Outcome of dogs with mast cell tumors in the inguinal or perineal region versus other cutaneous locations: 124 cases (1990–2001)

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Objective—To compare clinical outcome of dogs with cutaneous mast cell tumors (MCTs) in the inguinal or perineal region with outcome for dogs with MCTs in other cutaneous locations.

Design—Retrospective study.

Animals—37 dogs with MCTs in the inguinal or perineal region and 87 dogs with MCTs in other cutaneous locations.

Procedure—Information obtained from the medical records included sex, breed, age, histologic grade of all tumors, number and location of all tumors, tumor size (ie, diameter of the tumor), completeness of surgical excision, treatments administered in addition to surgery, and outcome. In all dogs, the primary treatment consisted of surgical excision.

Results—Disease-free interval and survival time for dogs with MCTs in the inguinal or perineal region were not significantly different from values for dogs with MCTs in other cutaneous locations. Dogs with incompletely excised tumors, dogs with grade III tumors, and dogs that received systemic treatment were 2, 2.5, and 4 times as likely, respectively, to have a relapse. Factors significantly associated with a shorter survival time were age > 8 years, metastatic disease at the time of initial diagnosis, and tumor relapse.

Conclusions and Clinical Relevance—Results of the present study suggest that dogs with MCTs in the inguinal or perineal region do not have a worse prognosis in regard to disease-free interval or survival time than do dogs with MCTs in other cutaneous locations. Treatment recommendations for dogs with cutaneous MCTs should be based on confirmed predictors of biological behavior, such as histologic grade and clinical stage. (*J Am Vet Med Assoc* 2005;226:1368–1374)

Numerous authors have suggested that **mast cell tumors (MCTs)** that develop in the inguinal, perineal, scrotal, and preputial regions in dogs have a more aggressive biological behavior, resulting in higher recurrence rates and shorter survival times, than do MCTs that develop in other cutaneous locations.[1-6] However, only a few studies[7-11] have objectively analyzed data to determine whether these anecdotal reports are valid. A recent study[12] of dogs with MCTs in the inguinal or perineal region found that many of these dogs had prolonged **disease-free intervals (DFIs)** and survival times, indicating that the prognosis for dogs with an MCT in the inguinal or perineal region is not uniformly poor. However, the study did not include a control group, making it difficult to compare results for these dogs with results for dogs with MCTs in other cutaneous locations.

The purpose of the study reported here was to compare the clinical outcome of dogs with cutaneous MCTs in the inguinal or perineal region with outcome for dogs with MCTs in other cutaneous locations. If anecdotal reports were true, we would have expected dogs with MCTs in the inguinal or perineal region to have had shorter times to disease recurrence and shorter survival times, compared with dogs with MCTs in other cutaneous locations. A secondary objective of the present study was to evaluate the prognostic importance of other factors putatively associated with DFI and survival time in dogs that have undergone excision of a cutaneous MCT.

Criteria for Selection of Cases

Medical records of all dogs examined at Cornell University, the University of Georgia, or the University of California at Davis between January 1990 and December 2001 because of a cutaneous MCT were reviewed. Dogs were eligible for inclusion in the study if the diagnosis of a cutaneous MCT had been confirmed by means of histologic examination, the anatomic location of the tumor was described in the medical record, the dog did not have any history of previous cutaneous MCTs, and adequate follow-up information was available. Dogs enrolled in ongoing studies at any of the participating institutions were excluded from the study.

Procedures

Information obtained from the medical records included sex, breed, age, histologic grade of all MCTs,[13]

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number and location of all tumors, tumor size (ie, diameter of the tumor), and completeness of surgical excision. For purposes of the present study, tumors were considered to be located in the inguinal region if they involved the skin of the caudoventral surface of the abdomen, including the prepuce, or the medial aspect of the thigh and were considered to be located in the perineal region if they involved the skin between the base of the tail and the scrotum or vulva. For dogs with multiple MCTs in which 1 of the tumors was located in the inguinal or perineal region, tumor size, histologic grade, and completeness of surgical excision were recorded for the tumor located in the inguinal or perineal region. For dogs with multiple MCTs in which none of the tumors were located in the inguinal or perineal region, tumor size and grade were recorded for the largest tumor and highest histologic grade, respectively, and tumor resection was considered incomplete if any of the tumors were incompletely excised. Information used to determine clinical stage (eg, results of cytologic examination of regional lymph node aspirates and abdominal ultrasonography) was recorded for each dog when available. Finally, treatments administered in addition to surgery (eg, administration of prednisone, chemotherapy, and radiation therapy) were recorded.

Duration of disease was defined as the interval between first appearance of an MCT and surgical excision. Relapse was defined as local recurrence of the tumor, metastasis to a regional lymph node or distant site, or development of another cutaneous MCT at a different site. Disease-free interval was defined as the time from surgical resection until tumor relapse; dogs with persistent gross evidence of disease after surgery were not included in analyses of DFI. Survival time was defined as time from surgical excision until death from any cause. Dogs alive or disease-free at the time of last follow-up were included in analyses until the day of last follow-up and then censored.

Potential prognostic factors for DFI and survival time that were examined included tumor location (inguinal or perineal region vs any other cutaneous location), age (≤ 8 years vs > 8 years), breed (brachycephalic vs retriever type vs other), sex (male vs female), neuter status (yes vs no), completeness of excision (complete vs incomplete), histologic grade (grade I vs grade II vs grade III), metastatic disease (yes vs no), number of tumors (1 vs ≥ 2), and treatment (local vs systemic). Because the anatomic boundaries of the inguinal and perineal regions may not be clear, we separately examined DFI and survival time for dogs with MCTs located on the prepuce or scrotum, 2 clearly defined regions.

Statistical analyses—Frequencies of potential categorical prognostic factors were compared between dogs with MCTs in the inguinal or perineal region and dogs with MCTs in any other cutaneous location by use of the χ^2 test of independence. Student *t* tests were used for analyses of continuous data that were normally distributed, and Wilcoxon rank sum tests were used for analyses of continuous data that were not normally distributed.[14]

Initially, the Kaplan-Meier product limit method was used to estimate DFI and survival time for dogs with MCTs in the inguinal or perineal region and for dogs with MCTs in other cutaneous locations. Similarly, survival curves for other potential prognostic factors were also estimated. For each variable, the log rank test for censored survival data was used to compare survival curves. To evaluate the joint and confounding effects of other variables in addition to location on DFI and survival time, multivariable survival analysis (Cox proportional hazards method) was used. Models were selected by means of backward elimination, following suggested methods.[15] Commercial software was used to perform χ^2 and log rank tests,[a] generate survival curves,[b] and build multivariable models.[b] For all analyses, values of $P \leq 0.05$ were considered significant.

Results

Patient and tumor characteristics—Six hundred eighty-nine dogs with MCTs were identified in the initial medical records search, of which 124 met the criteria for inclusion in the study (**Table 1**). Thirty-seven dogs had MCTs in the inguinal or perineal region, and 87 had MCTs in other cutaneous locations. Of the 37 dogs with MCTs in the inguinal or perineal region, 5 (14%) had MCTs on the scrotum and 7 (19%) had MCTs on the prepuce. The remaining dogs had MCTs in the inguinal (13 dogs [35%]) or perineal (12 [32%]) region. Of the 87 dogs with MCTs in locations other than the inguinal or perineal region, 31 (36%) had MCTs involving the extremities, 42 (48%) had MCTs on the trunk, and 14 (16%) had MCTs on the head or neck.

One hundred two (82%) dogs had a solitary MCT, and 22 (18%) had multiple cutaneous MCTs. Of the dogs with multiple MCTs, 15 had 2 tumors, 6 had 3 tumors, and 1 had 4 tumors. Median age of dogs with MCTs in the inguinal or perineal region was 8.0 years (range, 1.9 to 13.2 years); median age of dogs with MCTs in other cutaneous locations was 7.7 years (range, 2.1 to 15 years). Duration of disease prior to MCT removal ranged from 0.1 to 156 weeks (median, 5 weeks; n = 64). Information about tumor size was available for 78 dogs. Tumor size ranged from 1 to 150 mm (median, 15 mm). Only 10 tumors were ≥ 50 mm in diameter.

Information on histologic grade was available for 123 dogs (the histology report was not available for the remaining dog, which had an MCT in the inguinal region). Information on completeness of surgical excision was available for 120 dogs.

Results of cytologic examination of fine-needle aspirates of regional lymph nodes obtained at the time of initial diagnosis were available for 23 dogs. Eleven (48%) of these dogs had evidence of regional lymph node metastases. Abdominal ultrasonography was performed at the time of initial diagnosis in 52 dogs, and only 1, a dog with a grade I MCT on the prepuce, had evidence of visceral metastasis. In this dog, mild splenomegaly was evident ultrasonographically, and mast cells were seen during cytologic examination of a splenic aspirate. However, the dog also had positive results for heartworm infection. None of the other dogs had evidence of visceral metastasis at the time of initial diagnosis.

All dogs underwent surgical excision. In 93 dogs, tumors were treated locally; treatment in these dogs consisted of surgery alone (n = 85), surgery and intralesional

Table 1—Characteristics of dogs with mast cell tumors (MCTs) in the inguinal or perineal region (case dogs; n = 37) versus other cutaneous locations (control dogs; 87).

Characteristic	No. of case dogs (%)	No. of control dogs (%)
Sex*		
Male	22 (59)	29 (33)
Female	15 (41)	58 (67)
Breed		
Golden Retriever	4 (11)	13 (15)
Labrador Retriever	4 (11)	12 (14)
Boxer	1 (3)	5 (6)
Chinese Shar-pei	1 (3)	13 (15)
Cocker Spaniel	3 (8)	2 (2)
Mixed breed	8 (22)	16 (18)
Other pure breeds	16 (43)	26 (30)
Tumor grade		
I	5 (14)	18 (21)
II	25 (68)	57 (66)
III	6 (16)	12 (14)
Not available	1 (3)	0
Initial No. of tumors		
Solitary	28 (76)	74 (85)
Multiple	9 (24)	13 (15)
Lymph node metastases at diagnosis		
Yes	3 (8)	8 (9)
No	3 (8)	9 (10)
Not available	31 (84)	70 (81)
Visceral metastases at diagnosis		
Yes	1 (3)	0
No	19 (51)	32 (37)
Not available	17 (46)	55 (63)
Surgical margins		
Complete	17 (46)	57 (66)
Incomplete	17 (46)	29 (33)
Unknown	3 (8)	1 (1)
Additional treatment†		
Corticosteroids PO	4 (11)	5 (6)
Corticosteroids intralesionally	2 (5)	1 (1)
Chemotherapy	11 (30)	9 (10)
Radiation therapy	2 (5)	3 (3.4)
Chemotherapy and radiation therapy	1 (3)	1 (1)
None	17 (46)	68 (78)
Tumor relapse‡		
No	15 (41)	47 (54)
Yes	21 (57)	37 (43)
Location of tumor relapse		
Local	9 (24)	14 (16)
Regional lymph node	7 (19)	9 (10)
Distant site	1 (3)	0
New cutaneous MCT	9 (24)	23 (26)

*Dogs with MCTs in the inguinal or perineal region were significantly ($P = 0.007$) more likely to be males. †Dogs with MCTs in the inguinal or perineal region were significantly ($P < 0.001$) more likely to receive systemic treatment. ‡Relapse was defined as local recurrence of the tumor, metastasis to a regional lymph node or distant site, or development of another cutaneous MCT at a different site. Fourteen dogs (4 cases and 10 controls) had a relapse in > 1 site.

administration of corticosteroids (3), and surgery and radiation therapy (5). The remaining 31 dogs received systemic treatments, such as oral administration of corticosteroids (n = 9), cytotoxic chemotherapy (20), and radiation therapy and chemotherapy (2). Chemotherapy regimens and dosages were not standardized and consisted of corticosteroids combined with lomustine (n = 3), vinblastine (4), vinblastine and lomustine (5), vinblastine and cyclophosphamide (4), vincristine (2), or chlorambucil (4).

Comparison of groups—Dogs with MCTs in the inguinal or perineal region were comparable to dogs with MCTs in other cutaneous locations in regard to age, breed, tumor grade, number of tumors, presence of metastatic disease at the time of diagnosis, completeness of excision, and pattern of tumor relapse (Table 1). Dogs with inguinal or perineal tumors were significantly ($P = 0.007$) more likely to be male than were dogs with MCTs in other locations. Dogs with inguinal or perineal tumors were also significantly ($P < 0.001$) more likely to receive systemic treatment.

DFI and risk factors for relapse—Follow-up time ranged from 0.3 to 108 months (median, 17 months). Four dogs (1 with an MCT in the inguinal region and 3 with MCTs in other cutaneous locations) had gross evidence of disease after surgery and were not included in analyses of DFI. Of the remaining 120 dogs, 58 (48%) had a relapse and 62 (52%) had no evidence of relapse during the follow-up period. Median follow-up time for dogs without any evidence of tumor relapse was 18 months (range, 0.33 to 101 months). Twenty-one of 36 (58%) dogs with MCTs in the inguinal or perineal region had a relapse, compared with 37 of 84 (44%) dogs with MCTs in other cutaneous locations.

Disease-free interval for all dogs in the study ranged from 0.23 to 101 months (median, 24.7 months). Overall, estimated probabilities that dogs would be disease-free 6 months and 1, 2, and 5 years after surgery were 69%, 59%, 50%, and 40%, respectively. The DFI for dogs with MCTs in the inguinal or perineal region ranged from 0.33 to 83 months (median, 9.6 months), whereas the DFI for dogs with MCTs in other cutaneous locations ranged from 0.23 to 101 months (median, 33.9 months). For dogs with MCTs in the inguinal or perineal region, estimated probabilities that dogs would be disease-free 6 months and 1, 2, and 5 years after surgery were 60%, 43%, 43%, and 38%, respectively. For dogs with MCTs in other cutaneous locations, estimated probabilities were 73%, 65%, 53%, and 37%, respectively. The Kaplan-Meier curves for DFI were not significantly ($P = 0.14$) different (**Figure 1**). Because dogs with inguinal or perineal tumors were more likely to receive systemic treatment, we examined DFI curves for dogs that received only local treatment. For the 21 dogs with MCTs in the inguinal or perineal region that received only local treatment, estimated probabilities of being disease-free 6 months and 1, 2, and 5 years after surgery were 80%, 62%, 62%, and 62%, respectively. For the 69 dogs with MCTs in other cutaneous locations that received only local treatment, estimated probabilities were 81%, 74%, 61%, and 46%, respectively. The Kaplan-Meier curves for DFI for these 2 groups were not significantly ($P = 0.92$) different. Similarly, the Kaplan-Meier curve for DFI for dogs with MCTs in the inguinal or perineal region that received systemic treatment was not significantly ($P = 0.59$) different from the curve for dogs with MCTs in other cutaneous locations that received systemic treatment. Factors significantly associated with a shorter DFI when evaluated individually were incomplete excision ($P = 0.001$), high tumor grade ($P = 0.009$), metastatic disease at the time of initial diagnosis ($P = 0.06$), and systemic treatment ($P < 0.001$). Site of tumor, breed, sex, neuter status,

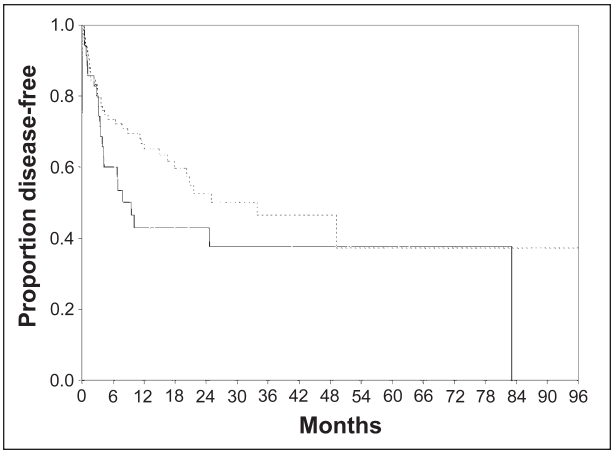

Figure 1—Kaplan-Meier curves depicting disease-free interval (DFI) for 36 dogs with mast cell tumors (MCTs) in the inguinal or perineal region (solid line) and 84 dogs with MCTs in other cutaneous locations (broken line). Median DFI for dogs with inguinal or perineal tumors (9.6 months) was not significantly ($P = 0.14$) different from median DFI for dogs with tumors in other cutaneous locations (33.9 months).

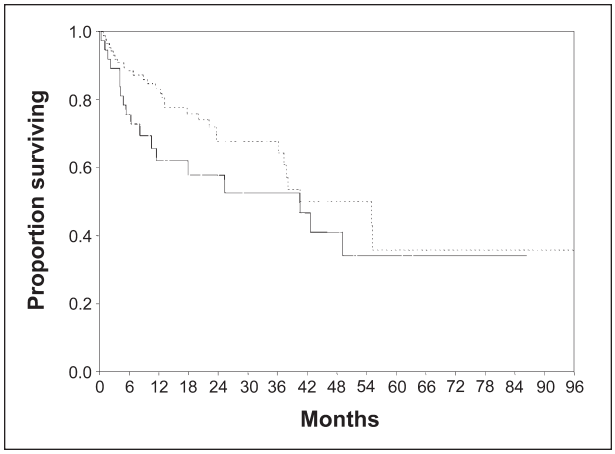

Figure 2—Kaplan-Meier curves depicting survival time for 37 dogs with MCTs located in the inguinal or perineal region (solid line) and 87 dogs with MCTs in other cutaneous locations (broken line). Median survival time for dogs with inguinal or perineal tumors (40.6 months) was not significantly ($P = 0.16$) different from median survival time for dogs with tumors in other cutaneous locations (55 months).

size of tumor, age, and initial number of tumors were not significant in univariate analyses.

The fact that several potential prognostic factors were highly associated with each other complicated building and interpreting the multivariable models. For example, grade of tumor and completeness of excision were closely associated in this data set. Similarly, location of tumor and type of treatment (local vs systemic) and type of treatment and completeness of excision were highly associated. Thus, multiple multivariable models were examined.

In multivariable analyses, tumor grade and type of treatment (local vs systemic) were significantly associated with DFI. Dogs that received systemic treatment were 4 times as likely to have a relapse as were dogs that received only local treatment (95% **confidence interval [CI]**, 2.3 to 7.0; $P < 0.001$). Also, dogs with grade III tumors were 2.5 times as likely to have a relapse as were dogs with grade I tumors (95% CI, 1.3 to 6.3; $P = 0.05$), regardless of type of treatment. However, dogs with grade II tumors were not significantly more likely to have a relapse than were dogs with grade I tumors (hazard ratio, 1.1; 95% CI, 0.5 to 2.4; $P = 0.71$). Because completeness of excision was associated with both tumor grade and type of treatment, it was examined in a model without these factors. Dogs with incomplete excision were 2 times as likely to have a relapse as were dogs in which excision was thought to be complete (95% CI, 1.1 to 3.3; $P = 0.02$).

Survival time—Overall, estimated probabilities of survival 6 months and 1, 2, and 5 years after surgery were 85%, 77%, 65%, and 35%, respectively. For dogs with MCTs in the inguinal or perineal region, estimated probabilities of survival 6 months and 1, 2, and 5 years after surgery were 76%, 62%, 58%, and 34%, respectively. Median survival time was 40.6 months (range, 0.33 to 86.4 months). For dogs with MCTs in other cutaneous locations, estimated probabilities of survival 6 months and 1, 2, and 5 years after surgery were 88%, 83%, 68%, and 36%, respectively. Median survival time was 55 months (range, 0.73 to 108 months). The Kaplan-Meier curves for survival time were not significantly ($P = 0.16$) different between groups **(Figure 2)**. Because dogs with inguinal or perineal tumors were more likely to receive systemic treatment, we examined survival curves for dogs that received only local treatment. For the 21 dogs with MCTs in the inguinal or perineal region that received only local treatment, estimated probabilities of survival 6 months and 1, 2, and 5 years after surgery were 86%, 86%, 79%, and 49%, respectively. For the 72 dogs with MCTs in other cutaneous locations, estimated probabilities were 92%, 90%, 78%, and 39%, respectively. The Kaplan-Meier curves for survival time were not significantly ($P = 0.9$) different. Similarly, the Kaplan-Meier curve for survival time for dogs with MCTs in the inguinal or perineal region that received systemic treatment was not significantly ($P = 0.78$) different from the curve for dogs with MCTs in other cutaneous locations that received systemic treatment. Factors significantly associated with a shorter survival time when evaluated individually were age > 8 years ($P = 0.001$), incomplete excision ($P = 0.005$), high tumor grade ($P = 0.03$), metastatic disease at the time of initial diagnosis ($P = 0.002$), systemic treatment ($P < 0.001$), and tumor relapse ($P = 0.002$).

In multivariable analyses, age, tumor relapse, and metastatic disease at the time of initial diagnosis were significantly associated with survival time. Dogs > 8 years old were 2.7 times as likely to die as were dogs ≤ 8 years old at the time of surgery (95% CI, 1.5 to 49; $P = 0.002$). Dogs with evidence of metastatic disease at the time of diagnosis were 3.2 times as likely to die as dogs with localized tumors (95% CI, 1.4 to 7.3; $P = 0.007$). Finally, dogs that had a relapse were 2.5 times as likely to die as dogs that did not have a relapse (95% CI, 1.3 to 4.7; $P = 0.005$).

Preputial and scrotal MCTs—Disease-free interval, tumor relapse, and survival time were analyzed in the 7 dogs with preputial MCTs and 5 dogs with scro-

tal MCTs. When the Kaplan-Meier curve for DFI for the 12 dogs with preputial or scrotal MCTs was compared with that for 84 dogs with MCTs in a location other than the inguinal or perineal region, dogs with preputial or scrotal MCTs had significantly ($P = 0.05$) shorter DFI (**Figure 3**). For the dogs with preputial or scrotal MCTs, estimated probabilities of remaining disease-free 6 months and 1, 2, and 5 years after surgery were 50%, 25%, 25%, and 25%, respectively. Nine dogs had a relapse by 11 months after surgery; the remaining dogs were still disease-free when lost to follow-up 21, 41, and 63 months after surgery. There was no difference with respect to pattern of tumor relapse between dogs with preputial or scrotal MCTs and dogs with MCTs in cutaneous locations other than the inguinal or perineal region. Because dogs with preputial or scrotal MCTs appeared to have a worse prognosis, we separately examined the curves for DFI for dogs with preputial or scrotal MCTs and dogs with MCTs in other inguinal or perineal locations. These curves were not significantly ($P = 0.20$) different.

For dogs with preputial or scrotal MCTs, estimated probabilities of survival 6 months and 1, 2, and 5 years after surgery were 58%, 58%, 58%, and 29%, respectively. Seven dogs had died by 43 months after surgery, 3 had been lost to follow-up, 1 was alive when lost to follow-up 49 months after surgery, and 1 was alive when lost to follow-up 63 months after surgery. Survival time for dogs with preputial or scrotal MCTs was not significantly different from survival time for dogs with MCTs in other cutaneous locations.

Number of dogs with preputial or scrotal MCTs was too small to allow for multivariate analysis. However, all of these dogs had grade I (4) or grade II (8) tumors, and only 3 had lymph node metastases at the time of initial diagnosis.

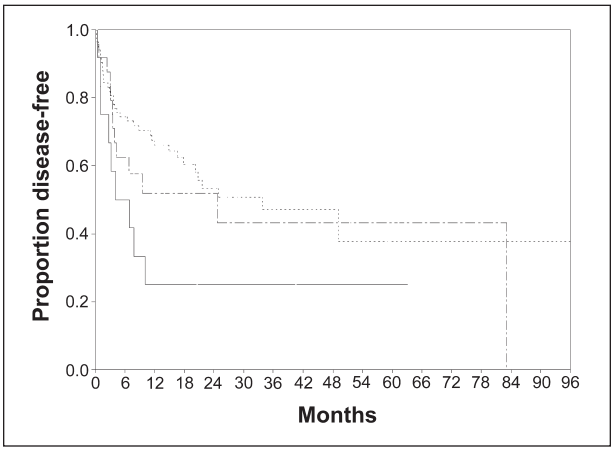

Figure 3—Kaplan-Meier curves depicting DFI for 12 dogs with MCTs on the prepuce or scrotum (—), 25 dogs with MCTs in other inguinal or perineal locations (— - —), and 84 dogs with MCTs in cutaneous locations other than the inguinal or perineal region (- - -). Median DFI for dogs with preputial or scrotal tumors (4.2 months) was significantly ($P = 0.05$) shorter than median DFI for dogs with tumors in cutaneous locations other than the inguinal or perineal region (33.9 months) but was not significantly ($P = 0.20$) different from median DFI for dogs with tumors located in other inguinal or perineal sites (24.7 months).

Discussion

In the present study, although median DFI for dogs with MCTs in the inguinal or perineal region was 9.6 months, compared with a median DFI of 33.9 months for dogs with MCTs in other cutaneous locations, and median survival time was 40.6 months, compared with a median survival time of 55 months for dogs with MCTs in other cutaneous sites, Kaplan-Meier and multivariable analyses indicated that DFI and survival time were not significantly different between groups. This suggests that the prognosis for dogs with MCTs in the inguinal or perineal region may be comparable to the prognosis for dogs with MCTs in other cutaneous locations.

The anatomic boundaries of the inguinal and perineal regions are indistinct and poorly defined. Thus, dogs were designated as having a tumor in the inguinal or perineal region on the basis of the attending clinicians' definitions of these anatomic boundaries. Because of the retrospective nature of this study, various clinicians examined dogs included in the study. Thus clinician variation in the definition of the boundaries of the inguinal and perineal regions may have led to improper placement of some dogs into study groups. To evaluate the effect of this type of error, dogs with MCTs of the scrotum or prepuce, 2 more clearly defined anatomic locations, were evaluated separately. When the 12 dogs with preputial or scrotal MCTs were compared with dogs with MCTs in locations other than the inguinal or perineal region, a significant difference in DFI was found (median, 4.2 vs 33.9 months). This suggests that these specific sites in the inguinal region may be biologically different. However, the DFI curve for dogs with scrotal or preputial MCTs was not significantly different from the DFI curve for dogs with other inguinal or perineal MCTs. Thus, studies with larger numbers of dogs with tumors in these locations are needed.

Another challenge researchers have faced when evaluating prognosis for dogs with MCTs is defining relapse. In particular, it is difficult to determine the clinical importance of new cutaneous MCTs at locations that are distant from the primary MCT. In this study, relapse was defined as local recurrence at the site of the excised MCT, development of metastatic disease, or development of a new cutaneous MCT at a different location. Metastasis is a characteristic of biologically malignant neoplasms. Local recurrence secondary to infiltration would also be a characteristic of aggressive biologic behavior. However, local recurrence may also be a result of limitations of surgical excision, especially in sites such as the perineum. In the present study, 9 of 36 (25%) dogs with inguinal or perineal tumors were classified as having had a relapse because they developed another cutaneous MCT at a different site. Although this was not significantly different from the percentage of dogs with MCTs in other cutaneous locations that were classified as having had a relapse for this reason, no large studies have evaluated whether these additional cutaneous tumors are new random events or extensions of existing disease.[10,11,16,17] Therefore, it is questionable as to whether these dogs should be considered as having had a relapse.

Nonetheless, MCT location was not a significant predictor of relapse in the present study.

Prognostic factors that were shown to affect the risk of relapse in the present study included histologic grade and systemic treatment. Dogs with grade III MCTs were 2.5 times as likely to have a relapse as were dogs with grade I tumors, after controlling for type of treatment. Similarly, dogs that received systemic treatment were 4 times as likely to have a relapse as were dogs that received only local treatment, regardless of tumor grade. Similar treatment effects were seen in other studies[7,12] when investigators considered the inguinal or perineal sites to be historically poor and administered chemotherapy, regardless of tumor stage or grade. However, many of the dogs treated with chemotherapy in the present study were those with evidence of metastatic disease at the time of diagnosis and dogs with grade III tumors. Therefore, the fact that dogs that received chemotherapy were more likely to relapse was expected. Finally, dogs with incompletely excised MCTs were 2 times as likely to have a relapse as dogs in which tumor excision was complete.

In the present study, tumor location was not significantly associated with survival time. One- and 2-year survival probabilities were 77% and 65%, respectively, and compared favorably with probabilities reported previously. For instance, a previous study[9] reported 1- and 2-year survival rates of 76.2% and 73.2%, respectively, and a more recent study[12] of dogs with inguinal or perineal MCTs reported 1- and 2-year survival probabilities of 79% and 61%, respectively. A separate study[18] reported 1- and 2-year survival rates for dogs with MCTs of 73% and 50%, and another study[19] reported a 45% survival rate 210 days after surgery. Again, other investigators have not found the inguinal or perineal region to have a negative impact on survival time.[7,19]

Prognostic factors associated with survival time in the present study were age, metastatic disease at the time of initial diagnosis, and relapse after initial treatment. Dogs > 8 years old were 2.7 times as likely to die as were younger dogs. In this study, however, death was defined as death attributable to any cause, not just death secondary to an MCT. Thus, it was expected that older dogs would be more likely to die than younger ones. Dogs with evidence of metastatic disease at the time of diagnosis were 3.2 times as likely to die as were dogs without evidence of metastatic disease after controlling for age and tumor relapse. These findings are in agreement with findings of previous studies[9,20,21] that have shown clinical stage to be a reliable negative prognostic factor for survival time in dogs with MCTs. Finally, dogs with evidence of relapse were 2.5 times as likely to die as dogs without evidence of relapse. Tumor recurrence has also previously been shown to be a poor prognostic indicator for survival time in dogs with MCTs.[20]

In the present study, males were more likely to have an MCT in the inguinal or perineal region than in another cutaneous site. We believe that errors attributable to the retrospective nature of the present study and the poor anatomic boundaries of the inguinal and perineal regions may have resulted in fewer females being classified as having inguinal or perineal MCTs. Therefore, we suspect that there was not a true difference that could be attributed to sex alone. Estrogen receptors have been described in the tumor cells of a small number of dogs with cutaneous MCTs.[22] However, the role of sex steroids in this disease has yet to be investigated. There were too few sexually intact dogs in the present study to further analyze any possible effects of sex steroids on outcome.

In the present study, 8 of the 21 (38%) dogs with an MCT of the inguinal or perineal region that had a relapse had a local recurrence, developed a new cutaneous MCT at a distant site, or both. Similarly, 27 of the 37 (73%) dogs with an MCT in another cutaneous site that had a relapse had a local recurrence, developed a new cutaneous MCT at a distant site, or both. Few dogs in either group had evidence of regional lymph node metastasis, and only 1 dog had evidence of distant metastasis. The standard treatment for local recurrence of an MCT or development of a new cutaneous MCT would involve additional surgery or radiation therapy. In contrast, chemotherapy is used to prevent systemic spread of disease. The fact that dogs in this study with MCTs in the inguinal or perineal region were often treated with systemic chemotherapy, despite a lack of dogs with systemic disease, clearly reveals a treatment bias in the study population. Given the lack of proof that new cutaneous MCTs are true metastases and the fact that dogs grouped on the basis of tumor location in the present study had similar recurrence rates and survival times, it is difficult to justify the use of chemotherapy in these dogs. In addition, results of a previous study[12] suggested that toxicoses associated with lomustine administration may have outweighed any potential benefits of the drug in dogs with MCTs for which local treatment was still an option. Given the risks associated with chemotherapy, it is difficult to justify treating dogs with inguinal or perineal MCTs more aggressively than is dictated by other well-known and proven prognostic factors, such as tumor grade and clinical stage, until more evidence that tumors in these regions are biologically more aggressive is documented.

Alternatively, we must also consider the possibility that it was the effectiveness of the additional chemotherapy that dogs in the present study with MCTs in the inguinal or perineal region received that prevented the development of distant metastases. These additional treatments, if in fact beneficial, may have also prolonged both the DFI and the survival time so that we were not able to identify differences between this group and the group of dogs with MCTs in other cutaneous locations. However, regardless of the type of treatment (systemic vs local), there was no significant difference in DFI or survival times between dogs with and without inguinal or perineal tumors. Similarly, after controlling for tumor grade and treatment type in the multivariate models, tumor location was not significantly associated with DFI or survival time. These findings do not rule out the possibility that bias in selection of dogs with inguinal or perineal tumors affected our ability to detect differences in outcome between groups. However, given that most dogs in

both groups received local treatment, the impact of this bias seems low. Nevertheless, our results must be interpreted with the study's limitations in mind. Additional limitations include the retrospective design of the study and the small sample size. Small sample size alone can make finding a significant difference between 2 groups with many confounding variables challenging. For this reason, a relatively large number of dogs with MCTs in locations other than the inguinal or perineal region were included in the study to help increase statistical power. Despite this, statistical power calculations following completion of the study indicated powers of approximately 65% and 73%, respectively, to detect true differences in the DFI and survival curves between dogs with inguinal or perineal tumors and dogs with tumors in other locations.

Results of the present study suggest that, contrary to prior beliefs, dogs with MCTs in the inguinal or perineal region do not have an inherently poorer prognosis than do dogs with MCTs in other cutaneous locations. Many of these dogs that have a relapse will have a local recurrence or develop additional MCTs at distant cutaneous sites. Therefore, treatment recommendations should focus on addressing these potential complications, and the question of whether systemic chemotherapy is indicated for these dogs remains unanswered.

a. Statistix, Analytical Software, Tallahassee, Fla.
b. Egret for Windows, Cytel Software Corp, Cambridge, Mass.

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Correction: What Is Your Neurologic Diagnosis?

In the article "What Is Your Neurologic Diagnosis?," published in the March 1, 2005, issue (2005;226:699–701), the units of measure are incorrect in the test results under serum thyroid hormone analyses on page 700. The sentence with the correct units should read "Thyroxine concentration, 14 nmol/L (reference range, 20 to 55 nmol/L); free thyroxine concentration, 11 pmol/L (reference range, 15 to 45 pmol/L); and thyrotropin concentration, 0.2 ng/mL (reference range, < 0.5 ng/mL)."