Braz J Vet Pathol, 2021, 14(1), 24 – 28
DOI: 10.24070/bjvp.1983-0246.v14i1p24-28

BJVP
Brazilian Journal of Veterinary Pathology
ISSN 1983-0246

Original Full Article

Veterinary approaches to canine mammary tumors and knowledge of the consensus statement in Brazil

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Submitted January, 27th 2020, Accepted November, 04th 2020

Abstract

Mammary gland tumors are one of the most commonly diagnosed tumors in female dogs, with a reported prevalence ranging from 26 to 73% in Brazil. In recognition of the importance of these tumors veterinary researchers and clinicians in Brazil produced the first consensus statement regarding canine mammary tumors in 2010. The intention was to establish criteria for diagnosis, prognosis, and treatment. This study evaluated the methods of prevention, diagnosis, treatment, and determination of prognosis used by veterinarians in Brazil, and sought to quantify the number of veterinarians who were aware of the consensus statement. One hundred and three veterinary clinics participated in the study, 87.37% of which recommend early neutering as a preventative treatment for mammary tumors. For diagnosis, 100% of these use laboratory testing, 94.17% perform chest radiography, 78.64% incisional biopsies, 44.66% cytological analysis, and 13.59% immunohistochemical analysis. The most common surgical procedure is unilateral mastectomy (72.81%), and chemotherapy is performed in 49.51% of the clinics. Of the 103 clinics, 66.01% were aware of the consensus. Although knowledge of the consensus statement is widespread among veterinarians in Brazil, not all its recommendations are being followed. Preventive actions for canine mammary tumors are well established in most parts of the country. However, the consensus statement has had little influence on informing prognostic and therapeutic approaches, with a poor uptake of surgical removal of lymph nodes and immunohistochemical examination.

Key words: Veterinary conduct, prevention, diagnosis, treatment, prognosis

Introduction

Neoplasia has become an increasingly important disease in animals over recent years (15). A higher prevalence of neoplasms in domestic animals is correlated with greater longevity and growing populations. The longer an animal lives, the more it is exposed to carcinogenic agents (9).

Mammary gland tumors are the most commonly diagnosed neoplasms in female dogs (22). These account for about 50% of all tumors (32). In Brazil, the prevalence of these tumors ranges from 26 to 73% (3, 2, 17, 19, 20), and approximately 85% are malignant (18). This incidence is three times higher than that reported in women worldwide (4). According to the National Cancer Institute, the number of breast cancer deaths in women in 2018 was 17,572 (16). It is estimated that in Brazil between 2020 and 2022 there will be 66,280 new cases annually, which corresponds to an estimated risk of 61.61 cases per 100,000 women (11).

The Brazilian Ministry of Health together with the National Cancer Institute (INCA), the Technical Area for Women's Health, and the Brazilian Society of Mastology issued in 2004 the "Breast cancer control consensus document" for human medicine. This defined criteria for clinical staging and evaluation of prognostic factors for breast cancer (5). Following the example of human medicine, a consensus statement to guide veterinarians regarding clinical staging, prognostic assessment and therapeutics for female dogs with this kind of tumor was created in Brazil.

In 2010, veterinary researchers and clinicians released the first consensus statement regarding canine

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Braz J Vet Pathol, 2021, 14(1), 24 – 28
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mammary tumors, to establish criteria for diagnosis, prognosis, and treatments for female dogs with mammary tumors. In 2013, the consensus was reviewed with discussions on how it had been applied over the preceding three years, what difficulties had been encountered in application, the results obtained, and which of the criteria could be improved and standardized. The researchers concluded that diagnostic criteria need to be improved and standardized. Furthermore, it was agreed that investment in studies that focused on prognostic markers for routine use by veterinary clinicians, surgeons, and pathologists was needed to guide appropriate treatments (8).

Given the above, this study aimed to determine approaches for prevention, diagnosis, treatment and prognosis used by veterinarians, and to evaluate the knowledge and application of the existing consensus statement in these approaches.

Materials and Methods

A questionnaire with closed multiple-choice questions relating to the approach used for the diagnosis, prognosis and treatment of female dogs affected by mammary cancer was sent to the veterinary centers (private clinics, teaching hospitals, and private hospitals). The questions included the mean number of consultations performed and numbers of presentations of female dogs with mammary tumors, as well the pre-surgical and diagnostic tests (biopsy and cytology), surgical procedures performed, use of chemotherapy and whether practices knew about consensus statement.

According to the Federal Council of Veterinary Medicine, in July 2017, when the study began, 341 veterinary hospitals and 17,287 veterinary clinics were registered. The website of the Ministry of Education reported 299 schools offered the veterinary medicine course. The sample size required was estimated at 5%, with a 95% confidence interval and a 5% statistical error (29), equivalent to 376 centers. The questionnaire was sent to 376 centers, however, only 103, from 21 Brazilian states, collaborated with the study. Four were private hospitals, four veterinary university hospitals, and 95 veterinary private clinics. Of these 40.77% were located in the Southern region of the country, 26.21% in the Southeast, 16.50% in the Northeast, 9.70% in the North, 5.82% in the Midwest, and 1% in the Federal District. As not all clinics completed a questionnaire the sample size for statistical significance was not met and there was no statistical analysis of the data.

This study was approved by the Ethics Committee for Research on Human Beings of the Federal Institute of Santa Catarina, under the report number 2.413.993.

Results

A total 10,750 animals were examined in the 103 sites, of which 650 (6.04%) were female dogs with mammary tumors. Prevention through early neutering was practiced by 87.37% of clinics (90/103), palpation of the mammary gland was performed in 96.11% (99/103), and clinical staging was done in 72.81% (75/103).

Among the evaluations performed, 100% (103/103) of the veterinarians requested laboratory tests, 94.17% (97/103) performed thoracic radiography, 78.64% (81/103) performed incisional biopsies on tumors for histopathological analysis, 44.66% (46/103) performed tumor cytological analysis, and 13.59% performed tumor immunohistochemical analysis. Moreover, 68.93% (71/103) of the clinics also performed preoperative cardiological evaluations in female dogs.

Tumor size was evaluated by 89.32% (92/103) of the clinicians; 81.55% of them (84/103) evaluated the number of mammary glands affected, 76.69% (79/103) evaluated the location of the mammary gland affected, and 56.31% (58/103) evaluated the possibility of lymphatic metastasis.

The most common surgical procedure performed at these veterinary centers was unilateral mastectomy, in 72.81% of the clinics (75/103), followed by block mastectomy in 12.62% of them (13/103), bilateral mastectomy in 8.73% (9/103), nodulectomy in 4.85% (5/103), and lumpectomy in 0.97% (1/103). Chemotherapy together with a surgical procedure was performed in 49.51% (51/103) by the clinics with some centers performing this on site and others referring the cases for treatment. The histologic tumor types most commonly requiring chemotherapy were carcinomas and sarcomas. The most commonly used chemotherapy drugs in the centers were doxorubicin, cyclophosphamide, carboplatin, vincristine, vinorelbine, and gemcitabine, based on the results of the histopathological exam.

Regarding the consensus statement on canine mammary gland tumors, 66.01% (68/103) of the veterinary clinics were aware of it, and of these, 88.23% (60/68) were applying its approaches within their routine practice.

Discussion

As previously mentioned, the prevalence of canine mammary tumors in Brazil has been found to range from 26 to 73% (3, 2, 17, 19, 20). However, there are few investigations of these tumors in general veterinary practice, with most studies being retrospective reports from academic institutions, such as universities. In the present study the total sample size was 6.04% of all veterinary clinics, which was insufficient to represent the situation in Brazil. During the study period, we tried to acquire information in a representative manner, but there were difficulties in obtaining responses from all the clinics that were approached.

Sorenmo, Worley and Goldschmidt, 2013 (27) reported that neutering performed before the first estrus prevented the occurrence of mammary tumors. Moreover, when performed before the first estrus, the risk of

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subsequently developing mammary cancer was only 0.5%, whereas this increased to 8% and 26% before the second and third estrus, respectively (24). However, in a study by Carvalho, 2018 (6) in Teresina, Piauí, Brazil, 71.87% of the owners who were interviewed did not know about the preventive role played by neutering on mammary tumors. Epidemiological studies conducted in Brazil have shown that high proportions of female dogs were entire at the time of diagnosis: 83.33% in Jaboticabal-SP, 87.50% in Salvador-BA, 85.88% in Santos-SP, and 94.0% in Realeza-PR (12, 30, 3, 28).

Clinical staging can be used to evaluate the animal's general state of health, to determine the extent of the tumor, to plan treatment, and to obtain prognostic information. For this, it is necessary to perform hemogram, a biochemical profile, to measure the tumor size, to perform histopathological classification, to evaluate regional lymph nodes, and to perform thoracic radiography and ultrasonography examinations (26). All the clinics interviewed perform hemograms and biochemical profiles. Another study, performed in Viçosa-MG, reported that abnormalities were present in 27 of the 44 animals evaluated: 5 had benign lesions and 22 had malignant lesions. The abnormalities comprised anemia (22.72%), increased alkaline phosphatase (20.45%), eosinophilic leukocytosis (15.91%), and hyperproteinemia (15.91%) (31).

In the clinics interviewed, 94.17% performed radiography on their patients but no detail on positioning was provided. Although most of these clinics were performing radiographic examinations, it was clear that this was not being done in a small proportion of the population. We did not ask the reasons why radiography was not performed, but it is likely that the cost of the examination was a reason for not pursing this option or the owners may have simply declined the procedure. According to the consensus, three-view thoracic radiography should be performed (ventrodorsal and right and left lateral) to assess for the presence of pulmonary metastasis (8). This can detect metastatic foci of 6 to 8 mm in diameter (26). Investigation of distant metastases is also important since the detection of pulmonary metastases is associated with an unfavorable prognosis (26).

Feliciano et al., 2012 (12) found no radiographic changes in the animals evaluated in their study conducted in Jaboticabal-SP. Toribio et al., 2012 (30) identified pulmonary metastases in 15.2% of the animals evaluated in Salvador-BA, and Valadares, 2017 (31) had a similar result in Viçosa-MG, in which 13.95% of the animals had metastases at time of diagnosis. These studies show the relevance of thoracic radiography, since if metastases are already visible at diagnosis the animal's prognosis is unfavorable. In these cases chemotherapy becomes the mainstay of treatment due to the risk of acceleration of the growth of metastatic foci after tumor excision. So for a small proportion of animals the lack of staging may result in inappropriate treatment and prognostic information.

The collection of samples for histopathological examination was performed by 78.64% of the clinics. However, in some cases the owner's financial limitations were an obstacle to this and in others the absence of a laboratory in the region meant histopathological examination was not possible. Histopathological examination allows clinicians to define prognosis and determine the need for combination chemotherapy, producing better treatment results. Failure to perform histopathological examination may influence survival time due to relapses and development of distant metastases. The clinician, therefore, needs to emphasize the importance of this examination to owners. Moreover, a lack of histological information slows our understanding of the types of tumor common in Brazil such as: how many and which tumors were benign or malignant, which tumors occurred most frequently and what their histological nature. This information is required to characterize the most prevalent mammary tumors more accurately.

In addition to taking into consideration financial limitations and limitations relating to the availability of facilities for examinations to be performed, veterinarians may be basing their approaches on the premise that most tumors can be treated surgically because they are benign or low grade. Although in many places the histopathological analyses performed do not follow the criteria established in the consensus statement, surgery has curative potential. This was reported by Sorenmo, 2003 (26), who stated that if an excisional biopsy were to be performed, this would be therapeutic for dogs with benign tumors and those with small and well-differentiated malignant tumors.

Cytological evaluation is recommended in the consensus statement but only 44.66% of clinics perform this. Cytology is important for making the initial diagnosis and for ruling out differential diagnoses (8), such as pseudocyesis, lactation, mastitis, and tumors of origins other than mammary tissue (33). It is also a safe method for identifying lymph node metastases (14). The advantage of this technique is that it is simple to perform, safe, non-invasive, and inexpensive. However, sample collection and interpretation may be challenging in some cases (23). Other difficulties relate to the heterogeneity of mammary tissue, in which cell morphology varies between different areas of the tumor (25), and to the presence of necrosis and inflammation (1). Although a simple non-invasive procedure, this technique was not frequently performed in the clinics.

Hormone exposure plays an important role in tumor development, and this is investigated through immunohistochemical analysis (27). This analysis also provides a more accurate prognosis (7). According to Ferreira et al., 2003 (13), immunohistochemical techniques are not routinely used in veterinary medicine because of their high cost. In this regard, the present study is in agreement with data in the literature, since only 13.59%. of the clinics used these techniques. Despite having prognostic and therapeutic value and being predictive for target therapies, a

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large number of animals in the country are not receiving the benefits of this technique.

The consensus statement recommends that surgeons should be familiar with lymphatic drainage since this system is considered the main route for metastasis from malignant mammary tumors (8). In the present study, only 56.31% of the clinics consider the lymphatic system in their surgical approach, and this is a risk in relation to prognosis, given the possibility of metastasis. Veterinarians should search for information and acquire qualifications relating to surgical approaches to lymph node excision.

As already described, most mammary tumors are malignant (3, 30, 10). However, in the present study, it was not possible to estimate which kinds of tumors were more frequently found in the mammary chain. Out of the 103 clinics surveyed, 96 performed more complex surgical procedures (unilateral, bilateral, and en bloc excision), which suggests that the tumors that affect female dogs are highly malignant. These procedures include the removal of tumors of larger diameter, which may or may not affect more than one gland, along with the lymphatic system. Another possibility is that surgeons choose treatments that are more aggressive to minimize the chance of recurrence. However, in many patients aggressive surgery may bring no benefit, given that many tumors do not require aggressive treatment. As proposed by the consensus statement, treatment should be matched to the animal's need.

Knowledge of the consensus statement is relatively widespread among veterinarians, since 66.01% of those interviewed were aware of it. However, a small proportion of the clinics were not following the proposed recommendations, despite being familiar with the consensus. We believe that this was related to difficulty in applying some of the approaches recommended by the consensus statement. These included the patchy distribution of laboratories to which diagnostic material could be sent, along with the owner's financial limitations. Another factor that may have influenced this result was the veterinarians' own preferences for personal approaches. To help update the consensus statement, the authors also surveyed veterinary clinics to understand how the consensus recommendations were being applied and what difficulties were encountered, but these data were not published.

Although the incidence of breast tumors in women has increased in developed countries, the mortality caused by these tumors has been decreasing. This is due to improved screening and treatment of these cases. In Brazil, incidence and mortality are increasing because of barriers to early detection and difficulty in using diagnostic resources and appropriate treatments (21). An estimate of the number of new cases of breast tumors in women is now published every year in Brazil, along with data on the mortality from these tumors. In contrast to our knowledge of breast cancer in women, there is a lack of information on this disease in dogs. Thus, it has been suggested that a reporting system with an annually published database should be created. This would also be available to the public to enable the analysis of the situation, planning of preventive actions in this area, and better awareness among owners, thereby ensuring early diagnosis and treatment. Through this database, it would be possible to verify whether the use of the consensus has any direct effect to decrease the mortality of animals affected by tumors.

Conclusion

Although knowledge of the consensus statement is widespread among veterinarians in Brazil, not all its recommendations are being followed. Many veterinary patients do not have access to immunohistochemistry, nor do they benefit from the removal of lymph nodes during surgery. This may be due to the lack of knowledge on the part of the professional, or to financial restrictions and/or lack of interest on the part of the owners. However, preventative measures (early neutering) are well established, which may possibly contribute to a decrease in the prevalence of canine mammary tumors in Brazil in the future.

References

1. Allen SW, Prasse KW, Mahaffey EA. Cytologic Differentiation of Benign from Malignant Canine Mammary Tumors. Vet Pathol. 1986; 23 (6): 649-655.
2. Andrade FHE, Figueiroa FC, Bersano PRO, Bissacot DZ, Rocha NS. Malignant mammary tumor in female dogs: environmental contaminants. Diag Pat. 2010; 5 (45): 1-5.
3. Biondi LR, Gentile LB, Rego AAMS, Noronha NP, Dagli MLZ. Canine mammary tumors in Santos, Brazil: clinicopathological and survival profile. Braz J Vet Res Anim Sci. 2014; 51 (3): 252-262.
4. Caicedo JA, Iregui CA, Cabarcas ME, Acosta BJ. Estudio comparativo de la frecuencia de tumores mamarios según sexo, edad y tipo histológico en caninos y humanos en los laboratorios de patología anatómica de la Universidad Nacional de Colombia sede Bogotá. Rev Colomb Cienc Ani. 2012; 5 (1): 7-46.
5. Câncer de Mama- Documento de Consenso [Internet]. Ministério da Saúde; 2004 April [updated 2018 June 20; cited 2020 Jan 24]. Available from: http://bvsms.saude.gov.br/bvs/publicacoes/Consensointegra.pdf.
6. Carvalho CJS. Tumor de mama em cadelas: Epidemiologia, características clínicas e morfológicas [dissertation]. [Teresina]: Universidade Federal do Piauí; 2016. 56 p.
7. Cassali G.D. Estudo morfológico, imunoistoquímico e citométrico de tumores mamários da cadela - Aspectos comparativos com neoplasias da mama humana [dissertation]. [Belo Horizonte]: Escola de Veterinária, Universidade Federal de Minas Gerais; 2000. 65 p.
8. Cassali GD, Lavalle GE, Ferreira E, et al. Consensus

for the Diagnosis, Prognosis and Treatment of Canine Mammary Tumors - 2013. Braz J Vet Pathol. 2014; 7 (2): 38–69.
9. Daleck CR, Calazans SG, De Nardi AB. Linfomas. In: Dalek CR, De Naedi AB, Rodaski S. Oncologia em Cães e Gatos. São Paulo: ROCA, 2009. p. 481-506.
10. Dias MLM, Andrade JML, Castro MB, et al. Survival analysis of female dogs with mammary tumors after mastectomy: epidemiological, clinical and morphological aspects. Pesq Vet Bras. 2016; 36 (3): 181-186.
11. Estimativa 2020- Incidência de Câncer no Brasil [Internet]. Ministério da Saúde; 2019 [updated 2020 October 06; cited 2020 October 18]. Availabre from: https://www.inca.gov.br/publicacoes/livros/estimativa-2020-incidencia-de-cancer-no-brasil.
12. Feliciano MAR, Silva AS, Peixoto RVR, Galera PD, Vivente WRR. Estudo clínico, histopatológico e imunoistoquímico de neoplasias mamárias em cadelas. Arq Bras Med Vet Zootec. 2012; 64 (5): 1094-1100.
13. Ferreira E, Bregunci GC, Schmitt FC, et al. Protocol for the anatomopathological examination of canine mammary tumors. Arq Bras Med Vet Zootec. 2003; 55 (1): 105-109.
14. Langenbach A, McManus PM, Hendrick MJ, et al. Sensitivity and specificity of methods of assessing the regional lymph nodes for evidence of metastasis in dogs and cats with solid tumors. J Am Vet Med Assoc. 2001; 218 (9): 1424-1428.
15. Maiti KS, Kumar DKM, Kumar S, et al. Mammary gland tumours in male dogs: a hormonal and tumour marker study. Vet arhiv. 2014; 84 (5): 537-548.
16. Mortalidade proporcional não ajustada por câncer de MAMA, mulheres, Brasil, no ano de 2018 [Internet]. Instituto Nacional de Câncer- Ministério da Saúde; 2018 [updated 2019 Oct 6; cited 2020 Oct 6]. Available from: https://mortalidade.inca.gov.br/MortalidadeWeb/pages/Modelo01/consultar.xhtml
17. Munson L, Moresco A. Comparative pathology of mammary gland cancers in domestic and wild animals. Breast Dis. 2007; 28: 7-21.
18. Nunes FC, Campos CB, Teixeira SV, et al. Epidemiological, clinical and pathological evaluation of overall survival in canines with mammary neoplasms. Arq Bras Med Vet Zootec. 2018; 70 (6): 1714-1722.
19. Oliveira Filho JC, Kommers GD, Masuda EK, et al. Estudo retrospectivo de 1.647 tumores mamários em cães. Pesq Vet Bras. 2010; 30 (2): 177-185.
20. Pérez-Alenza MD, Peña L, Del Castillo N, Nieto AL. Factors influencing the incidence and prognosis of canine mammary tumours. J Small Anim Pract. 2000; 41 (7): 287-291.
21. Pinheiro AB, Lauter DS, Medeiros GC, et al. Câncer de mama em mulheres jovens: análise de 12.689 Casos. Rev Bras Cancerol. 2013; 59 (3): 351-9.
22. Saba CF, KS Rogers, SJ Newman, Mauldin GE, Vail DM. Mammary gland tumors in male dogs. J Vet Intern Med. 2007; 21 (5): 1056-1059.
23. Santana AE, Siki MC, Gama FGV, et al. Citologia aspirativa com agulha fina aplicada ao estudo das neoplasias. In: Daleck CR, De Nardi AB, Rodaski S. Oncologia em Cães e Gatos. São Paulo: ROCA, 2009. p. 76-91.
24. Schneider R, Dorn CR, Taylor DON. Factors Influencing Canine Mammary Cancer Development and Postsurgical Survival. J Natl Cancer Inst. 1969; 43 (6): 1249–1261.
25. Simon D, Schoenrock D, Nolte I, et al. Cytologic examination of fine-needle aspirates from mammary gland tumors in the dog: diagnostic accuracy with comparison to histopathology and association with postoperative outcome. Vet Clin Pathol. 2009; 38 (4): 521-528.
26. Sorenmo K. Canine mammary gland tumors. Vet Clin Small Anim. 2003; 33 (3): 573–596.
27. Sorenmo KU, Worley DR, Goldschmidt MH. Tumors of the Mammary Gland. In: Withrow SJ, Vail DM, Page RL. Small Animal Clinical Oncology. 5th ed. St. Louis: Saunders Elsevier, 2013. p. 538-556.
28. Staziaki A. Avaliação dos aspectos patológicos, clínicos e epidemiológicos dos neoplasmas de glândula mamária, diagnosticados em cães e gatos no município de Realeza – PR [dissertation]. [Realeza]: Universidade Federal da Fronteira Sul; 2015. 40 p.
29. Thrusfield M. Epidemiologia veterinária. 2nd ed. São Paulo: ROCA; 2004. 556p.
30. Toribio JMML, Lima AE, Filho EFM, et al. Caracterização clínica, diagnóstico histopatológico e distribuição geográfica das neoplasias mamárias em cadelas de Salvador, Bahia. Rev Ceres. 2012; 59 (4): 427-433.
31. Valadares FD. O processo diagnóstico na abordagem das cadelas com tumor de mama atendidas no hospital veterinário da UFV: palpação linfonodal x pesquisa do linfonodo sentinela [dissertation]. [Viçosa]: Universidade Federal de Viçosa; 2017. 65 p.
32. Zatloukal J, Lorenzova J, Tichy F, Necas A, Kecová H, Kohout P. Breed and age as risk factors for canine mammary tumours. Acta Vet Brno. 2005; 74: 103-109.
33. Zuccari DAPC, Santana AE, Rocha NS. Correlação entre a citologia aspirativa por agulha fina e a histologia no diagnóstico de tumores mamários de cadelas. Braz J Vet Res Anim Sci. 2001; 38 (1): 38-41. omparative pathology of mammary gland cancers in domestic and wild animals. Breast Dis. 2007; 28: 7-21.