement, morphology, type of injuries and reactive lymph nodes during the clinical examination. Clinical and epidemiological characteristics of patients were reviewed by identifying their breed and age, as well as evaluating the main macro and microscopic features of pathological changes, as well as the frequency of their occurrence. In the only case allowed (carcinosarcoma), an immunohistochemistry exam was carried out with a 20% marked cells distribution, and moderate intensity to COX-2, with a final score of four.

Results and Discussion

Clinical-pathological data from 10 animals was collected along with their age and breed identification in all animals. The affected animals were 12 years old, in average, with a standard deviation of ± 2.86 . The animals between nine and eleven years old comprised 40% of the cases and the breed identification showed a greater incidence of the mongrel dogs breed 50%. Regarding the correlated reproductive information, 1/10 of the female

dogs were castrated and 1/10 had received the administration of estrus controlling hormones.

We obtained information on the tumor site in 10 animals, 30% in the abdominal mammary glands, 10% in the inguinal mammary glands and 60% had multicentric tumors. In the clinical analysis related to the tumor staging six and four animals showed tumors at stages III and IV, respectively (4). One animal showed second primary tumor with an average of appearance of 1,5 months. Three cases were identified with lymph node metastasis and five cases with distant metastasis, these last ones had the lungs as the predominant site (100%).

In the histopathological analysis of 10 mammary tumors, 100% were malignant neoplasms (8 carcinomas, 1 sarcoma and 1 carcinosarcoma). The histologic analysis of regional lymph nodes was only possible in 70% of the cases among those characterized as malignant and 43% of them had metastasis. In table 1, it is possible to identify the predominant neoplastic histologic types, their histologic graduation rates and expression of immunohistochemical markers. In one case of malignant tumor (carcinosarcoma), an immunohistochemical study was done and revealed positivity for COX-2.

Table 1. Histopathology findings of mammary tumors in female dogs.

Histologic type	N	COX-2 High score	Histologic Grade I/II/III	Global Survival
Micropapillary carcinoma with metastasis	1			36
Tubular carcinoma	3			192
Tubular carcinoma with metastasis	2			165
Solid carcinoma	2			113
Solid carcinoma with metastasis				
Carcinosarcoma				
Carcinosarcoma with metastasis	1	Pos*		210
Sarcoma	1			485

N: number; N/A: Does not apply; NI: not informed

*Immunohistochemistry marked cells distribution of moderate intensity to COX-2, final score of four.

Table 2. Clinical findings of mammary tumors in female dogs.

Histologic type	N	Surgery	Surgery + P1	Global survival
Carcinomas without metastasis	2	2		287
Carcinomas with aggressive profile without metastasis	2	2		113
Carcinomas with metastasis	6	5	1	165

P1: Protocol Paclitaxel (according to consensus)

All of the 10 female dogs evaluated went through surgical procedure. Two cases, not included in this work, observed during this period, which presented cytological diagnosis of inflammatory carcinoma, and very short survival time after diagnosis, <30 days, had not gone through chemotherapy treatment.

Conclusion

Based on this study, we found that the average age of the female dogs, treated at CenterVet Veterinary Hospital, which showed mammary lesions, was high and they arrived at a more advanced stage of the disease. Mammary tumors were more frequent in caudal mammary glands, according to Ferreira, *et al.*, 2009. Due to low a budget, no post-operative treatment was done in most cases. This procedure is important in order to increase the survival time of the patients. A low survival rate of the evaluated cases was observed, probably related to the high incidence of pulmonary metastases.

It is possible to notice the growing need of technical knowledge on behalf of veterinarians and pathologists about mammary neoplasia in female dogs and on behalf of the owners in order to have an earlier intervention, with safe margins, thus reducing relapses and improving the survival time of these patients.

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Clinical and Pathological Study of Canine Mammary Tumors at the Veterinary Teaching Hospital/UNOPAR

Neide Mariko Tanaka*, Sarah Rezende, Luciana Sayuri Takemura, Bernardo Kemper, Daniella Aparecida Godoi, Flávia Navas Padilha, Daniela dos Santos Corrêa, Silvia Manduca Trapp, Selwyn Arlington Headley

Veterinary Surgical Oncology - Biological and Health Science Center – UNOPAR, Londrina, PR, Brazil; Laboratory of Animal Pathology - Human, Health, Exact and Technological Sciences Center - UNOPAR, Arapongas, PR, Brazil.

* **Corresponding author:** Av. Paris, 675. Jardim Piza, 86041-120, Londrina/PR, Brazil. E-mail: neidemtanaka@gmail.com

The aim of this study was to evaluate the clinical and pathological data of dogs with mammary tumors presented to the Veterinary Teaching Hospital, North Paraná University- UNOPAR, Arapongas, Paraná, Brazil. Keywords: breast, cancer, dogs, diagnosis, survival.

Material and Methods

Medical records (2010-2012) of 44 female dogs diagnosed with mammary tumor at the Veterinary Teaching Hospital, North Paraná University – UNOPAR were reviewed. The diagnoses of mammary tumor were based on clinical and histopathological features. Complete medical records and the reproductive status of each dog (including dates of ovariohysterectomy and previous hormonal treatments) were obtained. Information of tumor (growth rate, size, and location), any previous surgery and type of mammary tumor were also recorded. Histopathology (including histological classification and grading of tumors) were evaluated. The clinical and pathological diagnoses based on the criteria described by authors (1) were statistically analyzed. Mammary tumors were classified for statistical analysis as benign and

malignant tumors to perform survival analysis using the free software R 2.15.3 Kaplan-Meier.

Results and Discussion

Forty-four female dogs were included in this study. The mean age of the animals was 10.8 (± 2.14) years old. The age group between 9 to 11 years represented 42% of the cases. Mongrel dogs were overrepresented and corresponded to 43.18% of the animals evaluated, followed by Poodle (11.36%). These data are similar to the findings described by authors (1,8).

Regarding the reproductive information, 6/44 (13.63%) female dogs were previously spayed, and 6/44 (13.63%) received hormone for controlling estrus cycle. Sexual hormones are involved on mammary gland tumorigenesis, and castration prior to the first estrus reduces the risk for developing these tumors (6). In this study, few female dogs were spayed, and hormone was

administered to control estrus, probably due to lack of preventive care.

The tumors were observed more frequently in 15/44 (34.09%) of the inguinal mammary glands, followed by 12/44 (27.27%) abdominal glands, 10/44 (22.72%) thoracic glands, and 7/44 (15.90%) in multiple glands. Clinical staging analysis revealed 18 (40.90%), 13 (29.54%), 5 (11.36%), and 8 (18.18%) animals presenting stages I, II, III and IV respectively. Tumor relapse was observed in six cases, with median development of 13 months. We identified 5/44 (11.36%) cases with regional lymph node metastasis, and 6/44 (13.63%) cases with distant metastases, mainly affecting the lungs. Similar results were reported by authors (9).

Histological classification of the tumors revealed that 47.72% were benign neoplasms (3 benign mixed tumors, 5 adenomas, and 3 fibroadenomas), and 52.27% were malignant neoplasms. Frequency and grading of mammary tumors are shown in Table 1

Table 1. Histological classification, grading and mean survival of 44 female dogs with mammary tumor from 2010-2012 at the Veterinary Teaching Hospital / UNOPAR.

Histologic Type	N	ER Pos	PR Pos	MIB-1 Medium Index	COX-2 High Score	Months Survival Global
Benign Mixed Tumor	3	NA	NA	NA	NA	10.5
Adenoma	8	NA	NA	NA	NA	17
Papilloma	0	NA	NA	NA	NA	0
Fibroadenoma	3	NA	NA	NA	NA	25
Myxoma	0	NA	NA	NA	NA	0
Sarcomas	2	NA	NA	NA	NA	10
Comedocarcinoma	0	NA	NA	NA	NA	0
Hemangiopericitoma	0	NA	NA	NA	NA	0
Simple cribriforme carcinoma	1	NA	NA	NA	NA	8
Simple cribriforme carcinoma with metastasis	0	NA	NA	NA	NA	0
Cystic papillary carcinoma	0	NA	NA	NA	NA	0
Tubular simple carcinoma grade I	2	NA	NA	NA	NA	12
Tubular simple carcinoma grade II	2	NA	NA	NA	NA	11
Tubular simple carcinoma grade III	0	NA	NA	NA	NA	0
Carcinoma <i>in situ</i>	1	NA	NA	NA	NA	0
Carcinoma into mixed tumor	0	NA	NA	NA	NA	0
Carcinoma into mixed tumor with metastasis	0	NA	NA	NA	NA	0
Complex carcinoma grade I	2	NA	NA	NA	NA	16
Complex carcinoma grade II	2	NA	NA	NA	NA	13
Complex carcinoma with metastasis grade I	0	NA	NA	NA	NA	0
Complex carcinoma with metastasis grade II	0	NA	NA	NA	NA	0
Invasive papillary carcinoma grade I	1	NA	NA	NA	NA	13
Invasive papillary carcinoma grade II	2	NA	NA	NA	NA	11
Invasive papillary carcinoma grade I with metastasis	0	NA	NA	NA	NA	0
Micropapillary carcinoma	0	NA	NA	NA	NA	0
Micropapillary carcinoma with metastasis	0	NA	NA	NA	NA	0
Tubular carcinoma grade I	1	NA	NA	NA	NA	8
Tubular carcinoma grade III	0	NA	NA	NA	NA	0
Tubular carcinoma grade III with metastasis	0	NA	NA	NA	NA	0
Solid carcinoma	4	NA	NA	NA	NA	6
Solid carcinoma with metastasis	0	NA	NA	NA	NA	0
Carcinosarcoma	3	NA	NA	NA	NA	7
Carcinosarcoma with metastasis	0	NA	NA	NA	NA	0
Total	44					

NA: Not applicable; ER: Estrogen Receptor; PR: Progesterone Receptor

Table 2. Clinical characteristics of 44 female dogs with mammary tumor from 2010-2012 at Veterinary Teaching Hospital UNOPAR.

Histological type	N	Surgery	OSH therapeutic	Months Survival Global
Benign tumors	11	9 (Mastectomy + OH) 2 (Mastectomy)	2	17.5
Sarcomas	2	Mastectomy	1	10
Simple cribriforme carcinoma	1	Mastectomy + OH		8
Tubular simple carcinoma grade I	2	Mastectomy + OH		12
Tubular simple carcinoma grade II	2	1 (Mastectomy + OH) 1 (Mastectomy)		11
Carcinoma <i>in situ</i>	1	Mastectomy	1	10
Complex carcinoma grade I	2	1 (Mastectomy + OH) 1 (Mastectomy)		16
Complex carcinoma grade II	2	1 (Mastectomy + OH) 1 (Mastectomy)		13
Invasive papillary carcinoma grade I	1	Mastectomy	1	13
Invasive papillary carcinoma grade II	2	1 (Mastectomy + OH) 1 Mastectomy	1	11
Tubular carcinoma grade I	1	Mastectomy + OH		8
Solid carcinoma	4	1 (Mastectomy + OH) 3 (Mastectomy)		6
Carcinosarcoma	3	Mastectomy + OH)		7
Total	44			

OSH: Ovarioalpingohysterectomy

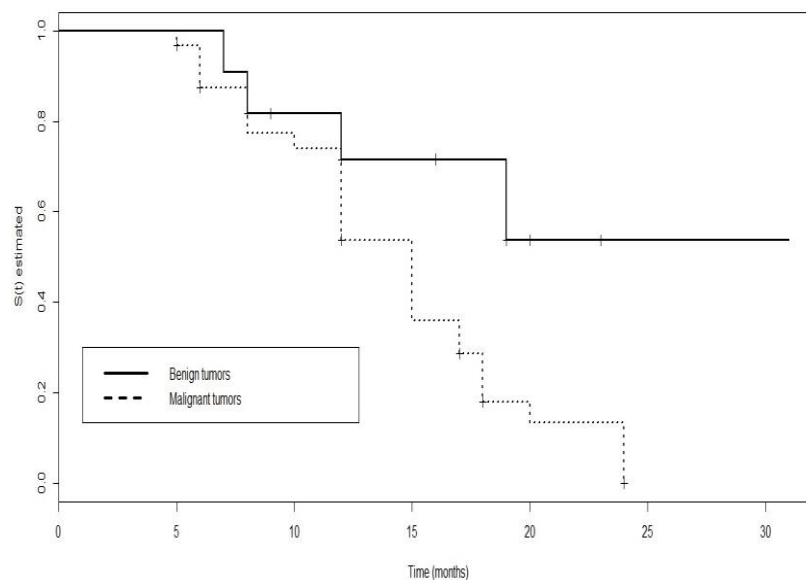


Figure 1. Kaplan-Meier survival curves for 44 dogs with 33 malignant and 11 benign tumors obtained from medical records (2010-2012) at the Veterinary Teaching Hospital UNOPAR.

Conclusion

This study may provide clinical and pathological evidence suggesting that the surgical

(mastectomy plus ovariohysterectomy) treatment is the main procedure. Pathological diagnosis is pivotal role to predict early clinical stage of the disease, together with

combined modality therapy for improving survival time of patients.

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Clinical-Pathological Study of Mammary Tumors in Dogs at the Veterinary Hospital of the Federal University of Rio Grande do Sul

Luciana Oliveira de Oliveira*, Luciane Cristina Vieira, Kelly Cristine Rocha da Silva Ferreira, Paula Azambuja de Quadros

HCV - UFRGS, Porto Alegre, RS, Brasil

* Corresponding author: Av. Bento Gonçalves, 9090. Agronomia, 91540-000, Porto Alegre/RS, Brasil. E- mail: luoliv@gmail.com

The purpose of this study was to analyse epidemiologic and pathological data related to clinical evaluation of dogs with mammary tumors admitted at the Veterinary Hospital of UFRGS, Porto Alegre, Brazil.

Materials and Methods

From 2010 to 2012, mammary tumors from 111 animals admitted at the Oncology Service at the Veterinary Hospital of UFRGS were studied. Epidemiologic and clinical data from these patients were analyzed, breed and age of the animals were identified, macro and microscopic pathological alterations, and the frequency of these alterations were recorded.

Results and Discussion

Clinical and pathological data from 110 animals were obtained. Breed and age of 110 bitches were analyzed. Affected animals had an average of 9.87 years,

standard deviation of 2.76. Animals between 9 and 11 years-old were 41.44% of cases. Breed identification showed a higher incidence of mixed breed dogs (28.83%). Age distribution and breed were similar to other reports in dogs (2, 5).

In relation to reproductive information, 27/110 females were spayed and 18/110 had previously received hormonal treatments. The influence of hormones contributes to tumor development. Ovarian hormones may influence the early development of mammary tumors (1, 3, 4).

Information about tumor location was obtained in 104 animals, 13.33% showed tumors located on thoracic mammary glands, 18.09% on abdominal glands, 10.47% on inguinal glands, and 58.09% showed multicentric tumors. Multiple tumors are commonly observed in dogs with mammary tumors, and the caudal abdominal and inguinal mammary glands are the most affected glands (5). In relation to tumor staging, 47, 20, 38, and 5 animals had tumors staged I, II, III, and IV, respectively. Stage I and III were the most prevalent. Mammary tumors showing clinical staging II or higher have decreased survival (1, 5).

Seven animals developed tumor recurrence, within an average of 6 months. Seven cases had lymph node metastasis. Seven cases showed distant metastasis,

the prevalent site was the lung (71%). Both lymph node and lungs are considered the most prevalent sites of metastasis (1, 3, 5).

Histopathology analysis of 106 mammary tumors revealed 4.70% non-neoplastic mammary lesions, 10.37% benign tumors and 84.90% malignant tumors (52 carcinomas, 3 sarcomas and 35 carcinosarcomas). Although international literature shows an average of approximately 50% for malignant mammary tumors in dogs (3, 4), this study and other Brazilian studies showed higher percentages of malignant tumors (2, 5). Histological analysis of regional lymph nodes was possible in only 47.25% cases of malignant tumors and 16.28% presented metastasis. According to literature, approximately 10% of the dogs with malignant mammary tumors develop lymph node metastasis (1).

Four animals showed mammary tumors clinically compatible with inflammatory carcinomas. These animals were not submitted to surgery or biopsy, they received palliative treatment with COX-2 inhibitors, and two of them received chemotherapy.

Table 1 shows the predominant histopathological findings. Immunohistochemical study of these cases was not performed.

Table 1. Type, immunohistochemical profile, mitotic index, histological grade and overall survival of canine mammary gland neoplasms.

Histological Type	N	ER Positive	PR Positive	MIB-1 Median index	COX-2 High level	Mitosis Median index	Histological grade I/II/III	Overall Survival
Hyperplasia	4						NA*	471
Adenoma	6						NA	951
Benign mixed tumor	5						NA	534
Benign mioepitelioma	1						NA	381
Complex carcinoma	14							548
Complex carcinoma with metastasis	1							212
Solid carcinoma	8							769
Solid carcinoma with metastasis	1							92
Tubulopapilar carcinoma	14							642
Carcinoma	7							830
Carcinoma with metastasis	1							1075
Anaplastic carcinoma	2							465
Anaplastic carcinoma with metastasis	2							327
Comedocarcinoma with metastasis	1							464
Squamous cell carcinoma	1							1061
Fibrosarcoma	2							1269
Sarcoma	1							417
Carcinosarcoma	34							571
Carcinosarcoma with metastasis	1							780

NA: do not apply. RE: Estrogen Receptor; RP: Progesterone Receptor

In relation to treatment, 86 cases underwent surgical treatment only, and 24 patients received additional

treatments (Tab. 2). Among treated animals, it was possible to observe tumor recurrence in 12% of cases.

Overall survival media of 606 days was observed for animals with malignant tumors. Animals were considered alive up to 06.30.2013. Figure 1 shows overall survival data for 110 female dogs according to therapy. Figure 2 shows the comparison of overall survival time between tubulopapillary carcinoma (14 cases) and aggressive

mammary tumors (35 carcinosarcomas, 9 solid carcinomas and 4 anaplastic carcinomas). Analysis revealed no statistical significance. Tumor type was considered an important prognostic factor in many studies, tumor size was also a prognostic factor in most prospective studies (1, 3).

Table 2. Therapeutical conduct for canine mammary neoplasms according to histopathological classification.

Histologycal Type	N	Surgery	OH* therapeutic	Surgery carboplatin	+	Surgery doxorubicin	+	Surgery+5FU+ cyclophosphamide	Overall Survival
Benign tumors	16	16	6						570
Carcinomas without metastasis	36	36	13					4	672
Agressive carcinomas without metastasis	43	43	18	10		5		1	615
Carcinomas with metastasis	9	9	2	3		1			284

OH: Ovariohisterectomy

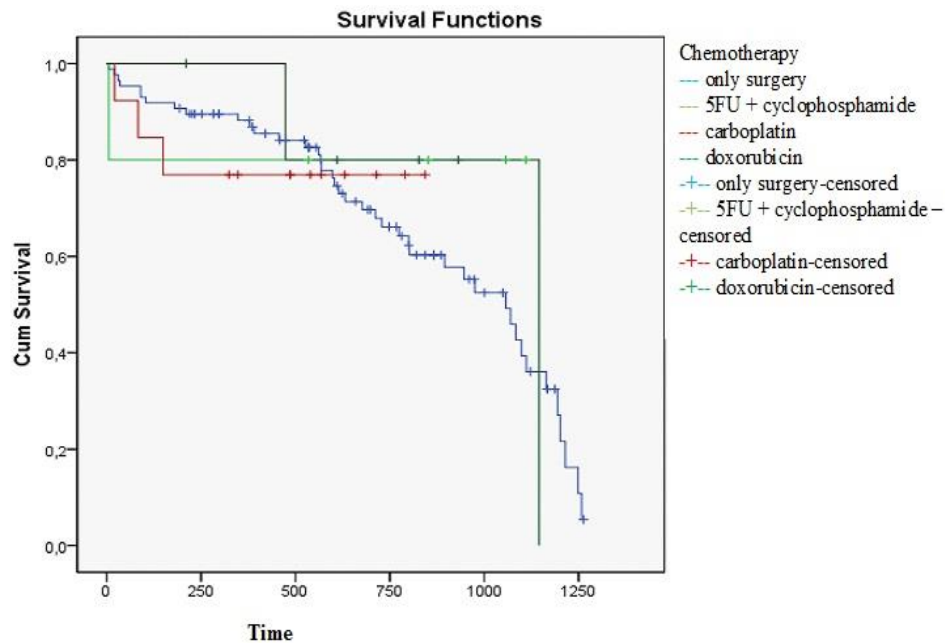


Figure 1. Overall survival curves for 110 female dogs according to therapy. Patients submitted to surgery alone (blue), 86 cases; surgery, 5-fluorouracil and cyclophosphamide (green), 5 cases; surgery and carboplatin (red), 13 cases; surgery and doxorubicin (dark green), 6 cases.

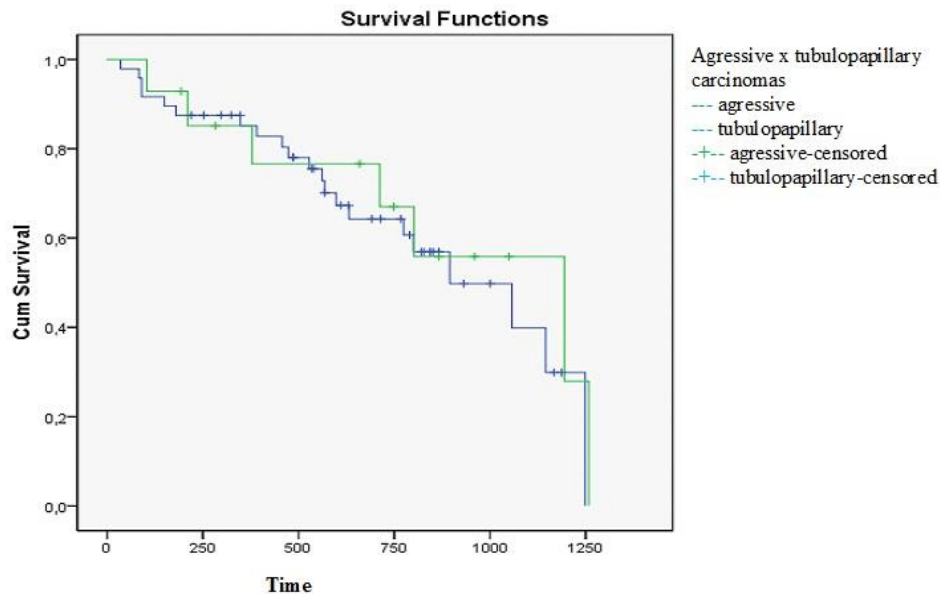


Figure 2. Comparison of overall survival time between tubulopapillary carcinoma (14 cases) and aggressive mammary tumors (35 carcinosarcomas, 9 solid carcinomas and 4 anaplastic carcinomas).

Conclusion

The results of this study show a higher incidence of malignancy in pathological examinations from animals with mammary neoplasms. Most common sites of metastasis were the regional lymph nodes and the lungs. Survival does not seem to be affected by histological type alone, staging of the tumor and treatment should also be considered.

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Clinicopathological Evaluation of Mammary Lesions in Dogs Treated at the Hospital of Veterinary Medicine Teacher Firmino Marsico Filho (HUVET) - University of Federal Fluminense (UFF)

Franciele Basso Fernandes Silva, Cristina Mendes Pliego, Tábata Maués, Livia Yumi Suzuki, Juliana da Silva Leite, Marcela Freire Vallim de Mello, Maria de Lourdes Gonçalves Ferreira, Ana Maria Reis Ferreira*

Laboratory of Pathological Anatomy Veterinary – Department of Pathology and Clinic Veterinary – Faculty of Veterinary Medicine – University of Federal Fluminense – Niterói/RJ, Brazil
* **Corresponding author:** Rua Vital Brazil Filho, 64. Santa Rosa, 24230-340, Niterói/RJ, Brazil. E-mail: anatotopatovet@vm.uff.br

The aim of this study was to characterize epidemiological and pathological data related to the clinical evaluation of mammary lesions in dogs treated at Hospital of Veterinary Medicine Teacher Firmino Marsico Filho (HUVET) - University of Federal Fluminense (UFF) in Niterói – Rio de Janeiro.

Material and Methods

During the period from 2010 to 2012, a clinical anatomo-pathological survey was conducted that included 124 mammary tumors in female dogs diagnosed at HUVET-UFF. The epidemiological and clinical characteristics of the patients were reviewed to identify the breed and age of the animals and to evaluate the main macroscopic and microscopic characteristics of the pathological changes, as well as the frequency of their occurrence.

Results and Discussion

Clinicopathological data were obtained for 124 animals; the age was available for 117 of these dogs, and the breed was identified for 121. The affected animals had an average age of 9.8 years, with a standard deviation of 2.3, and animals between 9 and 11 years old made up 44.4% (52/117) of the cases. These data corroborate those of Cassali (3) and Pliego (19), who state that the most affected age group is from 9 to 12 years of age, and the risk of developing cancer increases with age. A higher incidence of Poodle breeds (33%) and mongrel dogs (24%) was observed in the breed identification. Regarding breed-specific predisposition, there is no consensus among authors on whether breed is linked to the occurrence of cancer, but studies corroborate the present study in revealing a greater involvement of Poodle breeds (2, 8, 11, 12). Mongrel dogs were the second most affected; the high incidence in this group is due to the fact that these animals compose the majority of the canine population treated at HUVET-UFF. These data corroborate those of Daleck et al. (6), who argue that the greater predisposition to mammary tumors in mongrel dogs animals is due to the larger population of these animals compared to animals of defined breed.

Regarding reproduction data, 28/124 bitches were spayed, and only one had received estrus controlling hormones. Ovariohysterectomy (OSH) as prophylactic choice is well described in the literature. According to O'Keffe (17), the risk of developing mammary cancer in dogs that undergo OSH before the first estrous is smaller than that of dogs that undergo this procedure after two or more estrous cycles. However, in this study, it was not possible to identify at what age the bitches had undergone ovariohysterectomy because of insufficient information provided by the owner, making it impossible to determine whether the OSH was performed before or after sexual maturity. Nevertheless, only 22.6% of the females with mammary tumors were castrated.

Information about tumor localization was obtained for all 124 animals and revealed that 6.5% (8/124) of the bitches had thoracic mammary gland tumors, 12.1% (15/124) had abdominal mammary gland tumors, 17.7% (22/124) had inguinal mammary gland tumors, and 63.7% (79/124) had multicentric tumors.

According to the literature, it is common to find multiple nodes of the same type or different histological types in bitches (7, 19). The increased frequency of mammary neoplasms in the abdominal and inguinal glands observed in this study may be related to an increased activity of those glands during lactation (21) and to the fact that those glands have a higher amount of mammary parenchyma (1). The occurrence of single and multiple nodules were 36.5% and 63.5%, respectively, with a higher percentage of multiple nodules than the 50% found by other authors (10, 12, 22).

Clinical evaluation revealed 74, 15, 19 and 9 animals with stage I, II, III and IV cancers, respectively. This result is similar to the results found by Schoenrock (23), in which clinical stage I represented 50% of the diagnosed cases, clinical stage II 21%, clinical stage III 25% and clinical stage IV 4%. However, the present results differ from those found by D'Assis (5). In their study, clinical stages II and III prevailed, suggesting that the animals had a delayed diagnosis and treatment.

Two animals had tumor recurrence, at 60 and 360 days, respectively, after surgery. Eleven (11.6%) of the studied animals had lymph node metastasis, and nine (9.5%) had distant metastasis, among which the most prevalent site was the lungs (7/9). Similar data were found by Cavalvanti and Cassali (4), in which 10% of the bitches affected by malignant mammary cancer showed regional lymph node metastasis.

In histopathological analysis of mammary tumors from 124 animals, 4% were found to have benign non-neoplastic changes, 19.4% benign tumors, and 76.6% malignant tumors (92 carcinomas and 3 carcinosarcomas) (Table 1). This analysis considered only the nodule with the worse prognosis. These data corroborate those reported by Oliveira et al. (18), where the proportion of malignant and benign lesions was 4:1 (approximately 71.8% of cases were malignant). However, other authors claim that mammary tumors are divided almost equally between benign and malignant (50% of cases for each type) (6, 9, 13, 16). Considering the histological types of the malignant mammary gland tumors of the dogs in the present study, the higher incidence of carcinomas compared to carcinosarcomas was similar to the data found by Terzian et al. (25) and Martins (11). These studies diagnosed 65% and 77% of the tumors as carcinomas, respectively, and Martins (11) also observed that 14.8% were carcinomas in mixed tumors, and 8.2% were carcinosarcomas. Table 1 identifies the predominant neoplastic histological types, their histological graduation rates and the expression of immunohistochemical markers.

The literature reveals the high frequency of carcinomas in mixed tumors among malignant mammary gland tumors affecting bitches (14, 15). This information was confirmed in the present study, in which the most frequent tumor type found in mixed tumors was the carcinoma (43.5%, 54/124). Other authors had similar results, such as Brodey et al. (1), who found that 45.5% of

1625 canine mammary gland tumors were carcinomas in mixed tumors; Pliego (20), who found a percentage of 29.8% from 47 dogs; and Silva (24), with 35% from 49 dogs.

In the present study, the cell proliferation rate was higher than that of apoptosis in canine mammary neoplasms. Similar data were found by Martins (11), who evaluated the expression of PCNA, Ki-67 and cleaved caspase-3 and also noted a lower number of cells positive for the last marker.

Regarding treatment, 113 cases were surgically treated, and in 21 of these animals, complementary

treatments were performed - adjuvant chemotherapy with 5-fluorouracil and cyclophosphamide. Among these animals, tumor recurrence was observed in only two cases, and these dogs received no further treatment. One of these dogs had lung metastases after 120 days.

In the 46 female dogs with malignant tumors, a median survival rate of 468.7 days was determined; these animals were followed for up to 540 days after surgery. The present study showed that in tumors in which the immunohistochemical analysis showed a high rate of cell proliferation and apoptosis, the prognosis was considered unfavorable, and the patient showed a lower survival rate.

Table 1. Anatomopathological data for the histological samples of 124 female dogs studied at Hospital of Veterinary Medicine Teacher Firmino Marsico Filho (HUVET) - University of Federal Fluminense (UFF) in Niterói – Rio de Janeiro.

Histological Type	N	PCNA (% positive cells)	Cleaved Caspase-3 (% positive cells)	Mitotic Index*			Histological Grade*			Overall Survival
				1	2	3	I	II	III	
Benign mixed tumor	13	-	-	-	-	-	NA	NA	NA	-
Adenoma	9	-	-	-	-	-	NA	NA	NA	-
Papilloma	2	-	-	-	-	-	NA	NA	NA	-
Carcinoma in mixed tumor	48	27.8	24.7	10	11	-	6	13	1	479
Carcinoma in mixed tumor with metastasis	6	47.6	9.3	1	-	1	-	-	2	400
Complex carcinoma	17	19.4	11.7	8	1	-	5	3	1	540
Complex carcinoma with metastasis	1	-	-	-	-	-	-	-	-	-
Papillar carcinoma	10	11.1	9.45	1	-	3	-	1	1	540
Tubular carcinoma	1	13.2	10.4	-	-	-	-	-	-	540
Solid carcinoma	3	34.5	16.5	2	1	0	1	1	1	410
Spindle cell carcinoma	3	51.2	3.5	-	-	1	-	-	1	465
Mucinous carcinoma with metastasis	2	41.7	34.3	-	1	-	-	1	-	270
Anaplastic carcinoma	1	-	-	-	-	-	-	-	-	120
Anaplastic carcinoma with metastasis	1	26.1	18.8	1	-	-	-	1	-	485
Carcinosarcoma	3	32.4	10.6	1	-	2	-	1	2	426
Hyperplasia	4	-	-	-	-	-	-	-	-	-

NA: Not applicable. PCNA: Proliferating Cell Nuclear Antigen

* Number of evaluated and classified cases in each index/grade.

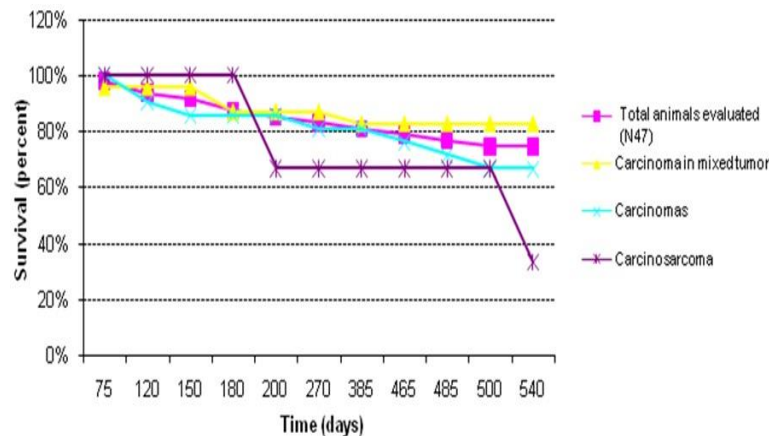


Figure 1. Survival curve for 47 female dogs from Hospital of Veterinary Medicine Teacher Firmino Marsico Filho (HUVET) - University of Federal Fluminense (UFF) that underwent a 540-day follow-up period after surgical treatment. Among the 47 animals evaluated, 23 were diagnosed with carcinoma in mixed tumor, 21 with carcinoma (complex, simple and special) and 3 with carcinosarcoma.

Conclusion

Malignant neoplasms, particularly carcinomas in mixed tumors, were the most frequent mammary lesions among the patients from HUVET-UFF. The proliferation index of the analyzed mammary tumors was higher than the apoptotic rate, and the incidence of metastasis was unusual. Surgical excision of the mammary cancer proved to be an effective treatment, providing good survival, without disease recurrence for the majority of the canine population evaluated.

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Epidemiological and Histological Aspects of Canine Mammary Tumors Diagnosed at the Veterinary Teaching Hospital/Uel

Michele Salmon Frehse¹, Ana Paula F. R. Loureiro Bracarense^{2*}, Giovana Wingeter di Santis², Elisângela Olegário da Silva², Roberta Lemos Freire¹, Marco Antônio Machado³, Maria Isabel Mello Martins³

¹Department of Preventive Veterinary Medicine - Agricultural Sciences, Center – UEL, Londrina/PR, Brazil

²Laboratory of Animal Pathology, Department of Preventive Veterinary Medicine - UEL, Londrina/PR, Brazil

³Department of Clinical Veterinary - Agricultural Sciences Center – UEL, Londrina/PR, Brazil

* **Corresponding Author:** Rodovia Celso Garcia Cid, PR 445 Km 380, Campus Universitário Cx. Postal 10.011, 86051-970, Londrina/PR, Brasil
E-mail: ana.bracarense@pq.cnpq.br

This study aims to characterize epidemiological and histopathological data of canine patients with mammary tumors treated at the Veterinary Teaching Hospital of the Universidade Estadual de Londrina (HV/Uel), Paraná-Brazil.

Material and Methods

From 2010 into 2012, medical records on canine patients with mammary tumors attended at HV/Uel were reviewed. Epidemiological (age, breed, time of survival), clinical (number of pregnancies, progesterone administration, metastasis, treatment) and pathological (affected glands, histological classification and grading of tumors) data were recorded. Histological classification followed the criteria proposed (6). Data were processed and tabulated with the statistical software for epidemiology EPI INFO 3.5.4. The survival analysis was performed in free software R 2.15.3 using the Kaplan-Meier test.

Results and Discussion

Seventy-five animals with mean age of 10.1 (\pm 2.4) years were included in this study. The group aged 9 to 11 years corresponded to 44.7% of the cases. Mixed breed dogs had higher frequency 53.3% of the disease, followed by Poodles 33.3%. Regarding reproductive information, 22.7% (17/75) female dogs were previously spayed and 21.3% (16/75) have received progesterone for controlling the estrous cycle.

The tumors were observed more frequently in abdominal mammary glands 69% (49/71) followed by

inguinal glands 53.5% (38/71) and thoracic glands 38% (27/71). In 64.8% (46/71) of the animals, multiple glands were affected by tumors. We identified 16% (12/75) cases with regional lymph node metastasis, and 14.7% (11/75) with distant metastases, mainly affecting the lungs. Histological classification of the tumors revealed that 16% were benign neoplasms, and 84% were malignant neoplasms (59 carcinomas, 3 sarcomas and 1 carcinosarcoma), as shown in Table 1. Non-neoplastic cellular changes were not diagnosed. Frequency and grading of mammary tumors are disposed in Table 2.

The most prevalent malignant tumor was simple tubular carcinoma, and grade II was the most frequent histological grading. Histological analysis of regional lymph nodes was performed in all cases, showing metastasis in 16% of the animals. All animals were submitted to surgical treatment that consisted of total unilateral mastectomy and ovariosalpingohysterectomy. Chemotherapy was not performed.

Survival analysis was performed in 46 female dogs with malignant tumors. Figure 1 exhibits the survival analysis curve for the group with malignant tumors (46 animals). The survival rate for: Simple tubular carcinoma grade I, was 33% at 15 months after surgery [(standard error (SE) = 0.157, 95% CI (0.132 to 0.840)]; Simple tubular carcinoma grade II, 29,6% at 25 months after surgery [(standard error (SE) = 0.164, 95% CI (0.10 to 0.87)]; Simple tubular carcinoma grade III, 33% at 17 months after surgery [(standard error (SE) = 0.27, 95% CI (0.06 to 1.00)]; Complex carcinoma grade I, 72,9% at 20 months after surgery [(standard error (SE) = 0.13, 95% CI (0.50 to 1.00)] and Complex carcinoma grade II, 58,7% at 22 months after surgery [(standard error (SE) = 0.15, 95% CI (0.34 to 1.00)]. The mortality rate until May 2013 was 47.6% (30/63) for all malignant tumors. Survival was considered from the first one mastectomy, with the average time after removal of tumors was 11.7 months. The small size (≤ 3 cm) accounted for 52.7%, followed by tumors of medium size (4-10cm) 35.5% and large size (>10 cm) represented 11.8%.

Several studies reported that mammary tumors

affect middle-aged and older intact or spayed female dogs, which is in accordance with the present study (3,4). In addition, similar results on the average age of affected females was reported in the literature (8,2). In this study, Poodle was the most affected breed similarly to data reported in other Brazilian study (9). The risk of developing mammary tumors in spayed females prior to the first heat cycle is 0.5%, showing the protective effect of castration at a young age, as well as hormone-dependent mammary cancer (2). However, as only 22.7% dogs had been castrated prior to mastectomy, such effect could not be observed in the present study. The use of progesterone contraceptives increases the chance of developing benign mammary tumors. The results found in this study showed that 21.3% of the patients underwent hormonal treatment, and 16% of these had benign neoplasms (1). Concerning the location of tumors, 69% and 53.5% tumors were located in the abdominal and inguinal mammary glands, respectively, similar to previous studies (9). The high incidence of inguinal mammary gland tumors has been associated with an increased amount of parenchyma and hormone receptors (5). Regarding neoplastic changes, 16% were benign and 84% were malignant, resembling to other studies (4, 9). This high prevalence of malignant mammary tumors may be due to the long period between the onset and clinical evaluation (9). The most prevalent malignant tumor was simple carcinoma, similar to other studies (8,9,7), and grade II was the most frequent histological grading.

Conclusion

The epidemiological results observed in this study were similar to data reported in the literature. Interestingly, the survival rates observed for tubular carcinoma grade III was worse compared with other carcinomas. These data reinforces the need to improve the diagnosis and treatment of mammary tumors, considering the histological types, leading patients to a good quality of life.

Table 1. Clinical aspects of 75 female dogs with mammary tumors attended from 2010-2012 in the Veterinary Hospital at Universidade Estadual de Londrina, Londrina, PR, Brazil.

Histological type	N	Surgery	OSH therapeutic	Surgery + P1	Months Survival Global (mean)
Benign tumors	11	All	Yes all	Yes all	14
Carcinomas <i>in situ</i>	1	All	Yes all	Yes all	15
Carcinomas without metastasis	25	All	Yes all	Yes all	17.89
Carcinomas with aggressive features without metastasis grade II/III	29	All	Yes all	Yes all	12.16
Carcinomas with metastasis	5	All	Yes all	Yes all	6.37
Sarcomas	3	All	Yes all	Yes all	9.66
Carcinosarcoma	1	All	Yes all	Yes all	13
Total	75				

P1: Protocol 1 (Total unilateral mastectomy + Ovariosalpingohysterectomy)

*The Survival Analyses Curve was not done for each kind of tumor due the low number of samples.]

Table 2. Histological classification, grading and mean survival of 75 female dogs with mammary tumors attended from 2010-2012 in the Veterinary Hospital at Universidade Estadual de Londrina, Londrina, PR, Brazil.

Histologic Type	N	ER Pos	PR Pos	MIB-1 Medium Index	COX-2 High Score	Mitosis Medium Index	Months Survival Global (mean)
Benign mixed tumor	8	NA	NA	NA	NA	scarce	10.37
Adenoma	1	NA	NA	NA	NA		20
Papilloma	0	NA	NA	NA	NA		0
Fibroadenoma	1	NA	NA	NA	NA		27
Mixoma	1	NA	NA	NA	NA		12
Sarcomas	3	NA	NA	NA	NA		9.66
Comedocarcinoma	1	NA	NA	NA	NA		9
Hemangiopericytoma	1	NA	NA	NA	NA		1
Simple cribriforme carcinoma	0	NA	NA	NA	NA		0
Simple cribriforme carcinoma with metastases	1	NA	NA	NA	NA		20
Cystic papillary carcinoma	1	NA	NA	NA	NA		23
Simple tubular carcinoma grade I	9	NA	NA	NA	NA		14.44
Simple tubular carcinoma grade II	10	NA	NA	NA	NA		18.4
Simple tubular carcinoma grade III	3	NA	NA	NA	NA		8.66
Carcinoma <i>in situ</i>	1	NA	NA	NA	NA	1	15
Carcinoma into mixed tumor	0	NA	NA	NA	NA		0
Carcinoma into mixed tumor with metastases	0	NA	NA	NA	NA		0
Complex carcinoma grade I	11	NA	NA	NA	NA	≤1/until3	23.09
Complex carcinoma grade II	13	NA	NA	NA	NA		15
Complex carcinoma with metastasis grade I	1	NA	NA	NA	NA	≤1/until3	1
Complex carcinoma with metastasis grade II	1	NA	NA	NA	NA		20
Invasive papillary carcinoma grade I	2	NA	NA	NA	NA	≤1/until3	16.5
Invasive papillary carcinoma grade II	2	NA	NA	NA	NA		17
Invasive papillary carcinoma grade I with metastasis	1	NA	NA	NA	NA	≤1	0
Micropapillary carcinoma	0	NA	NA	NA	NA		0
Micropapillary carcinoma with metastasis	0	NA	NA	NA	NA		0
Tubular carcinoma grade III	0	NA	NA	NA	NA		0
Tubular carcinoma grade III with metastasis	2	NA	NA	NA	NA	>3	4.5
Solid carcinoma	0	NA	NA	NA	NA		0
Solid carcinoma with metastasis	0	NA	NA	NA	NA		0
Carcinosarcoma	0	NA	NA	NA	NA		0
Carcinosarcoma with metastasis	1	NA	NA	NA	NA		13
Total	75						

NA: Not applicable; ER: Estrogen Receptor; PR: Progesterone Receptor

*The Survival Analyses Curve was not done for each kind of tumor due the low number of samples.

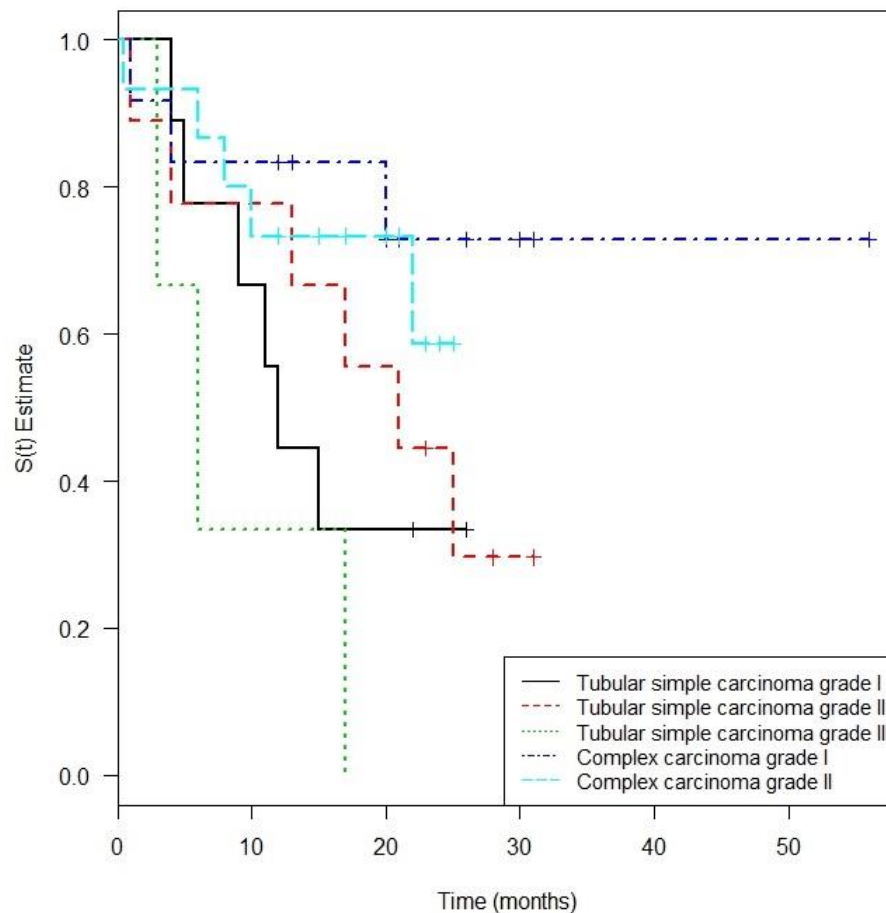


Figure 1. Survival Analyses Curve of 46 female dogs show the most frequent histologic types of malignant mammary tumors, attended from 2010-2012 in the Veterinary Hospital at the Universidade Estadual de Londrina, Londrina, PR, Brazil.

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Analysis of Clinico-Pathological Data, Therapeutical Conduct and Overall Survival of Canine Mammary Lesions Attended at the Veterinary Hospital of the Federal University of Minas Gerais (UFMG)

Fernanda Camargo Nunes, Conrado de Oliveira Gamba, Karine Araújo Damasceno, Cecília Bonolo de Campos, Rodrigo dos Santos Horta, Marina Rios de Araújo, Lidianne Narducci Monteiro, Gleidice Eunice Lavalle, Enio Ferreira, Geovanni Dantas Cassali*

Laboratory of Comparative Pathology – Department of General Pathology

Institute of Biological Sciences – Federal University of Minas Gerais - UFMG, Belo Horizonte, MG, Brazil

* **Corresponding author:** Av. Antonio Carlos, 6627. Pampulha, 31270-901, Belo Horizonte/MG, Brazil. Email: cassalig@icb.ufmg.br

The aim of this study was to present clinico-pathological data, therapeutical conduct and overall survival of canine mammary lesions attended at the Veterinary Hospital of the Veterinary School of the Federal University of Minas Gerais (UFMG) in Belo Horizonte, Minas Gerais, Brasil.

Material e Methods

Information related to canine patients attended during the period from 2011 to 2012 at the Veterinary Hospital of the UFMG was obtained. Mammary lesions were diagnosed at the Laboratory of Comparative Pathology (UFMG). In the present study, epidemiological

characteristics (breed, sex, and age), clinical data (hormone administration, castration, clinical staging, and overall survival), pathological data (macroscopic and microscopic characteristics of the lesions and their occurrence), and therapeutic conducts applied to patients with mammary tumors were reviewed. Overall survival was evaluated by univariate analysis (Kaplan-Meier estimated survival curves). Values were considered statistically significant when $P < 0.05$ by the Log-rank Test (Cox-Mantel).

Results and Discussion

A total of 1072 mammary lesions affecting 285 female dogs were obtained. Age was informed in 223/285 (78.24%) animals with a median of 9.7 ± 2.8 years old. Animals aged from 9 and 11 years constituted 41.25% of cases. The described age is similar to findings in most studies that indicate a higher susceptibility between 9 and 11 years (4, 11, 12, 16).

Breed identification was informed in 240/285 (84.21%) animals and a larger incidence of poodles 73/240 (30.41%) was observed, as described by Misdorp (2002) and Toribio et al. (2012). The increased frequency of poodles may be determined by the increased number of poodles in several veterinary centers (4, 5, 12, 16).

The frequency of mammary tumors increases with higher life expectancies and with prolonged use of progestogens, while decreasing when young animals are ovariectomized (15). Therefore, the disease is considered hormone-dependent (14). In the present work, 39/140 (27.85%) bitches were spayed and solely 3/132 (2.27%) received progestogen treatment.

Tumoral location was informed in 273 animals presenting 811 mammary lesions. The majority of tumors were located in abdominal mammary glands 353/811 (43.52%), followed by 224/811 (27.62%) in inguinal mammary glands, 178/811 (21.94%) in thoracic mammary glands, and 56/811 (6.90%) presented multicentric tumors. Misdorp (2002) affirms that the abdominal and inguinal mammary glands are the most affected by mammary lesions due to larger amount of mammary parenchyma and consequently increased possibility of proliferative response to reproductive hormones.

Clinical staging revealed that most animals were classified as stage I (150/283, 53%), followed by stage II (58/283, 20.49%), III (36/283, 12.72%), IV (35/283, 11.30%), and V (4/283 1.41%). Regarding tumor size, 159/276 (57.60%) animals presented lesions smaller than 3 cm, 65/276 (23.55%) presented lesions between 3-5 cm, and 52/276 (18.84%) presented lesions larger than 5 cm. Previous studies demonstrate that tumors smaller than 3 cm and free from lymphatic invasion (stage I) present better prognosis than tumors larger than 5 cm or tumors that present lymph node invasion (4, 6, 7, 16).

The main metastasis sites associated to mammary gland tumors are regional lymph nodes and lungs and occur through lymphatic and hematogenous routes,

respectively (12,13). However, the risk and metastatic pattern are mainly influenced by the histologic type (4). In the present work, 43/187 (22.99%) cases presented lymph node metastasis and 14/285 (4.91%) presented distant metastasis mainly located in the lung (78.57%), as found by previous studies (4, 6, 16). Lymph node involvement and the presence of metastasis indicates unfavorable prognosis (2).

Histopathological classification of mammary tumors is notably important in predicting the biological behavior of tumors (1). Therefore, morphologic evaluation of all nodules is essential to better define the prognosis and choice of therapy (2). Histopathological analysis of primary tumors revealed 194/1072 (18.09%) benign neoplastic alterations, 236/1072 (22.01%) benign neoplasms, and 642/1072 (59.88%) malignant neoplasm. Malignant neoplasms were composed of 631/642 (98.28%) carcinomas, 7/642 (1.1%) carcinosarcomas, and 4/642 (0.62%) other histological types. Tumors displaying multiple morphological patterns were classified according to the pattern considered to have worse prognosis, which determines the therapeutic conduct (2). Among the carcinomas, the carcinoma in mixed tumor was the most frequent 338/631 (53.56 %) and is considered to have the best prognosis (2), followed by papillary carcinomas 68/631(10.77%). Solid and micropapillary carcinomas,

considered as aggressive histological subtypes (2), presented 34/631 (5.38%) and 17/631 (2.69%) cases, respectively. Histological findings are similar to previous literature findings (4, 6).

The evaluation of molecular markers through immunohistochemistry techniques may indicate prognostic and predictive values of the neoplasm (2). In the present work, immunohistochemistry was performed in 17/642 (2.64%) cases of malignant tumors, revealing positivity for estrogen receptors (ER) in 13/17 (76.47%) of cases, for progesterone receptor (PR) in 5/17 (29.41%) of cases, for cyclooxygenase-2 (Cox-2) in 8/17 (47.05%) of cases, and for Ki67 in 1/17 (5.88%) case that revealed a cellular proliferation index of 13.20%. The histological type and grade, immunohistochemical profile, mitotic index, and overall survival of all studied mammary lesions are presented in Table 1.

Regarding treatment, 234/285 (82.10%) of cases were submitted solely to a surgical treatment and 35/285 (12.28%) of animals received complementary treatments. The surgical approach considered the extension of the disease, size and location of the lesion and lymphatic drainage, according to Sorensen, Worley and Goldschmidt (2013). Patients diagnosed with solid carcinoma, micropapillary carcinoma, and carcinosarcoma, even

Table 1. Histological type, immunohistochemical profile, mitotic index, histological grade and overall survival of canine mammary gland neoplasms.

Histological type	N	ER Positive	PR Positive	Ki-67 Median Index	COX-2 High Score	Overall Survival
Benign mixed tumor	150					769
Carcinoma in mixed tumor	338	5	3	1	2	524
Carcinoma in mixed tumor with metastasis	9	4	1		2	416
Invasive papillary carcinoma	32					584
Invasive papillary carcinoma with metastasis	4					572
Non-invasive papillary carcinoma	39					682
Micropapillary carcinoma	17					523
Micropapillary carcinoma with metastasis	7				1	233
Tubular carcinoma grade I and II	18					631
Tubular carcinoma grade I, II, and III with metastasis	3					553
Solid carcinoma	34	4	2	1	4	397
Solid carcinoma with metastasis	9	4	1	1	3	300
Carcinosarcoma	7					180
Carcinosarcoma with metastasis	3					173
Malignant phyllodes tumor	1	1		1	1	409

NA: No applicability. RE: Estrogen receptor; RP: Progesterone receptor

when no regional or distant metastasis was evidenced, received the recommendation of complementary chemotherapy treatment. Adjuvant chemotherapy was also recommended to all patients with regional or distant metastasis regardless of histological type. Among these animals that were submitted to complementary treatment following tumor excision, tumor recurrence was observed in 11/35 (31.42%) cases, with a two month median appearance period. Therapeutic conducts are presented in

Table 2.

Prognosis determination in canine malignant mammary gland neoplasms is notably important for clinicians. However it remains a challenge due to marked variation of the biological behavior of tumors (4). In the present work, the overall survival was evaluated in 132/285 (46.31%) animals. Patients with benign neoplasms presented a higher median overall survival (997 days) than those with malignant neoplasms (404 days). Higher overall

survival associated to malignant neoplasms was observed in carcinomas in mixed tumors (median was not reached at 980 days); invasive papillary carcinomas (median reached at 717 days); tubular carcinomas (median reached at 299 days); solid carcinomas and carcinosarcomas (median reached at 193 days); and micropapillary carcinomas (median reached at 188 days) (Fig. 1). This data is similar to findings (3, 6, 8, 16) that observed higher overall survival in bitches diagnosed with carcinomas in mixed tumors when compared to other histological types.

Regarding the animals that were submitted solely to surgical treatment, the group of patients diagnosed with

solid carcinomas presented a median overall survival of 332 days. While patients with the same diagnosis treated with surgery and adjuvant chemotherapy did not reach median survival during the period of the present study. These results reaffirm the importance of adjuvant treatment that may contribute towards higher overall survival. Unfortunately, reports regarding overall survival periods of treated patients according to specific histological subtypes are not available in the literature.

Figures 1 and 2 present the overall survival of animals regarding histopathological diagnosis and different proposed treatments, respectively.

Table 2. Therapeutical conduct for canine mammary neoplasms according to histopathological classification.

Histopathological Type	N	Surgery	Therapeutical OH	Surgery + P1	Surgery + P2	Surgery + P3	Another protocol	Overall Survival
Benign tumors	34	34						769
<i>In situ</i> carcinomas	16	16						607
Carcinomas without metastasis	184	184	5					524
Poor prognosis								
Carcinomas without metastasis	12	12	6	5	6	1		311
Carcinomas with metastasis	23	23	4	12	7	1	3	394

P1: Protocol 1 (segundo consenso); P2: Protocol 2; OH: Ovariectomia

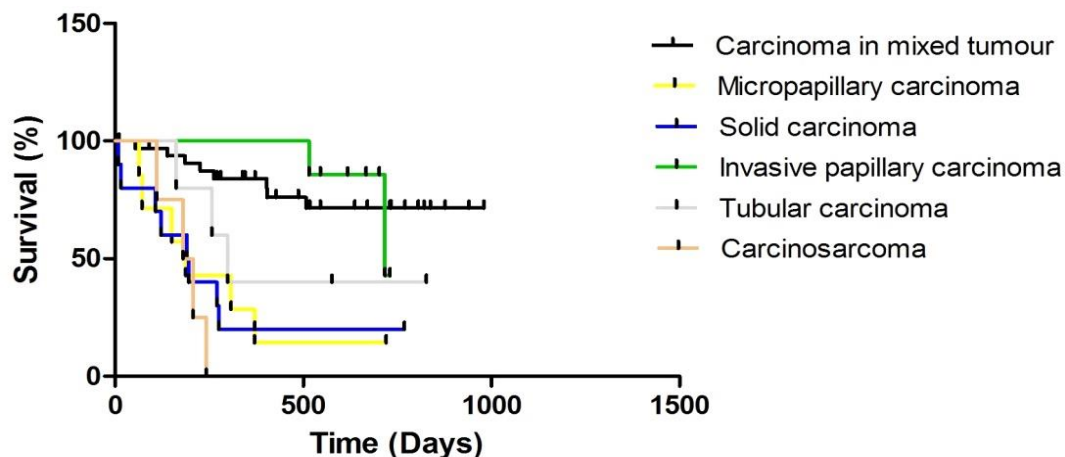


Figure 1. Overall survival analysis of malignant mammary tumors (34 carcinomas in mixed tumor; 7 invasive micropapillary carcinomas; 10 solid carcinomas; 7 invasive papillary carcinomas; 5 tubular carcinomas; 4 carcinosarcomas) ($p=0.0001$).

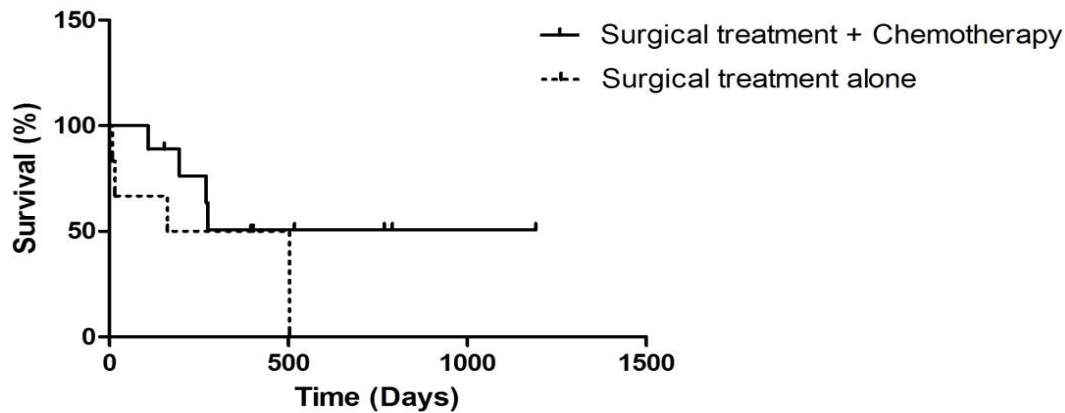


Figure 2. Overall survival curves for 15 solid carcinomas of the canine mammary glands according to therapy. Patients submitted to surgical treatment alone (6 cases); Surgical treatment + Chemotherapy (9 cases) ($p=0.70$).

Conclusion

Based on the observed results it is possible to conclude that the study of classic prognostic factors such as tumor size, lymph node involvement, and histological type is crucial for clinical and pathological approaches of canine mammary neoplasms. These data allow appropriate choices of therapeutical conducts for animals with different prognosis due to different biological characteristics.

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Clinical Pathological Study of Mammary Tumors in Female Dogs from the Veterinary Hospital of UFBA – Bahia, Brazil

Alessandra Estrela Lima*, João M. Costa Neto, Arianne Pontes Oriá, Eduardo Luiz T. Moreira, Tiago C. Peixoto, Caterina Muramoto, Mário Jorge M. H. D'Assis, Carlos H. C. Vieira Filho, Marília C. A. Machado, Nara A. Nascimento, Danielle N. Silva, Emanuel F. Martins Filho, Emanuelle A. Gomes, Laís P. Silva, Luciano G. T. Requião, Thanielle N. Fontes.

Veterinary Pathology Laboratory - Department of Anatomy, Pathology and Clinics EMEVZ-UFBA. Salvador/BA, Brazil.

* **Corresponding author:** Av Adhemar de Barros, 500, 40170-110, Ondina, Salvador/BA, Brazil. E-mail: alestrela@gmail.com

The aim of this study was to characterize the pathological and epidemiological data related to the clinical evaluation of canine patients with mammary lesions presented at the Veterinary Hospital of Federal University of Bahia, Salvador – Bahia, Brazil.

Material and Methods

During the period of May 2011 to April 2013 a retrospective study of clinical and pathological data of 348 female dogs with mammary lesions treated at the Clinic and Surgery sector of the Veterinary Hospital, Federal

University of Bahia was performed. We reviewed the main epidemiological and clinical aspects of patients and performed an assessment of macro and microscopic features of mammary cancer related to the animals survival rates.

Results and Discussion

During the study period, 348 female dogs with neoplastic lesions were clinically diagnosed with possible mammary tumor. Among the animals evaluated nine dogs were suffering from inflammatory carcinomas and only 174 underwent mastectomy with subsequent histopathological confirmation of the neoplastic lesions. The predominant age group was nine to eleven years, representing 41.67% of the cases (145/348) with an average of 10.54 years - standard deviation of ± 2.75 . These data are in agreement with the literature, in which the risk of developing mammary cancer in dogs increases significantly with age, affecting most frequently animals at an age from nine to eleven, with a low occurrence in female dogs with less than five and are rare when the animal has less than two years of age (13). Based on breed identification we observed a higher incidence of Poodle 150/348 (43.10%) followed by mixed breed dogs 104/348 (29.88%). Apparently there is no breed predisposition for the development of mammary tumors in dogs (4,5,16). Thus, the high incidence in mongrel dogs and poodles can be associated with the fact that these animals represent the majority of the dog population in Brazil (8, 10, 11, 20). In all 348 cases we were able to identify the tumor location. Most dogs had bilateral involvement of the mammary chains 143/348 (41.09%). The multicentric tumors represented 256/348 (73.56%), and/or multiple 90/348 (25.86%). Tumors with the worst prognosis were located, by order of importance, in the inguinal mammary glands 152/348 (43.68%), abdominal (glands 133/348 (38.22%) and thoracic glands 63/348 (18.10%). The caudal abdominal and inguinal glands are the most frequent sites of tumor development, possibly due to their larger amount of parenchyma, thus maintaining the secretory ability longer than others, or by a greater possibility of proliferative response to the action of hormones (14). Regarding their reproductive history, only 34/348 (9.77%) were previously treated with exogenous progesterone. According to Cavalcanti (2006), the prolonged use and high doses of this exogenous hormone lead to predisposition of benign mammary tumors. Also, only 37/348 (10.63%) of the female dogs had been previously spayed, however with no indication as to when the surgical procedure had taken place. Most authors disagree with the protective capability of OSH after the third estrous cycle, regardless of the presence of the neoplastic process (12, 15, 18, 21). However, Sorenmo et al. (2000) reported a higher survival rate of female dogs that underwent to mastectomy associated with spaying or when this was performed within 24 months prior to the primary node

excision. Data from clinical staging performed on all animals revealed 116/348 (33.34%), 71/348 (20.40%), 77/348 (22.13%), 45/348 (12.93%) and 22/348 (6.32%) of tumors at stages I, II, III, IV and V respectively. During the evaluated period the stage I tumors were more often observed smaller tumors and better prognosis was observed. These data differ from previous surveys conducted in this institution, in which the large, ulcerated and metastatic tumors were predominant, accounting for up to 90% of cases (8, 9, 20). Histological analysis of lesions was performed in only 174 of the 348 cases, since 50% of patients did not return to the Veterinary Hospital for mastectomy consequently we did not have a histological diagnosis. According to the microscopic evaluation benign neoplasms represented 13/174 (7.47%) and malignant neoplasms 161/174 (92.53%). The predominant histological type in the malignant tumors group were carcinomas 150/161 (93.17%), followed by carcinosarcomas 10/161 (6.21%). Among the malignant tumors, the carcinoma in benign mixed tumor (CaTMB) was the most commonly subtype observed 50/161 (31.06%) confirming the findings of Bertagnolli et al., 2009 and Damasceno et al., 2012. CaTMB are the result of malignant transformation of epithelial components of the benign mixed tumor (1, 7). These results, with a predominance of malignant tumors, show the reality of the Veterinary Hospital of the Federal University of Bahia, where socioeconomic factors related to the owners interferes in mammary tumor diagnosis and prognosis of the disease (20). In Table 1 it is possible to identify the predominant neoplastic histologic type and their histological grade. Histological evaluation of regional

lymph nodes of patients with malignant tumors was performed in 158/161 (98.14%). However, during clinical staging lymph nodes from 45 patients that were enlarged were considered affected, in those cases the assessment was presumptive based exclusively on physical examination. Therefore, we emphasize the necessity and importance of carrying out the lymph nodes cytology for a more accurate diagnosis.

We identified 30/174 (17.24%) animals with metastasis, 25/174 (14.37%) had metastasis exclusively in lymph nodes and 05/174 (2.87%) had distant metastasis. The lymph node involvement is considered one of the most important prognostic factors, together with tumor size and histologic type (14). Surgical treatment was performed in 174/348 (50%) animals, which is the most appropriate therapeutic procedure (except for inflammatory mammary carcinoma) for mammary tumor in dogs (2, 17). Chemotherapy treatment with carboplatin (300 mg/m²) was performed in 7/174 (4.02%) animals that have undergone mastectomy. According to Daleck (2008), cancer chemotherapy is a neoadjuvant treatment method to surgery, which promotes destruction of micrometastases, thereby reducing the potential for recurrence of mammary tumors. In Table 2 it is possible to identify the predominant neoplastic histological types and their recommended treatment. With respect to inflammatory mammary carcinoma, 9/348 (2.59%) animals were clinically diagnosed with this type of cancer, only 3/9 (33.34%) underwent chemotherapy with carboplatin, associated with palliative firocoxib (5mg/kg) and only 1/9 (11.12%) used firocoxib not associated with neoadjuvant treatment.

Table 1. Histopathology findings of mammary tumors in female dogs.

Histologic Type	N	Histological grade I/II/III	Global survival
Mixed benign tumor	5	NA	530.75
Adenoma	6	NA	517.50
Papilloma	2	NA	454.5
Carcinoma <i>in situ</i>	1	NA	-
Carcinoma in mixed tumor without metastasis	44	31/13/0	402.7
Carcinoma in mixed tumor with metastasis	6	03/03/00	210.33
Complex carcinoma without metastasis	17	11/06/0	412.5
Complex carcinoma with metastasis	4	02/02/00	225.5
Invasive papillary carcinoma without metastasis	28	14/14/0	312.7
Invasive papillary carcinoma with metastasis	5	1/4/00	252.0
Tubular carcinoma without metastasis	7	5/2/0	323.00
Carcinoma tubulopapillary without metastasis	9	7/2/0	261.00
Carcinoma tubulopapillary with metastasis	1	0/1/0	149.00
Solid carcinoma without metastasis	9	0/9/0	290.0
Solid carcinoma with metastasis	10	0/10/0	116.0
Carcinosarcoma without metastasis	7	NA	256.4
Carcinosarcoma with metastasis	3	NA	-
Carcinomas (special types) without metastasis	9	5/4/0	290.5
Carcinomas (special types) with metastasis	1	0/1/0	220.5

NA: Not applicable

Table 2. Clinical findings of mammary tumors in female dogs.

Histologic Type	N	Surgery	OH therapeutic	Surgery + P1	Global survival
Benign tumors	13	13	6	0	500.91
Carcinomas in situ	1	1	0	0	-
Carcinomas without metastasis	123	123	76	4	255.56
Carcinoma with metastasis	27	27	20	3	138.3

P1: Protocol 1 - Chemotherapy with Carboplatin (according to consensus); OH: ovariectomy.

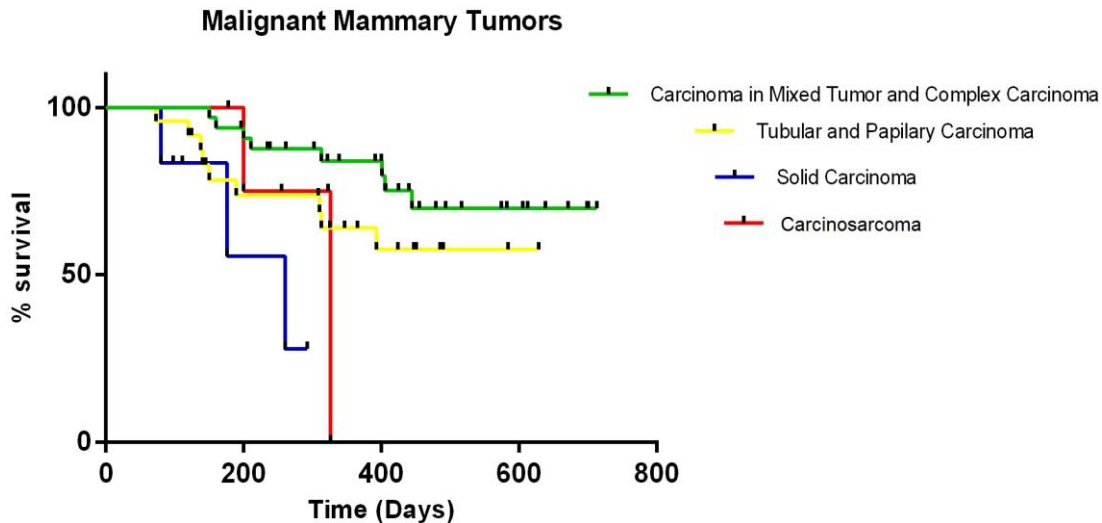


Figure 1. Comparison of overall survival time malignant mammary tumors in female dogs.

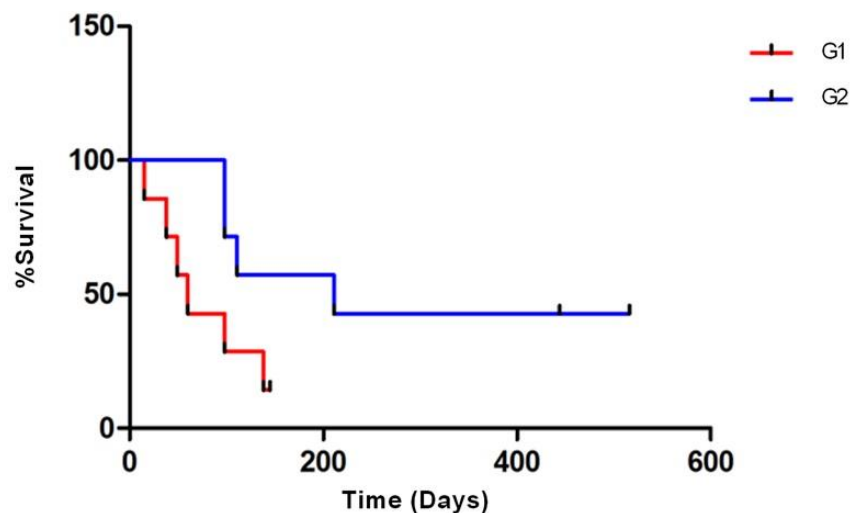


Figure 2. Overall survival curves for 97 female dogs according to therapy. Patients with advanced stage submitted to surgical treatment alone (G1), 7 cases; conventional surgical excision and carboplatin (G2), 7 cases.

The overall survival is defined (in days) as the period between the surgical excision of the primary tumor and the date of death due to the disease. In this survey an average of 500.91 days for female dogs with benign mammary tumors and 359.5 days for those with malignant mammary tumors were observed. Carcinomas have a specific biological behavior, evidenced by short survival rate and frequent occurrence of metastases, with worse prognosis compared to benign tumors (13). Surgical excision of the tumor combined chemotherapy with carboplatin was performed in seven dogs (4,02%) these

patients had higher survival time than dogs with advanced stage not submitted to the chemotherapy protocol.

According to the literature the presence of metastases markedly reduces the survival time of the patient and in such cases the treatment is purely palliative with the purpose of improving the quality of life. On Figures 1 and 2 it is possible to observe the survival rate of animals with malignant tumors as well as the survival rate depending on the type of treatment used, respectively.

Conclusion

The epidemiological and clinicopathological aspects allow us to conclude that there is a high incidence of mammary tumors in the oncology routine from the veterinary hospital of UFBA. We found a higher frequency of malignant tumors with histological grade I, standing out specially the carcinoma in benign mixed tumor (CaTMB) and the stages I and III were the most frequent. Considering the results observed in this study, the classification of the tumors will be a priority in the future. Clinical staging, histologic grade and the use of analysis with immunohistochemical prognostic and predictive markers will be implemented. Subsequently, since currently the treatment is based almost exclusively on surgical excision, we intend to intensify routine cancer chemotherapy, aiming to provide the patient a higher survival rate and a better quality of life.

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Clinical-Pathological Study of Canine Mammary Tumors at the Veterinary University Hospital of the Federal University of Pampa – UNIPAMPA

Tainã Normanton Guim^{1*}, Shana Letícia Garmatz¹, Adriano Krabbe², Bruno dos Anjos²

¹Veterinary University Hospital

²Veterinary Pathology Laboratory

UNIPAMPA. Uruguaiana, RS, Brazil

* Corresponding author: Br 472 - Km 592, Uruguaiana, RS, 97500-970 Brazil. Email: tainaguim@unipampa.edu.br

This study aims to characterize pathologic and epidemiologic data associated to clinical evaluation of dogs with mammary lesions at the Veterinary University Hospital of the Federal University of Pampa - Unipampa, Uruguaiana, Rio Grande do Sul, Brazil.

Material and Methods

The clinical-pathological survey of 10 tumoral

mammary lesions in canines, diagnosed at the Veterinary University Hospital of Unipampa, was performed during the period of 2011 to 2012. The clinical and epidemiologic aspects of these patients were reviewed, with identification of their breed and age, and evaluation of the characteristics and frequency of the main macroscopic and microscopic mammary lesions.

Results and Discussion

Clinical and pathological data from 10 dogs were gathered. The affected animals were on average 10.6 years, with a standard deviation of 4.06 years. Animals between the ages of 9 and 11 years represented 40 percent of the cases. In this study, the results were similar to those in the literature, which describe middle-aged to older dogs being mostly affected by mammary neoplasms (6). Similar average age was observed by some authors (1,12), while others (7,10) found average ages of 9.3 and 9.2 years, respectively.

The breed identification showed that 40 percent of the cases were mongrel female dogs and 60 percent of the cases were equally distributed among the breeds Dachshund, Yorkshire, Basset Hound, Boxer, Brazilian Fila and Poodle. Similar to Cavalcanti and Cassali (2006) (4) and Daleck *et al.* (1998) (6) findings, there was not breed predisposition to the development of the disease in this survey. However, some breeds such as Poodle, Cocker Spaniel, Dachshund, German Shepherd and Pinscher seem to be more predisposed to mammary tumors (5,9,10,12).

The reproductive signalment in this study indicated that 1 out of 10 bitches were spayed and 3 out of 8 bitches had received hormones for controlling estrus cycle. According to Daleck *et al.* (2009) (5), hormones like estrogen, progesterone and growth hormone have an influence in the carcinogenesis. Data of this report show that the majority of the females were not spayed and susceptible to hormonal influences. This data did not allow the evaluation of the ovariectomy preventive effect as described in the literature (3,5,9) since there were not records of spayed bitches before puberty. As for exogenous hormones, there is a correlation between the use of progestogens and the growth of benign tumors (5,9,11), which does not occur with estrogens (5). However this type of correlation was difficult to apply in this study, since the information regarding the types of hormones administered were not available in the patients records.

The prevalent locations of the mammary tumors were evaluated in all of the 10 cases. Twenty percent of the dogs presented tumoral growths located in the abdominal mammary glands, 20 percent had tumors in the inguinal mammary glands and 60 percent had multicentric tumors. In this report, tumoral lesions were not found in the thoracic mammary glands. According to Cassali *et al.* (2011) (3) and Misdorp (2002) (9), multiple tumors in the same mammary gland or involving simultaneously several

glands (multicentric mammary tumors) are frequently observed. In one study Daleck *et al.* (1998) (6) found that 20 out of 23 dogs with mammary neoplasms had multiple nodules. Other studies show the multicentric form was prevalent in 77.6 percent (11) and 80.1 percent (12) of the cases. This present report corroborates the results obtained by these authors.

According to the clinical tumoral staging, 3, 2, 4 and 1 animals had tumors in stages I, II, III and IV, respectively. One case had a distant site metastasis, in the mediastinum. In one study Toribio *et al.* (2012) (12) found stage III tumor also as the most frequent tumor, followed by tumors in stages IV and V.

The histopathological analysis of 10 mammary tumors revealed that 10 percent of them were benign non-neoplastic lesions; 40 percent were benign neoplasms and 50 percent were malignant neoplasms (3 carcinomas and 2 sarcomas) (Table 1). According to Misdorp (2002) (9), simple mammary carcinomas are the malignant neoplasms most commonly found in dogs and cats. In this present study, the results were similar to those observed by other authors, varying only as to the histological subtypes (6,10,11,12). In one study performed by Andrade *et al.* (2012) (1), the carcinosarcoma was the predominant histological type followed by the simple mammary carcinoma.

Table 1. Histopathological diagnoses and survival rates of the affected animals.

Histological type	N	Global survival (days)
Epithelial hyperplasia	1	-
Mixed benign tumor	1	-
Adenoma	2	-
Complex adenoma	1	-
Tubulopapillary carcinoma	2	-
Complex carcinoma	1	360
Carcinosarcoma	1	150
Osteosarcoma	1	120

Eight animals were submitted to surgical therapy and two animals were submitted to euthanasia due to the severe advanced stage of the disease. It was possible to detect tumoral recurrence in 10 percent of these cases. According to Daleck *et al.* (2009) (5) and Cassali *et al.* (2011) (3), the complete surgical removal of the tumors without metastasis still is the therapeutic procedure with the higher cure probability for the disease. In this present report, the surgical therapy proved to be efficient; recurrence was observed in only one case.

An average of 210 days of post treatment survival was identified in the animals carrying malignant tumors (Table 1). The 24-month period follow-up of the cases, as suggested by Benjamin *et al.* (1999) (2) was not possible to conduct in this survey since the data were gathered only over a period of 12 months. Only the survival rates data of the dogs that died during this period were registered.

According to this data, the dogs affected by mammary sarcomas had a short period of survival, metastasis and tumoral recurrence, which is also observed by other authors (8,9).

Conclusion

The results in this study allow us to conclude that old-aged, purebred, female dogs were most commonly affected by mammary neoplasms. Tumors with multicentric distribution, malignant tumors and non-metastatic tumors were predominant. Surgery applied as the only treatment was shown to be efficient to control the disease. With a few number of cases and the short post-surgical follow-up period it was not possible a thorough analysis of the survival rates of the affected animals.

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The Epidemiological and Pathological Characteristics of Canine Mammary Neoplasia Cases Diagnosed at the Veterinary Teaching Hospital of the Universidade de Franca (UNIFRAN), Brazil

Geórgia Modé Magalhães*, Priscila Pavini
Cintra, Sabryna Gouveia Calazans

Veterinary Hospital – Universidade de Franca
(Unifran), São Paulo, Brazil.

* **Corresponding author:** Av: Armando Salles Oliveira, 201, Parque
Universitário, Franca, São Paulo, Brazil.
E-mail: georgiamode@hotmail.com

The objective of this study was to conduct a retrospective analysis of the pathological and epidemiological characteristics of the mammary tumors of female dogs admitted to the Veterinary Teaching Hospital of the Universidade de Franca (Unifran), Franca-SP, Brazil.

Materials and Methods

Thirty-nine bitches, diagnosed with mammary tumors between 2010 and 2013, were included in this study. Clinical and epidemiological data were analysed considering breed, age, main macroscopic and microscopic characteristics of the tumors and their frequency of occurrence as variables.

Results and Discussion

The average age of the affected animals was 9.1 ± 2.4 years, with 64% of patients between 7 and 11 years of age. These results are in agreement with those of an epidemiology study that reported the prevalence of neoplasia in patients between 7 and 12 years old (1). Thirty-three per cent of the patients were of mixed breeds, 15% were Poodles and 12% Dachshunds. The breed diversity found in the different regions of the country made comparisons between studies challenging; however, our results are in agreement with those which reported that Poodles are amongst the most affected breeds by mammary tumors (2). Regarding the reproductive history of the patients, nine animals had been spayed and five had been treated with hormonal contraceptives in the past. Information on tumor site was obtained in 38 of the 39 cases: 60.5% were multicentric tumours, 26.3% were located in the abdominal mammary glands, 7.8% in the inguinal mammary glands and 5.2% in the thoracic mammary glands. Our results contrasted with those of a study that found a higher incidence of tumors in the inguinal mammary glands (3).

Histopathological analysis revealed that two (5.1%) cases were benign and non-neoplastic while 37 (94.8%) were of various malignant varieties; including 35 carcinomas, 1 sarcoma and 1 carcinosarcoma. The carcinoma cases were classified as follows: 12 carcinomas in mixed tumors grade II, 11 carcinomas in mixed tumors grade I, 4 tubular carcinomas grade I, 4 solid carcinomas grade II, 2 carcinomas *in situ*, 2 tubular carcinomas grade II, 2 invasive papillary carcinomas grade II and 1 solid carcinoma grade III. The high incidence of malignancy in canine mammary tumors has been reported in several studies (1, 2, 3) and the high percentage of malignant varieties observed in the present study support those findings. Histological analysis of the regional lymph nodes was possible in four of the cases and revealed the presence of four metastases.

Table 1. Anatomopathological classification of mammary tumors of bitches admitted between 2010 and 2013 into the Veterinary Teaching Hospital of the Universidade de Franca (Unifran), Franca-SP, Brazil.

Histological Type	N	Mitotic Mean Index	Histological Grade I/II/III	Global Survival (days)
Mixed benign tumour	1	-	NA	-
Carcinoma <i>in situ</i>	2	-	NA	-
Carcinoma in mixed tumour	11	1	I	713
Carcinoma in mixed tumour	12	1	II	492
Carcinoma in mixed tumour with metastasis	1	2	II	850
Invasive papillary carcinoma	2	-	-	-
Solid carcinoma	5	3	II/III	530
Carcinosarcoma with metastasis	1	-	-	240

N: number of tumors; NA: not applicable

The histological classification and grade of the neoplasms are shown in Table 1. Thirty-eight patients underwent surgical treatment alone while one received complementary treatment in addition to surgery. Two animals showed tumor recurrence within 30 months post-treatment. Lymph node metastases occurred in three animals, whereas distant metastasis was observed in only one patient.

Conclusion

It can be concluded that most of the cases of mammary tumors analysed were malignant, with a high incidence of carcinomas in mixed tumors. The mean age of the affected patients was nine years and mixed breed dogs were the most prevalent, followed by Poodles and Dachshunds. Most tumors were multicentric and the incidence of lymph node and distant organ metastases was low.

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Clinical-Pathologic Study of Canine Mammary Tumors at the Oncologic Veterinary Service of FV/UFPel

Thomas Normanton Guim, Daniela Silva da Silva, Cristine Cioato da Silva, Rosimeri Zamboni, Bianca Lemos dos Santos, Josiane Bonel-Raposo, Cristina Gevehr Fernandes*

Hospital de Clínicas Veterinárias - Depto de Clínicas Veterinárias, Depto de Patologia Animal - Laboratório Regional de Diagnóstico / Faculdade de Veterinária – UFPel. Pelotas, RS, Brasil

* Corresponding author: Campus Capão do Leão, s/ nº, 96010-900, Pelotas/RS, Brasil. Email: crisgevf@yahoo.com.br

The aim of this study was to characterize the epidemiological, clinical and pathological data of canine mammary tumors at the Service of Veterinary Oncology of the Veterinary Hospital and Veterinary Diagnostic Laboratory of UFPel, at Pelotas, Rio Grande do Sul from 2010 to 2012.

Materials and Methods

A retrospective chart review was carried out to obtain the clinical and pathological features of the patients and mammary tumors diagnosed from 2010 to 2012. Every case was entered in a form that contained basic identification, including case number, breed, age and history of spaying. Specific macroscopic data, such as tumor size and number, location of affected mammary glands and lymph node involvement, were also tabulated. Histological characteristics, such as tumor type, grading and surgical margins, were categorized. The survival time was also considered in a study where patients were followed for a 24-month period.

Results and Discussion

Clinical data were obtained from 175 animals, in which a total of 305 tumors were diagnosed. Only one tumor occurred in a male. All other tumors occurred in females, and 63.6% of tumors occurred in dogs 9 to 17 years old. The mean age of the diagnosed animals was 9.6 years. Nearly 40% of the cases occurred in crossbred animals. Among purebred animals, tumors were most prevalent in poodles (16%). Information regarding reproductive status was obtained in 143 cases, and only 23 bitches were spayed after mastectomy. It was also observed that 33/87 received contraceptive hormones. In 88 animals this information was not available.

The anatomical locations of the tumors were determined in 153 cases and in 22 cases this information was not available in our records. Multicentric tumors predominated (67.3%). Tumors were located in the thoracic glands in 6.5% of cases, abdominal pairs in 5.9% of cases and inguinal glands in 20.3% of cases. Caudal abdominal and inguinal mammary glands were affected with higher frequency than thoracic glands (2). Clinical staging was determined according to the TNM system established by the World Health Organization (WHO) (2, 6). The staging was performed in 56 cases and revealed that 19, 6, 10, 14 and 7 animals presented grade I, II, III, IV and V tumors, respectively. Tumor relapse was observed in 3 patients. Lymph node metastases was clinically detected in 28 cases and distant metastasis in 9 cases, of which 77.8% had localization in the lungs. This pattern of metastasis is well reported in dogs (5).

Methods of classifying canine mammary tumors vary considerably (1). In this paper we adopted the classification system proposed by the Consensus for the Diagnosis, Prognosis and Treatment of Canine Mammary Tumors (2). Pathological data were obtained from 305 tumors, as mentioned above. Only 13 benign lesions were observed; malignant lesions accompanied the benign lesions in dogs with multiple tumors. The most prevalent malignant lesions were carcinosarcomas (78/305-25.57%), followed by complex carcinoma (62/305-20.33%) and tubulopapillary carcinomas (52/305-17.05%). Table 1 shows the histologic types of specific tumors and their rates.

Histological grading of tumors was determined by the Nottingham system and modified by Elston and Ellis (3). The tumor grade was determined in 32.46% (99/305) of the cases, with a preponderance of grade III tumors followed by grade II, and finally, grade I. Table 2 shows the histologic types of specific tumors. Similar results were observed by Mendes et al (4). A histological evaluation of the lymph nodes was performed in 46.2% (141/305) of cases with malignant tumors; 23.3% of these cases presented metastasis. Evaluation of surgical resection margins was performed in 177/305 cases. Whenever there were neoplastic cells in the area stained with Indian ink, the sample was considered as having "compromised

margins" (2). Neoplastic cells were observed within the margins of 20 cases. Survival time was determined in 66/175 animals, which were followed up to 720 days (24 months) after mastectomy. The mean survival time of 440 days (14.6 month) was observed in animals with mammary tumors. Figure 1 shows the overall survival time of 59 females with carcinosarcomas, complex carcinomas and tubular/tubulopapillary carcinomas. Surgical therapy was performed in 142 patients, and only 2 received complementary chemotherapy. Concurrent castration was done in 42 animals (Table 3). The number of followed up patients need to be increased to obtain conclusive data.

Table 1. Frequency of each mammary histologic tumor type.

Histologic type	N	%
Carcinosarcoma	78	25.57
Complex carcinoma	62	20.33
Tubulopapillary carcinoma	52	17.05
Tubular carcinoma	37	12.13
Carcinoma in mixed tumor	18	5.90
Solid carcinoma	13	4.26
Anaplastic carcinoma	9	2.95
Adenoma	8	2.62
Papillary carcinoma	8	2.62
Spindle-cell carcinoma	5	1.64
Benign benign tumor	4	1.31
Malignant myoepithelioma	3	0.98
Papiloma	1	0.33
Carcinoma <i>in situ</i>	1	0.33
Micropapillary carcinoma	1	0.33
Hemangiosarcoma	1	0.33
Pure condrosarcoma	1	0.33
Osteosarcoma	1	0.33
Lipid-rich carcinoma with metastasis	1	0.33
Squamous carcinoma	1	0.33
Total	305	100.00

Conclusion

In this study, mammary tumors were most highly prevalent in middle-aged animals. Multicentric anatomical locations predominated over the others. Although metastasis was uncommon based on clinical examinations, histological evaluation revealed an increase in the number of affected lymph nodes. In our oncologic service, malignant tumors are the most frequent type, and carcinosarcomas are the predominant histologic type. Furthermore, surgical treatment is routinely performed. As the evaluation period comprised only the 3 most recent years, only a few cases were followed for 24 months. Follow-up times need to be increased to obtain conclusive data.

Table 2. Tumor type, histologic grade and global survival mean time.

Histologic type	N	Grade				Global survival* (n)
		I	II	III	NI	
Benign mixed tumor	4	3			1	360 (1)
Adenoma	8	3			5	720 (4)
Papilloma	1				1	-
Carcinoma <i>in situ</i>	1				1	-
Carcinoma in mixed tumor	17				17	-
Carcinoma in mixed tumor with metastasis	1			1		540 (1)
Complex carcinoma	57		10	8	39	217 (11)
Complex carcinoma with metastasis	5	1			4	-
Solid carcinoma	9			4	5	360 (1)
Solid carcinoma with metastasis	4			2	2	-
Tubular carcinoma	32		2	4	26	435 (2)
Tubular carcinoma with metastasis	5			5		570 (4)
Papillar carcinoma	7		2	1	4	660 (3)
Papillar carcinoma with metastasis	1				1	-
Tubulopapillar carcinoma	41	2	13	6	20	493 (14)
Tubulopapillar carcinoma with metastasis	11		2	2	7	247 (3)
Micropapillar carcinoma with metastasis	1				1	-
Anaplastic carcinoma	6		1	3	2	-
Anaplastic carcinoma with metastasis	3			1	2	-
Carcinosarcoma	66	2	5	8	51	405 (15)
Carcinosarcoma with metastasis	12			3	9	360 (2)
Malignant myoepithelioma	3			2	1	-
Lipid-rich carcinoma	1				1	-
Squamous cell carcinoma	1				1	-
Spindle-cell carcinoma	3		1	2		630 (3)
Spindle-cell carcinoma with metastasis	2				2	-
Hemangiosarcoma	1				1	360 (1)
Pure Condrosarcoma	1				1	-
Osteosarcoma	1				1	-
Total	305	11	36	52	206	440 (66)

*Animals followed for 720 days (24 months) after mastectomy.

NI: not informed.

Table 3. Clinical and therapeutic procedures in patients with mammary tumors.

Histologic type	N	Surgery	Therapeutic OH	Survival Global* (n)
Benign tumors	2	2	2	720 (1)
Carcinomas without metastasis	22	22	15	309 (3)
Aggressive Carcinomas without metastasis	3	3	1	465 (2)
Carcinomas with metastasis	17	15	7	150 (4)
Carcinosarcomas without metastasis	13	13	8	-
Carcinosarcomas with metastasis	14	14	9	309 (6)

PI-other: Protocol 1 to other protocol (according to Cassali et al, 2011).

OH: Ovariohysterectomy

*Animals followed for 720 days (24 months) after mastectomy.

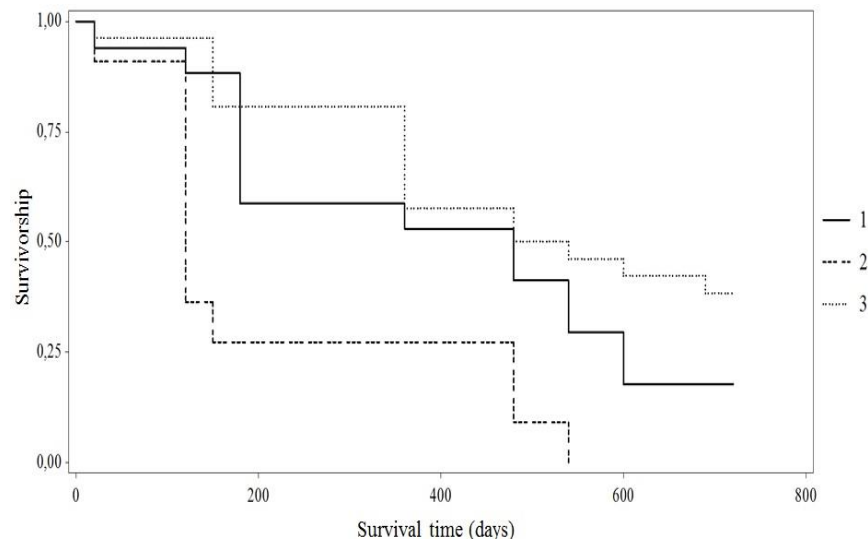


Figure 1. Comparison of overall survival times between carcinosarcomas (1), complex carcinomas (2) and Tubular/tubulopapillary carcinomas (3).

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Mammary Tumors in Dogs - Clinic and Pathology Survey at the Onco Cane Veterinary Clinic

Sobral, RA.*, Silva, GRO., Honda, ST., Fernandes, SC., Cesar, JR., Zoppa, A., Afonso, ECA., Rosa, AL., Bianchi, FC., Alves, TG.; Arakaki FS., Packness, J., Rossi, A., J. Tedardi, MV.

Onco Cane Clínica Veterinária Ltda - São Paulo, Brazil
* **Corresponding author:** Avenida Miruna, 591, CEP 04084-002, São Paulo/SP, Brasil. Email: renatasobral@oncocane.com

The survey shows epidemiology and pathology information related to female dogs diagnosed with mammary tumors attended at Onco Cane, a specialized Veterinary Oncology Clinic, São Paulo, Brazil.

Method

The survey considered 15 patients attended from May, 2012 to May, 2013. Four patients had more than one tumor nodule which were different histological types; the survival time was based on the worst tumor prognosis.

Epidemiologic and clinical characteristics of all patients were studied including breed, age, neoplasm macro and microscopic characteristics and their occurrence.

Results

The average age at diagnosis time was 8 years and 5 months (± 2 years) with 40% of the bitches (6/15) ranged between 9 to 11 years. Related to breed predisposition, Poodle (3/15), Yorkshire (3/15) and Maltese (3/15) represented 60% of all breeds included in the study.

According to the owners, 33,3% of the dogs were already spayed at the diagnosis. None of them reported the use of any hormone to regulate the estrus; in one case, however, the animal had been adopted when she was about 10 years old and was not spayed at that moment.

Regarding the location of the tumor, 20% (3/15) there were single nodules at thoracic mammary glands, 13% (2/15) at abdominal glands and 6% (1/15) at inguinal glands. Four bitches (26,6%) had multicentric tumors. The clinical stage of the patients was performed according to TNM system. Ten patients were classified in stage I (66%), four in stage III (26,6%) and one patient in stage IV (6,6%).

Complex carcinoma (3/15) and carcinoma in mixed tumors (4/15) represented 46,6% among other types (Table 1). Regional metastasis was observed only in patients with large tumors (T3) and in a micropapillary carcinoma with an inflammatory presentation. Pulmonary metastasis, at diagnosis, was related just in a large (10 cm) carcinosarcoma.

Most of the patients (12/15 = 80%) were treated only by surgery. Two patients (13,5%) were treated by surgery and chemotherapy and one was treated by surgery plus chemotherapy and also 6 sessions of radiation therapy (Table 2).

Regional nodes were removed from all patients during the mastectomy and submitted to histological analysis. Regional nodal metastasis was confirmed in 3 patients (20%), all in advanced clinical stage (2 patients with large tumor (T3) and one as inflammatory carcinoma). Pulmonary metastasis was confirmed in one patient.

Two patients showed recurrence of the disease in about 4 months after surgery. One of these developed recurrence from a primary neoplastic lesion as an

inflammatory carcinoma, and another developed recurrence from a fixed carcinosarcoma (10 cm diameter, T3NxM1).

The Figure 1 shows the overall survival time among different histological types, there was not statistical difference among the groups. Patients which died during the follow up had the average survival time of 219 days and, all of them had aggressive clinical and histological tumors.

Discussion

The results show that middle age small pure breeds, which were spayed later (after the 5 year old), has a profile for a risk for mammary cancer (1). Treatments were conducted according with the clinical stage and, because of that 80% of the patients were treated just by surgery, even those that patient with multicentric tumors.

The prevalence of carcinoma in mixed tumors and complex carcinoma was expected, these histological types are very common at mammary gland in bitches (2). The occurrence of metastasis was related to more aggressive histological type or to advanced clinical stage (3). The median survival time of the patients with metastatic disease was 219 days. All patients classified as ECI were alive at the end of the follow up which confirm that a longer survival time is related to initial clinical stages (3). The patient diagnosed as a micropapillary inflammatory carcinoma lived for 429 days. This patient was treated by surgery, chemotherapy and radiation therapy and, probably, the more complex combination of treatment contributed for the quite long survival time

Conclusion

According to the study, we concluded that complex carcinoma and carcinomas in mixed tumors were the most common histological tumors in middle age small pure breed and not spayed.

Clinically, most patients were classified in initial clinical stages. The treatment was strongly based on surgery and, in the case of more aggressive disease, additional treatment such as chemotherapy and radiation therapy was indicated. The overall survival time showed that patients diagnosed at ECI had longer survival than patients in advanced clinical stage.

Acknowledgements

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Table 1. Histopathological x overall survival.

Histological types	N	Histologic Grade I/ II/ III	Overall survival
Carcinoma in mixed tumor	3	Grade I (n=1) Grade II (n=1) Grade III (n=1)	All alive
Complex Carcinoma	4	Grade I (n=2) Grade II (n=2)	All alive
Papillary carcinoma (without metastasis)	2	Grade II (n=1) Grade III (n=1)	All alive
Papillary carcinoma (with metastasis)	1	Grade III (n=1)	Alive
Micropapillary carcinoma (without metastasis)	1	Grade III (n=1)	73 days
Micropapillary carcinoma – inflammatory (with metastasis)	1	Grade III (n=1)	429 days
Tubular carcinoma (without metastasis)	2	Grade I (n=1) Grade II (n=1)	All alive
Carcinosarcoma (with metastasis - lung)	1	NA (n=1)	155 days

Table 2. Clinical treatment x overall survival.

Histological types	N	Only mastectomy	Spay together mastectomy	SUR + (P1)	SUR + (P2) + Radiation therapy	Overall Survival
Carcinomas without metastasis	8	8/8	6/8	-	-	Patient 1 (alive – follow up 106 days) Patient 2 (alive – follow up 145 days) Patient 3 (alive - follow up 183 days) Patient 4 (alive - follow up 119 days) Patient 5 (alive - follow up 207 days) Patient 6 (alive - follow up 174 days) Patient 7 (alive - follow up 243 days) Patient 13 (alive - follow up 181 days)
Carcinomas (agressive profile without metastasis)	4	3/4	2/4	1/4	-	Patient 8 (alive – follow up 43 days) Patient 10 (alive - follow up 300 days) Patient 14 (alive - follow up 185 days) Patient 9 (died - 73 days)
Carcinomas with metastasis	2	-	-	1/2	1/2 (inflammatory)	Patient 11 (alive – follow up 71 days) Patient 12 (died - 429 days)
Carcinosarcoma	1	1/1	-	-	-	Patient 15 (died - 155 days)

P1 (chemotherapy based doxorubicin); P2 (chemotherapy based doxorubicin+carboplatin)

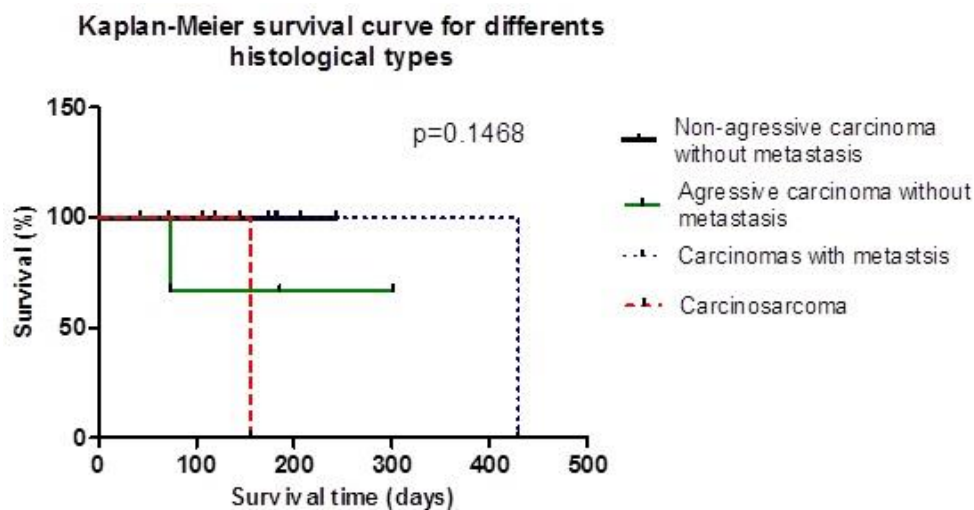


Figure 1. Overall survival time among different histological types.

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Clinical-Pathological Study of Mammary Tumors in Bitches at the Governador Laudo Natel Veterinary Hospital – UNESP – Jaboticabal

Erika Maria Terra*, Talita Mariana Morata Raposo, Rosana da Cruz Lino Salvador, Giovanna Rossi Varallo, Marília Gabriele Prado Albuquerque Ferreira, Paulo César Jark, Giovanni Vargas Hernandez, Reinaldo Juan Garrido Palacios Junior, Lívia Maria Souza Semolin, Rafaela Bortolotti Viéra, Josiane Morais Pazzini, Mayara Caroline Rosolem, Geórgia Modé Magalhães, Felipe Augusto Ruiz Sueiro, Thais Larissa Lourenço Castanheira, Eduardo Garrido, Renée Laufer Amorim, Geovanni Dantas Cassali, Rosemeire de Oliveira

Vasconcelos, Andrigo Barboza de Nardi, Mirela Tinucci Costa

Governador Laudo Natel Veterinary Hospital – Dept. of Clinic and Surgery, Faculdade de Ciências Agrárias e Veterinárias– UNESP. Jaboticabal, SP, Brazil

* **Corresponding author:** Governador Laudo Natel Veterinary Hospital– Dept. of Clinic and Surgery, Faculdade de Ciências Agrárias e Veterinárias– UNESP - Jaboticabal, SP, Brazil. Email: erikamterra@hotmail.com

This study describes the pathological and epidemiological data related to clinical evaluation of bitches with mammary lesions treated at the Veterinary Hospital of the Universidade Estadual Paulista Júlio de Mesquita Filho, in Jaboticabal, São Paulo, Brazil. The study was based on clinical and pathological guidelines proposed at the First Meeting of Mammary Pathology: Diagnosis, Prognosis and Treatment of Canine Mammary Neoplasia, held on 6 and 7 November 2010, in Belo Horizonte, Minas Gerais, Brazil, sponsored by the Laboratory of Comparative Pathology - UFMG, with the support of the Brazilian Association of Veterinary Pathology (ABPV) and the Brazilian Association of Veterinary Oncology (ABROVET).

Material and Methods

During the period 2011-2013, we conducted a clinical and pathological survey of 346 mammary lesions diagnosed in bitches at the Veterinary Oncology Service of UNESP, in Jaboticabal. Epidemiological and clinical characteristics of patients were reviewed; their breed was determined, as well as their age, main macro and microscopic features of lesions and the frequency of their occurrence.

Results and Discussion

Clinical-pathological data of 148 patients plus reported age and breed of all bitches were evaluated. Bitches affected were 10.43 years on average (10.43 ± 2.3 years), corroborating previous results on the age of highest incidence of mammary tumors (1, 3, 6, 16, 17).

Regarding animal breed, mixed breed animals were the most affected (36.48%) agreeing with De Nardi et al. (3). From the affected bitches, 64.87% (96/148 bitches) were intact females and despite the fact that the reproductive status effects on the development of mammary tumors in bitches is somewhat controversial, some studies suggest that these tumors are hormone dependent, and thus intact or late-spayed females are more predisposed to the onset of this disease (6, 16).

Contraceptives were administered in 10.13% (15/148) of the bitches. Of these 15, four had benign and malignant tumors concomitantly. These results disagree with those observed by Oliveira et al. (2003) (9), who reported that the correlation between progesterone

administration and the incidence of benign tumors was higher compared to malignant tumors.

As for tumor location in all 148 patients, 3.37 % had tumors in thoracic mammary glands; 20.27% in abdominal glands; 14.2% in the inguinal mammary glands; and, 62.16 % had tumors in multiple glands. Although the abdominal and inguinal mammary glands are usually the most affected, possibly due to greater amount of mammary tissue; it is common to have multiple nodules involving the same mammary gland or simultaneously affecting more than one gland while presenting different histological types, as observed in this study (3, 8, 15).

Regarding the tumor stage at diagnosis, 70 bitches had stage I; 24 bitches, stage II; 29 bitches, stage III; 17 bitches, stage IV; and, 5 bitches, stage V. During follow-up, 9 bitches had recurrences. Evaluation of regional and distant metastases revealed that 19 bitches had regional lymph node metastases and 22 patients had distant metastases, and the prevalent location sites were the lung (40.9%); followed by liver and spleen (22.73%); adrenal, skin and spine (4.5%). These sites of metastases were also described by other authors as the main sites of metastatic mammary tumors (3, 5, 7, 16).

Histopathological analysis of 346 breast lesions revealed that 5.78% were benign non-neoplastic changes; 10.11% were benign; and 83.53% were malignant tumors (290 carcinomas and 3 sarcomas). This high incidence of malignant tumors corroborates other Brazilian studies that report an incidence of malignant neoplasms higher than 70%, unlike American studies whose reported incidence is approximately 50% (9, 10, 14). Table 1 identifies the neoplastic histological types of worse prognosis of each patient and the histological grades. Some animals had benign and malignant lesions concomitantly. Overall survival was determined by evaluating the patients during follow-up or by phone; however, we were unable to get information about some patients.

The overall survival was an average 377.6 days, based on the data reported for 119 patients, out of 131 bitches that were diagnosed with malignant neoplasms. Figures 1 to 4 show the survival of patients in relation to histopathological diagnosis and recommended treatment. The comparison of histological types shows significant differences in relation to overall survival ($p < 0.0001$), as shown in Figure 1.

Table 1. Neoplastic histological types of worse prognosis for each patient and their histological grades.

Histological type	N	Histological grade I/II/III	Overall survival (days)
Benign Mixed Tumor	2	NA	
Adenoma	2	NA	
Complex Adenoma	3	NA	
Hyperplasia	3	NA	
Fibroadenoma	1	NA	
Chondroma	1	NA	
Carcinoma in mixed tumor	33	I=27 II=6 III=0*	374.28
Ca in mixed tumor with metastasis	2	I=2 II=0 III=0	377
Complex Carcinoma	10	I=8 II=1 III=1	927.75
Complex Ca with metastasis	4	I=2 II=2 III=0	633.34
Papillary Carcinoma without metastasis	18	I=6 II=12 III=0	339.29
Invasive Papillary Ca with metastasis	3	I=2 II=1 III=0	664
Micro-papillary Carcinoma	0		
Micro-papillary Ca with metastasis	3	I=0 II=0 III=3*	222
Ductal Carcinoma	38	I=30 II=7 III=1*	430.01
Ductal Ca with metastasis	2	I=0 II=1 III=1*	221.4
Solid Carcinoma	11	I=2 II=8 III=1*	352.57
Solid Ca with metastasis	5	I=0 II=2 III=3	182.5
Anaplastic Ca with metastasis	1	I= 0 II=1 III=0	
Carcinosarcoma	0		
Sarcoma without metastasis			458
Sarcoma with metastasis	1	NA	100

NA: Not applicable. * refers to graded tumors.

On the other hand, overall survival of ductal carcinomas (solid and tubular) and micro-papillary carcinoma patients was not significantly different ($p = 0.5778$) (Figure 2). The overall survival of patients diagnosed with mixed tumor and simple carcinomas (papillary, tubular, solid and anaplastic) ($p = 0.2727$) was also not significantly different, as shown in Figure 3. About tumor grade, overall survival time was significantly different for different histopathologic grades ($p = 0.0022$). This correlation between tumor grade and survival time has been observed in other studies, which state that overall survival (in days) decreases with an increase of tumor grade of malignancy (12) (Figure 4).

Regarding treatment, 136 patients underwent surgical treatment only, of which 18 underwent associated anti-neoplastic chemotherapy (Table 2). Among animals

treated with chemotherapy, tumor recurrence (local) was observed in 22.22% (4/18 cases) while distant metastasis was observed in 22.22% (4/18 cases). The combination of adjuvant chemotherapy and/or administering COX-2 inhibitor did not influence survival when compared with surgical resection only (Figure 5). Surgical treatment with complete removal of the non-metastatic neoplasia is considered the procedure with the best chance of cure (2, 4) while the efficacy of the surgery combined with adjuvant chemotherapy is still not known (14). However, the use of selective COX-2 inhibitors has been associated with increased survival and improved clinical status of dogs with inflammatory carcinomas (18). Furthermore, increased expression of the COX-2 is related to increased malignancy of mammary carcinomas in female dogs (11, 13).

Table 2. Clinical data of bitches diagnosed with mammary tumors with and without metastasis regarding treatments as: mastectomy, ovariectomy (OH), chemotherapy (CTP) and COX-2 inhibitor (Previcox).

Histological type	N	Surgery	OH therapeutic	CTP	Inhibitor of COX-2
Non-metastatic carcinoma	115	115	81	9	7
Metastatic carcinoma	21	21	15	9	6

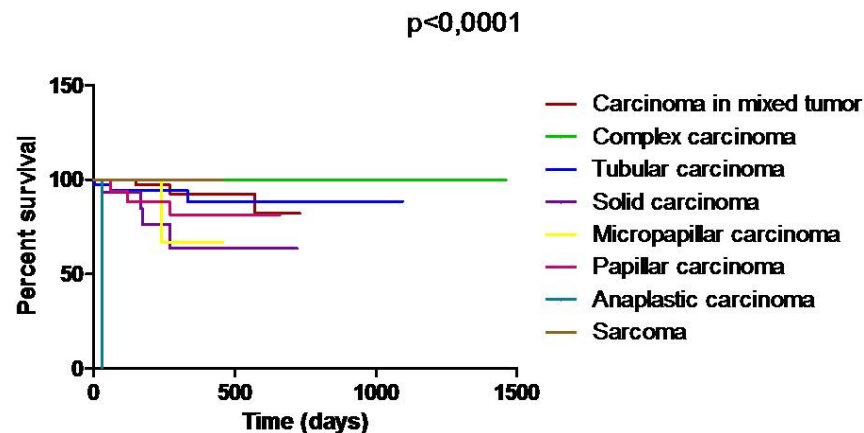


Figure 1. Comparison of overall survival for the different histological types of 119 patients.

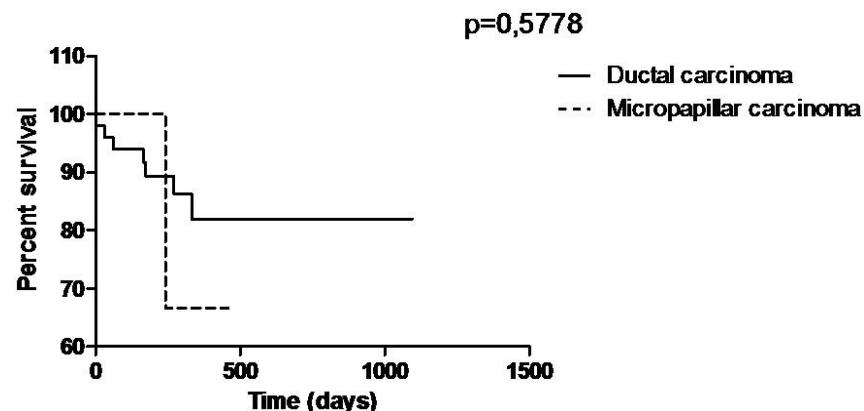


Figure 2. Comparison of overall survival time between invasive micro-papillary and ductal carcinoma (solid and tubular carcinoma).

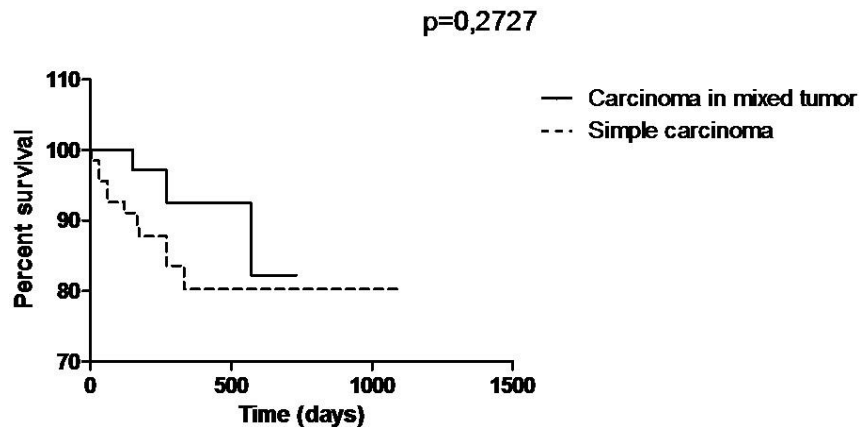


Figure 3. Comparison of overall survival between carcinoma in mixed tumor and simple carcinomas (papillary, ductal, solid and anaplastic).

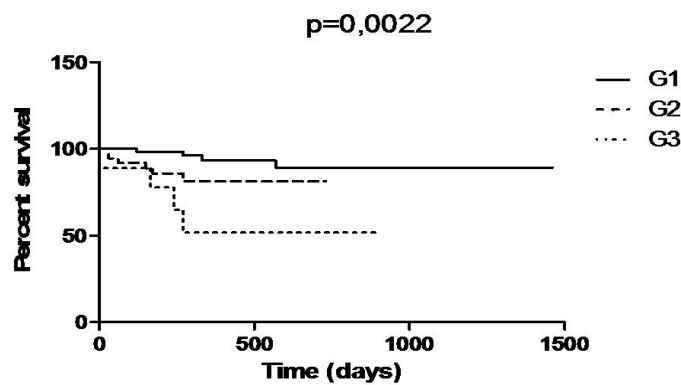


Figure 4. Comparison of overall survival for the different grades of tumor malignancy.

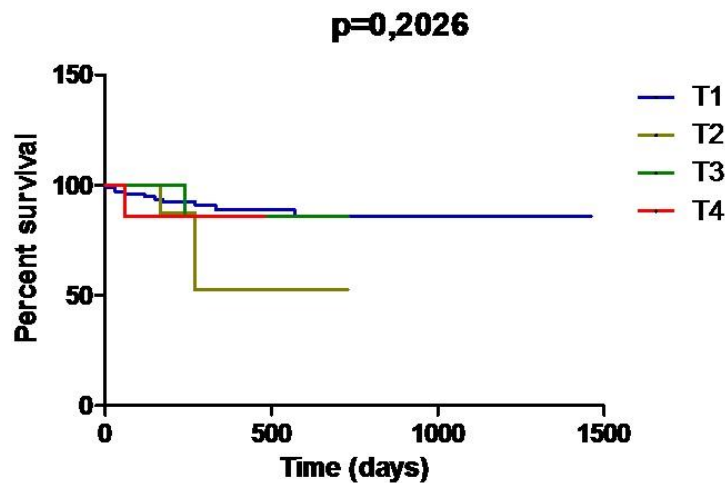


Figure 5. Percent survival of bitches according to the therapy. Patients treated only surgically (T1), 96 cases; surgery associated with chemotherapy (T2), 9 cases; surgery associated with previcox (T3), 7 cases; and, surgery associated with adjuvant chemotherapy and previcox (T4), 7 cases.

Conclusion

During the period 2011-2013, we tried to implement the guidelines proposed by the I Consensus for the Diagnosis, Prognosis and Treatment of Canine Mammary Tumors, especially regarding their classification and histopathological grade. However, was not easy to

choose and standardize the protocol of the antineoplastic chemotherapy as well as the surgical procedure, since unilateral mastectomy is the procedure established in this institution. Despite the fact that the clinical follow-up was performed in most patients, it is still difficult to get the owners to treat and continue with the follow-up of the animals.

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