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Original Scientific Article

CLINICOPATHOLOGICAL SURVEY OF 56 CANINE MALIGNANT MAMMARY TUMOURS IN SLOVENIA - PROGNOSTIC VALUE OF CLINICAL STAGE AND HISTOLOGICAL GRADE

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Summary: Mammary gland tumours are the most frequent class of neoplasm seen in female dogs; some breeds are reported to be at increased risk. This retrospective study describes the clinical and histopathological findings in 56 female dogs with mammary carcinomas that underwent surgery at the Clinic for Small Animal Medicine and Surgery of the Veterinary Faculty University in Ljubljana. Data relating to age, breed, spaying and history of pseudopregnancy were collected and survival analyses performed. The prognostic value of clinical stage and histological grade, based on 2 year survival after surgical removal of the tumour, was evaluated. Mammary carcinomas most often developed in dogs at 10 years or older (64.3 %), most falling into the 10 and 11 age group. Occurrence was the highest in Saluki (5.56 per 100 dogs), Miniature Schnauzer (0.44 per 100 dogs) and Medium Poodle (0.41 per 100 dogs) breeds. Survival times differed significantly for dogs with simple and complex tumours ($P<0.05$). Significant differences in survival were revealed between groups of dogs with different histological grades ($P<0.05$). Kaplan–Meier survival curves for dogs classified by clinical stage differed between dogs with stages I and IV and also II and IV ($P<0.05$). All dogs in subgroups with clinical stage I or II and histological grade I survived a 2-year follow up period (2-YFUP) after surgical removal of the tumours. In contrast, the average survival of dogs with clinical stage IV and histological grade III was less than 200 days. Our results reveal the high prognostic value of the combination of clinical stage and histological grade, based on survival of bitches after surgical removal of mammary gland tumour.

Key words: canine mammary gland tumour; clinical stage; histopathological diagnosis; histological grade; prognostic value

Introduction

Mammary gland tumours (MGTs) are the most frequent class of neoplasm seen in dogs (1, 2, 3). Early ovariectomy is a key element in decreasing the risk for MGTs (3). Genetic influence is apparent as the incidence of MGTs differs between breeds (4), although depending on the study, contradicting results can be found (3).

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The average age at diagnosis is between 10 and 11 years (5). Older dogs with MGTs have poorer prognosis, probably due to the fact that malignancy increases with age (6, 7, 8, 9, 10). However, age is not necessarily regarded as a prognostic factor (3, 8), given that older dogs are more likely to die from other causes. Dogs with tumours that ulcerate overlying skin and dogs with rapid and invasive growth of tumours also have shorter survival times (5, 6, 7, 11).

Surgical excision is the treatment of choice for most types of local MGTs (3, 12). The extent

of surgery is usually determined by the surgeon, the decision being based on whether treatment is seen as curative or palliative, taking into account the owner's consent. Many factors have been examined for their possible influence on the post-treatment survival of dogs and for their ability to predict recurrence and/or metastasis. Tumour size is considered one of the most important determinants of clinical staging in cancer (13). Additionally, vascular or lymphatic invasion and lymph node metastases have been associated with decreased survival and increased risk of tumour recurrence (3). Based on the clinical data of tumour size (T designation), presence of lymph node metastases (N category) and of distant metastases (M category), MGTs can be clinically staged according to the original World Health Organization's (WHO) TNM system (14) or the modified version (15). The TNM system is a prognostic factor for breast cancer in women that could also be used for canine MGTs (11, 13).

Histopathological examination shows that hyperplastic tissue, benign and malignant tumours can be present throughout the mammary glands of dogs in a variety of histologically defined forms, and with combinations of histogenetically different cells inside a single tumour (16, 17, 18). Tumours are classified as complex when they are composed of epithelial and myoepithelial cells, and simple when only one of these cell types is present (16). Inconsistencies between histopathological features and biological behavior or prognosis (19) have been documented, since approximately 10 % of the MGTs in the dog can be histologically misdiagnosed as benign (16). Due to these discrepancies, histological grade should be used for MGTs, as it could be helpful for classification and prognosis (20, 10). In human medicine, for the characterization of breast cancer, the grading system according to Elston and Ellis (20) is the most widely used (21). This method has also been applied for the grading of canine mammary carcinomas (22, 23, 24), and Karayannopoulou et al. (8) found it predictive for prognosis. In the prospective study of Pena et al. (10) the canine-adapted version of this method was evaluated and the authors identified it as significantly and independently associated with clinical outcome.

The aim of our study, therefore, was to evaluate the clinical and pathological characteristics of 56 mammary carcinomas with respect to the breed, age, spaying and history of pseudopregnancy, clinical stage, histopathological diagnosis and histological grade. Factors potentially associated with 2 year survival following surgical removal of the tumour were also evaluated.

Material and methods

Dogs and data collection

For this retrospective study fifty-six tissue samples were obtained from fifty-six bitches with malignant primary tumours that underwent surgery at Clinic for Small Animal Medicine and Surgery of the Veterinary Faculty University in Ljubljana (CSAMS VF, UL) between 2003 and 2009. In the case of the presence of multiple tumours, data were recorded but only the most malignant tumour, according to histopathological estimation, was included in the study. Data about age, breed, spaying and history of pseudopregnancy, surgical procedures and survival were collected from the medical records of the bitches, written questionnaires and interviews with owners. Clinical staging according to the TNM system was made at the time of surgeries. For every bitch a radiograph of the thorax was obtained before surgery. Routine 3-view (2 laterolateral projections and a dorsoventral projection) thoracic radiographs were taken. Re-check on 3 months, 6 months and then once a year was recommended. In the case of regional lymph node involvement, re-check was recommended 1 month after surgery. Follow-up data were collected over a 2 year follow-up period (2-YFUP) and expressed as survival time (the time between surgery and death due to the tumour or death from other causes or euthanasia). In the case of the recurrence of the disease the disease free time was recorded.

Histopathological and clinical evaluation

Histological type. Tissue samples were fixed in 10 % buffered formalin immediately after surgery and processed routinely. Histopathological diagnoses were based on haematoxylin and eosin-stained sections according to the WHO criteria (16).

Histological grading. Histological grading was evaluated in accordance with Elston and Ellis (20). Criteria of tubule formation, nuclear pleomorphism and mitotic counts were scored on scales from 1 to 3. The scores for each category

were added together and the total score converted to give the histological grade: 3 - 5 points: grade I (well-differentiated carcinoma), 6 - 7 points: grade II (moderately-differentiated carcinoma) and 8 - 9 points: grade III (poorly differentiated carcinoma). Histological grades were determined by at least two histopathologists.

Clinical staging. Dogs without regional lymph node or distant metastases were categorized as stage I, II or III, depending on tumour diameter (3 cm; 3 to 5 cm; more than 5 cm respectively). Dogs with regional lymph node involvement were classified as stage IV and dogs with distant metastasis as stage V, regardless of the tumour size (15). Metastases in regional lymph nodes and the presence of tumour cells in the lymphatic vessels of the primary lesion were confirmed by histopathological analysis.

Statistical analysis

Given the small consistency of the groups of age and breed, these two parameters were not taken into account for the statistical evaluation.

Survival time was defined as the time from surgical removal of the tumour to the date of death or recurrence of the disease (two years follow up period). For dogs that died of causes unrelated to the MGTs or had recurrence of the disease, the date of death/recurrence was defined as the censored date for calculating survival time (13, 25). Survival curves were constructed using the Kaplan–Meier method and the differences in survival between groups assessed using the log rank test for the following potential prognostic factors: clinical stage, histological grade, spaying, multiple tumours present, history of pseudopregnancy, histological tumour type (simple/complex) and combinations of clinical stage/histological grade. Histopathological classification was not included in the preparation of the survival curves because of the small number of cases in individual subgroups. The only dog with clinical stage V was included in the group of dogs with clinical stage IV. Variables for which the difference between survival curves was significant or near statistical significance were included in a multivariate model. The Cox proportional hazard model was used for multivariate analysis on factors potentially associated with survival 2-YFUP (26). For a categorized variable, a hazard ratio (HR, also called ''relative risk'') shows the hazard of a category compared with the reference category. For a continuous variable, HR shows the hazard ratio of two individuals that differ by one unit for the variable in question. An HR greater than 1.0 corresponds to an increase in risk and an HR less than 1.0 to a decreased risk.

Values of $P<0.05$ were considered significant for all analyses; data were analysed using software IBM SPSS Statistics 17.0.

Results

Of the 56 bitches included in our study, 12 (21.4 %) were spayed and 9 (16.1 %) had histories of pseudopregnancy. All the ovariectomies were made late in life. Multiple tumours developed in 18 dogs (32.1 %). 36 dogs (64.3 %) were 10 years or more, with most falling into the group of age 10 or 11.

The most frequently presented breed with MGT was English Cocker Spaniel (19.6 % from all dogs with MGTs), followed by mixed breeds (16.1 %) and Medium Poodle (7.1 %). Comparing the number of the dogs of an individual breed with the number of that breed in Slovenia (according to data from the Veterinary Administration of Slovenia, December, 2011), mammary carcinomas developed most frequently in Saluki (2/36 dogs; 5.56 %), followed by Miniature Schnauzer (3/459; 0.44 %) and Medium Poodle (4/976; 0.41 %) (*Table 1*). The prevalence of MGTs regarding the breed were not taken into account for the statistical evaluation given the small consistency of the groups.

Histopathological diagnosis included 4 carcinomas in situ, 29 simple type carcinomas (17 tubulopapillary carcinomas, 10 solid carcinomas and 2 anaplastic carcinomas), 19 complex type carcinomas and 1 case of malignant mixed tumour, mucinus carcinoma, squamous cell carcinoma and malignant myoepithelioma. From the 50 carcinomas 22 (44 %) were grade I, 13 (26 %) were grade II and 15 (30 %) were grade III.

Regarding clinical stage, 23 (41.1 %) dogs were stage I, 11 (19.6 %) stage II, 7 (12.5 %) stage III, 14 (25 %) stage IV and 1 (1.8 %) was stage V.

Of the 56 dogs, 29 (51.8 %) were still alive 2 years after surgical removal of MGTs, 14 (25 %) died within this period, in 7 dogs (12.5 %) recurrence of the disease was recorded, and 6 (10.7%) dogs died of causes unrelated to MGTs.

Table 1: Number and proportion of dogs with mammary gland tumours in separate breeds presented to Clinic for Small Animal Medicine and Surgery of the Veterinary Faculty University in Ljubljana between 2003 and 2009 and included in our study

BREED	n° DOGS WITH TUMOURS	n° DOGS IN SLOVENIA*	THE PROPORTION OF PRESENTED DOGS WITH MGTs**
Saluki	2	36	5.56
Miniature Schnauzer	2	459	0.44
Medium Poodle	4	976	0.41
English Cocker Spaniel	11	3157	0.35
Doberman Pinscher	2	746	0.27
Samoyed	2	1513	0.13
Pekingese	3	3030	0.10
Maltese	2	5231	0.04
Golden Retriever	2	9093	0.02
German Sheperd Dog	3	22589	0.01
Mixed	9	92934	0.01

*According to data from the Veterinary Administration of Slovenia (December, 2011).
** (n° of dogs in our study of the given breed with MGT/n° of dogs of this breed in Slovenia) x100.

Table 2: Kaplan–Meier survival for variables possibly associated with survival 2 years after surgical removal of mammary gland tumours

Variable	Categories	n of dogs (%)	Survival time (days) (mean ± SE)	P Value
Clinical stage	I II III IV/V	23 (41.1) 11 (19.6) 7 (12.5) 15 (26.8)	700.0 ± 30.1 730.0 ± 0.0 553.0 ± 123.5 303.1 ± 76.9	<0.05
Histological grade	I II III	22 (44.0) 13 (26.0) 15 (30.0)	730 ± 0.0 602.0 ± 70.8 332.5 ± 82.0	<0.05
Ovariectomy	Yes No	12 (21.4) 44 (78.6)	594.5 ± 73.5 576.9 ± 41.9	0.930
Multiple tumours	Yes No	21 (37.5) 35 (62.5)	560.3 ± 63.0 592.1 ± 44.7	0.707
Pseudopregnancy	Yes No	9 (16.1) 47 (83.9)	576.7 ± 103.3 580.5 ± 39.0	0.813
Histological type	Simple Complex	29 (60.4) 19 (39.6)	507.9 ± 56.4 704.4 ± 25.9	<0.05

Table 3: Results of multivariate analysis of variables associated with survival 2 years after surgery in dogs that had undergone surgical removal of mammary gland tumours

Variable	Categories	Relative Hazard	95% Confidence Limits for HR	P Value
Clinical stage	I II III IV/V	0.179 0.237 0.353 Reference	0.071 – 0.448 0.082 – 0.683 0.101 – 1.235	<0.001 0.008 0.103
Histological grade	I II III	0.338 0.467 Reference	0.145 – 0.787 0.171 – 1.276	0.012 0.138

Total. 48; event: 36; censored: 12

Table 4: Number of survived and censored dogs in subgroups with different clinical stage and histological grade

Clinical stage	Histological grade	n	n censored (%)	n survived (%)
I	I	**11**	**2 (18.2)**	**9 (100.0)**
I	II	3	1 (33.3)	2 (100.0)
I	III	3	0 (0.0)	3 (100.0)
II	I	**7**	**1 (14.3)**	**6 (100.0)**
II	II	4	2 (50.0)	2 (100.0)
II	III	0	0	0
III	I	2	0 (0.0)	1 (50.0)
III	II	3	1 (33.3)	1 (50.0)
III	III	2	1 (50.0)	1 (100.0)
IV	I	2	1 (50.0)	1 (100.0)
IV	II	3	1 (33.3)	0 (0.0)
IV	III	**10**	**1 (10.0)**	**0 (0.0)**

*Groups which are included in further evaluation are bolded

Table 5: Kaplan-Meier survival for combination of clinical stage and histological grade associated with survival 2 years after surgery in dogs that had undergone surgical removal of mammary gland tumours

Clinical stage	Histological grade	n (%)	Survival time (days) (mean ± SE)	P Value
I	I	11 (39.3)	730.0 ± 0.0	<0.001
II	I	7 (25.0)	730.0 ± 0.0	0.001
IV	III	10 (35.7)	184.0 ± 58.8	

Figure 5 shows Kaplan-Meier survival curves for compared subgroups.

Factors associated with prognosis

Of all the variables included in the univariate study, histological grade, histological type (simple/complex) and clinical stage were associated significantly with survival at 2-YFUP of dogs that had undergone surgical removal of MGTs (P<0.05).

Kaplan–Meier survival curves differed for dogs with clinical stages I and IV, and also II and IV (P<0.05), whereas the difference between curves for dogs with stages I and III, and II and III, were near the level of significance (P=0.06 and P=0.053, respectively). There was no significant difference between the survival curves for dogs with stages I and II or for dogs with stages III and IV (P=0.489 and P=0.115, respectively) (*Figure 1*). Significant differences in survival were revealed between groups of dogs with different histological grades (P<0.05); mean survival time was calculated as 730 ± 0 days for grade I, 602 ± 70.8 days for grade II and 332 ± 82 days for grade III (*Figure 2*). Significant difference was observed between each pair of survival curves according to histological grade (P<0.05).

The difference in survival time between dogs with simple (mean survival time 507.9 ± 56.4) and complex (704.4 ± 25.9) tumours was significant (P<0.05) (*Figure 3*).

The survival curve for dogs with multiple MGTs did not differ from that for dogs with only one tumour (P=0.707). No association was found between survival of ovariectomized and non-ovariectomized dogs (P=0.930), or between groups of dogs with and without a history of pseudopregnancy (P=0.813) (Table 2).

Variables included in the multivariate analysis were clinical stage, histological grade and histological tumour type (simple/complex). The histological tumour type is shown not to be significant (P>0.05), therefore, in the final model, only clinical stage and histological grade were included.

Relative risk for clinical stage III was not significantly lower than that for stage IV/V (P>0.05), whereas dogs with stages I and II exhibit 5.6 and 4.2 times lower relative risk than dogs with stage IV/V. Relative risks for histological grades II and III did not differ significantly, whereas that for grade I was 3-fold less than that for grade III (Table 3).

Table 4 shows subgroups of dogs with different combinations of clinical stage and histological grade. Because of the low number of cases in several subgroups, only those with n≥6 were further evaluated.

Kaplan-Meier survival curves revealed significant differences when comparing groups 1 (clinical stage I/histological grade I) and 2 (clinical stage II/histological grade I) with group 3 (clinical stage IV/histological grade III) (P<0,001 and P=0.001 respectively), whereas groups 1 and 2 did not differ significantly (P>0.05) (Figure 4).

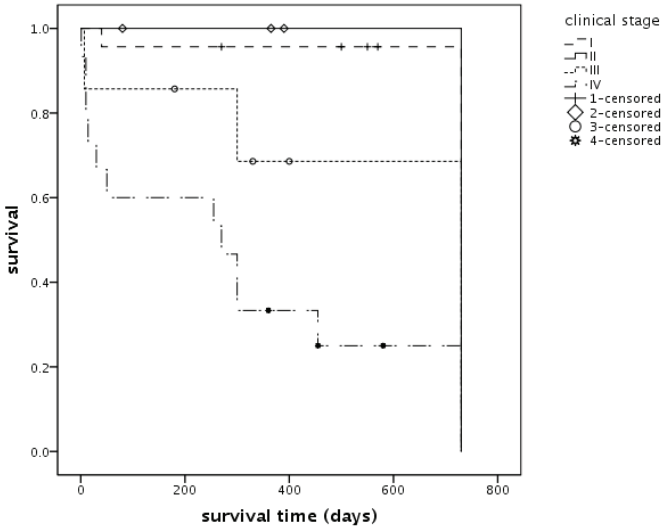

Figure 1: Kaplan–Meier survival curve for dogs with mammary gland tumours classified by clinical stage (P<0.05) (n=56)

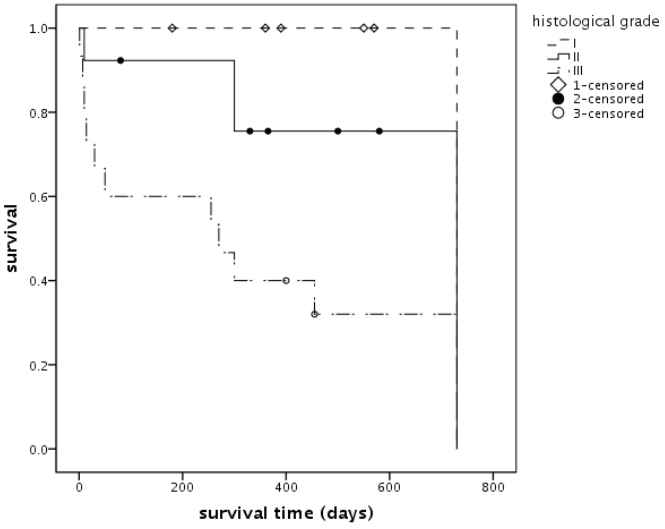

Figure 2: Kaplan–Meier survival curve for dogs with mammary gland tumours classified by histological grade (P<0.05) (n=50)

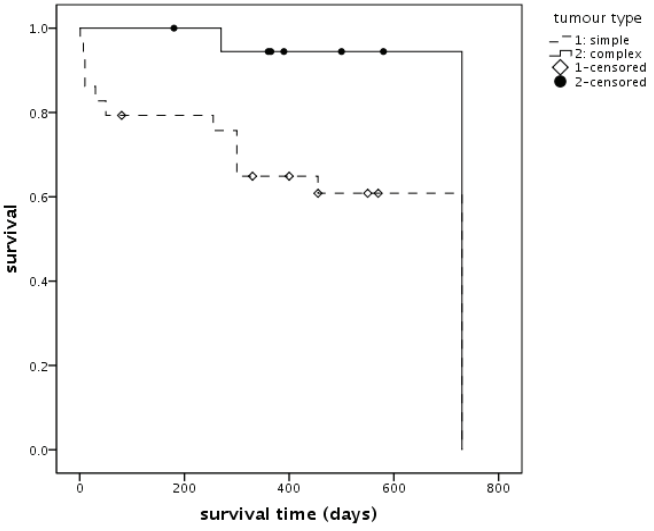

Figure 3: Kaplan–Meier survival curve for dogs with mammary gland tumours classified by tumour type – simple or complex (P=0.05) (n=48)

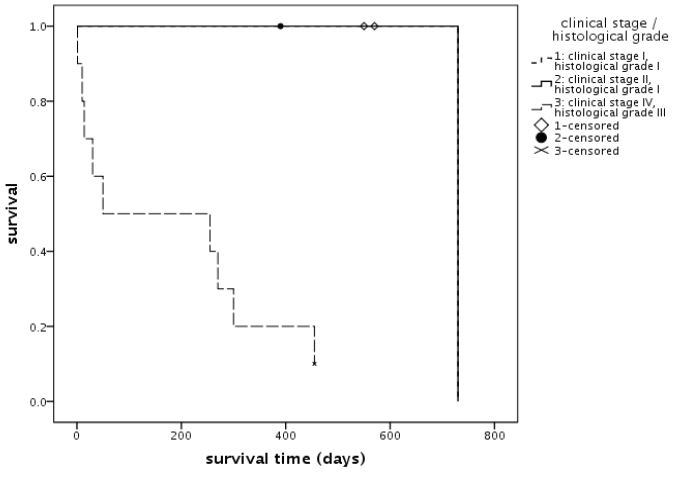

Figure 4: Kaplan–Meier survival curve for dogs with mammary gland tumours classified by combining clinical stage and histological grade (P≤0.01) (n=28)

Discussion

The most frequent neoplasms in intact female dogs are MGTs. It is therefore very important to have some protective actions to prevent the emergence of MGTs and, if they are diagnosed, to determine the prognosis. Neither of these is simple because of the many factors that can influence the biological behavior of the MGTs.

Steroid hormones play an important role in the etiology of MGT in dogs and ovariectomy of a bitch at an early age, modifying their levels is therefore the most effective way of preventing MGTs (3, 4). Some authors report that late spaying does not reduce the risk of malignant tumours (15), while others conclude that ovariectomy at any age may be beneficial to survival of dogs that develop MGTs (18, 3). In our patients with MGTs, none of the ovariectomies were made before the second estrous and 78.6 % dogs were intact, pointing to the protective effect of early ovariectomy. We found no association of survival in ovariectomized versus non-ovariectomized dogs with MGTs. In addition, the effect of pseudopregnancy on the development of MGTs is still the subject of debate (3, 27). In our study, 5 out of 9 dogs with a history of pseudopregnancy developed multiple MGTs. No association was found between survival of dogs with and without a history of pseudopregnancy (P=0.813). However, the small number of dogs with a history of pseudopregnancy makes it difficult to draw firm conclusions.

Contradictory results have been reported regarding breed predisposition towards occurrence of MGTs. MGTs occur more frequently in purebred dogs (3, 11, 26, 28) and the same was found in our study.

MGTs develop mostly in middle-aged and old dogs (3, 11). In our study most dogs with diagnosed MGTs were age 10 or 11, and the youngest was 5 years old, which fits well with the reported data (3, 5). Given the small number of cases in several subgroups of age and breed we did not evaluate the possible influence of these two factors on survival. Furthermore, dogs of different breeds differ in their life span.

Survival after MGT surgery varies significantly, depending on different tumour and dog characteristics, and different parameters therefore need to be evaluated in order to obtain a significant prognosis. Significant differences in the survival of dogs with different histological tumour types have been reported (25, 29, 30, 31). Malignancy increases from non-infiltrating *in situ* carcinoma over anaplastic carcinoma to sarcoma (16). Moreover, simple carcinomas have a poorer prognosis than complex carcinomas (28), and in some authors' opinion myoepithelial cells could act as tumour suppressors in regulating the transition from *in situ* to invasive carcinoma in humans (32). In our study the difference in survival time between dogs with simple and complex tumours was significant ($P<0.05$). However, by multivariate analysis, histological tumour type was revealed as not being significant ($P>0.05$).

With regard to clinical stage, dogs with more advanced tumour stage exhibit significantly shorter survival than dogs with low-stage disease (3, 30). In our study there was no significant difference between survival for dogs with stages I and II and those with stages III and IV/V, while survival for dogs with stages I and IV/V differs significantly from those with II and IV/V. The same trend was shown by multivariate analysis, where dogs with stages I and II have 5 and 4.3 times lower relative risk than dogs with stage IV/V. While there is general agreement that tumour size is an important prognostic factor, there is conflicting evidence as to the size category, and therefore clinical stage, at which prognosis changes significantly for the worse (13, 15). Similarly to our observations, it has been reported (13, 25) that dogs with tumours larger than 5 cm (stage III) exhibit a significantly poorer survival than those with smaller tumours. On the other hand, Philibert et al. (30) found a significant difference in survival between dogs with stage I and those with stages II and III. In addition to large tumour size, lymph node status has been reported to be a poor prognostic factor in canine MGTs (11, 25). In our study, dogs with metastases in lymph nodes were associated with the shortest postoperative survival of all groups of clinical staging. Similarly, Karayannopoulou et al. (8) linked dogs with stage IV with poorer outcome, since 24 of 28 dogs with stage IV in their study died within 2-YFUP.

Numerous reports (3, 8, 33, 34) show that histological grading of malignant MGTs is significantly related to prognosis, with higher grade tumours having worse prognosis. The method of Elston and Ellis used in our study, was primarily developed for invasive adenocarcinomas of breast regardless of tumour type (20). Since

in veterinary medicine there are no generally accepted guidelines about which histological types of canine MGTs could be graded, the decision is left to the authors. Consequently, there are great variations in grading of canine MGTs between individual studies. Dutra et al (35) and Manuali et al. (24) have graded only simple and complex type carcinomas, Clemente et al (22) and Karayannopoulou et al (8) also carcinomas of special types, while Santos et al (23) have also graded carcinosarcomas and in situ carcinoma. Tumor samples in the study of Manuali et al. (24) and Clemente et al. (22) included carcinosarcoma, malignant mioepithelioma and sarcoma, but from their results it is not evident whether the tumors of this histological type were graded. The disadvantage of the Elston and Ellis method, when adapted to grading of canine MGTs, is that it does not include the evaluation of myoepithelial proliferation or mesenchymal areas (10). Namely, unlike in woman, complex and mixed carcinomas frequently occur in the dog (34) and if grading is restricted to simple type carcinomas, important prognostic information could be lost (20). Pena et al (10) therefore recommended some modifications of this method in relation to the evaluation of myoepithelial proliferation areas, mixed neoplasms and the evaluation of nuclear features. When these recommendations are taken into account, different histological tumour types can be graded. In our study, simple, complex and special type carcinomas were graded. Like Pena et al (10) we carefully graded complex tumours scoring the degree of tubule formation only in the epithelial parts of the tumours while the nuclear pleomorphism was evaluated throughout the tumour. There were significant differences in survival curves among groups of dogs with different histological grade ($P<0.05$). Karayannopoulou et al. (8) showed a 21-fold higher risk of death in the group of dogs with grade III carcinomas than in those with grade I and II carcinomas. We found that relative risks did not differ significantly between histological grades II and III, whereas dogs with grade I exhibited a 3-fold lower risk than dogs with grade III.

Further, we have studied the prognostic value of the combination of clinical stage and histological grade. Complete survival was recorded in subgroups of stage IV/grade I and stage I/grade III. However, due to the low number of cases, these two subgroups were not included in comparison. All dogs in subgroups with clinical stage I or II and histological grade I survived, in contrast to dogs with clinical stage IV and histological grade III, where average survival time after surgical removal of tumours was less than 200 days. Our results have demonstrated that a combination of clinical staging and histological grading is of high prognostic value, although corroboration is required on account of the small number of dogs in our study. Since MGTs are histologically very heterogeneous, clinical staging and histological grading could improve the estimation of their malignancy and therefore prognosis of dogs with MGTs.

Conclusion

In our study canine mammary carcinomas were most frequently recorded in Saluki, Miniature Schnauzer and Medium Poodle breeds. All dogs in subgroups with clinical stage I or II and histological grade I survived 2-years after surgical removal of the tumours. In contrast, average survival of dogs with clinical stage IV and histological grade III was less than 200 days. Our results show that the combination of clinical staging and histological grading provides a high prognostic value and should therefore be included in the diagnosis of every MGT.

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KLINIČNO PATOLOŠKA ŠTUDIJA 56 MALIGNIH TUMORJEV MLEČNE ŽLEZE PRI PSICAH V SLOVENIJI - PROGNOSTIČNA VREDNOST KLINIČNEGA STADIJA IN STOPNJE DIFERENCIACIJE TUMORJA

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Povzetek: Tumor mlečne žleze (TMŽ) je najpogosteje diagnosticirana oblika tumorja pri psicah in po poročilih avtorjev so posamezne pasme bolj nagnjene k nastanku te vrste tumorjev. Naša retrospektivna študija opisuje klinične in histopatološke ugotovitve pri 56 psicah z malignimi TMŽ, katerim so tumorje odstranili na Kliniki za kirurgijo in male živali Veterinarske fakultete Univerze v Ljubljani. Zbrali smo podatke o starosti, pasmi, sterilizaciji in morebitni, v preteklosti diagnosticirani, navidezni brejosti psic in izvedli analizo preživetja. Na podlagi 2-letnega preživetja po kirurški odstranitvi tumorjev, smo ocenili napovedno vrednost kliničnega stadija in stopnje diferenciacije tumorja. Maligni TMŽ so bili najpogostejši pri psicah starih 10 let ali več (64,3 %), z največjim deležem psic starosti 10 in 11 let. Maligni TMŽ so bili najpogostejši pri psicah pasme Saluki (5,56 na 100 psov), pritlikavem šnavcerju (0,44 na 100 psov) in srednjem kodru (0,41 na 100 psov). Razlika med preživetjem psic z malignimi TMŽ kompleksnega in enostavnega tipa je statistično značilna ($P<0.05$). Med skupinami psov z malignimi TMŽ različne stopnje diferenciacije je statistično značilna razlika v preživetju. Statistično značilna je razlika med Kaplan–Meierjevimi krivuljami preživetja psic s kliničnim stadijem I in IV in tudi II in IV ($P<0.05$). Vse psice s kliničnim stadijem I ali II in stopnjo diferenciacije I so preživele 2-letno obdobje po kirurški odstranitvi tumorjev. Povprečen čas preživetja psic s kliničnim stadijem IV in stopnjo diferenciacije III je bil krajši od 200 dni. Iz rezultatov naše študije je razvidno, da ima kombinirana ocena kliničnega stadija in stopnje diferenciacije tumorja visoko napovedno vrednost za preživetje psic po kirurški odstranitvi malignega TMŽ.

Ključne besede: tumor mlečne žleze pri psicah; klinični stadij; histopatološka diagnostika; stopnja diferenciacije; prognostična vrednost