Survival times in dogs with right atrial hemangiosarcoma treated by means of surgical resection with or without adjuvant chemotherapy: 23 cases (1986–2000)

Chick Weisse, VMD; Nancy Soares, VMD; Matthew W. Beal, DVM; Michele A. Steffey, DVM; Kenneth J. Drobatz, DVM; Carolyn J. Henry, DVM

Objective—To determine survival times in dogs with right atrial hemangiosarcoma treated by means of pericardectomy and tumor resection, with or without adjuvant chemotherapy, and identify complications associated with treatment.

Design—Retrospective study.

Animals—23 dogs.

Procedure—Dogs were included only if the diagnosis was confirmed histologically.

Results—The most common initial complaints included acute collapse (8 [35%] dogs), anorexia or inappetence (8 [35%]), and lethargy (8 [35%]). The most common physical examination abnormalities included muffled heart sounds (12 [52%] dogs), tachycardia (7 [30%]), and weak pulses (7 [30%]). Postoperative complications developed in 12 (52%) dogs; however, most complications were minor. Twenty (87%) dogs were discharged from the hospital. Survival time was significantly longer in the 8 dogs that received adjuvant chemotherapy (mean, 164 days; median, 175 days) than in the 15 dogs that did not receive chemotherapy (mean, 46 days; median, 42 days). Dogs that received chemotherapy were significantly younger and had significantly lower WBC counts than did dogs that did not receive chemotherapy.

Conclusions and Clinical Relevance—Results suggested that in dogs with right atrial hemangiosarcoma, surgical resection of the tumor was associated with a low complication rate and complications that did arise typically were minor. In addition, use of adjuvant chemotherapy following resection was associated with significantly longer survival times, compared with resection alone. (J Am Vet Med Assoc 2005;226:575–579)

Hemangiosarcomas (HSAs) are aggressive, malignant tumors of endothelial cell origin that can potentially develop in any vascularized site in the body. Previous reports document tumor recurrence rates and survival times in dogs following surgical resection and chemotherapy of splenic and subcutaneous HSAs. In contrast, little information is available concerning the outcome of dogs with right atrial HSAs. One study reported survival times of 1 and 4 months in 2 dogs with right atrial HSA treated with pericardectomy alone. Similarly, 3 studies involving a total of 14 dogs with right atrial HSA that underwent pericardectomy and tumor resection reported survival times ranging from 2 days to 8 months. Five of these dogs died of confirmed metastatic disease without evidence of local tumor recurrence; the remaining 9 died of suspected metastatic disease. None of these 14 dogs received adjuvant chemotherapy. An additional 2 dogs with right atrial HSA that underwent pericardectomy and tumor resection received adjuvant chemotherapy because gross metastatic disease was identified at the time of surgery; survival times for these 2 dogs were between 3 and 5 months. Finally, a single dog with right atrioventricular junctional HSA treated with chemotherapy alone survived for at least 4 months but subsequently died of metastatic disease.

Metastasis typically occurs early in the course of disease in dogs with right atrial HSA. Therefore, surgical resection is considered only palliative. Because of this and the relatively short survival times that have been reported, clinicians often recommend only subtotal pericardectomy for palliation of cardiac tamponade associated with pericardial effusion, rather than tumor resection, for dogs with cardiac HSA. Unfortunately, although most affected dogs die of metastatic disease, dogs in previous studies generally did not receive adjuvant chemotherapy, even though chemotherapy has been shown to prolong survival times in dogs with splenic HSA. In addition, completeness of tumor resection and complete tumor staging have rarely been addressed.

The purposes of the study reported here were to determine survival times in dogs with right atrial HSA treated by means of pericardectomy and tumor resection, with or without adjuvant chemotherapy, and identify complications associated with treatment.

Criteria for Selection of Cases

Medical records of all dogs examined at the Veterinary Hospital of the University of Pennsylvania between 1986 and 2000 in which a diagnosis of cardiac...
HSA had been made were reviewed. In addition, the Veterinary Medical Data Base at Purdue University was searched to identify dogs with histologically confirmed cardiac HSA.

Dogs were included in the study if the diagnosis of cardiac HSA was confirmed histologically. Dogs were excluded if biopsy specimens were obtained at necropsy; the origin of the tumor was not identified as the right atrium, right auricle, or right atrial appendage; another tumor had been identified previously; or follow-up information was not available.

**Procedure**

Medical records of dogs identified through the Veterinary Medical Data Base were obtained by contacting the medical records department of the submitting institution. Information obtained from the medical records included breed; age; sex; date of initial examination; initial complaint; physical examination findings; results of clinicopathologic testing; abdominal and thoracic radiography; abdominal and cardiac ultrasonography; and pericardiocentesis; date of surgery; surgical procedures performed (eg, surgical approach and resection technique); operative and postoperative complications; postoperative treatment; results of histologic examination of biopsy specimens; discharge date; chemotherapy protocol, including date chemotherapy was initiated; date of death, necropsy results; and time from surgery to death. Follow-up information was obtained through telephone or mail contact with owners and referring veterinarians or both. All dogs were followed up until the time of death.

**Statistical analyses**—Continuous variables were assessed for normality by means of visual inspection of graphically displayed data and the Shapiro-Wilk test. A Wilcoxon rank sum test or unpaired t test was used to compare continuous variables between groups, depending on data distribution. The Fisher exact test was used to compare categorical variables between groups. For survival analyses, Kaplan-Meier curves were generated and the log-rank test was used to compare median survival times between groups. For all analyses, values of \( P < 0.05 \) were considered significant. Standard software was used for all statistical analyses.

**Results**

Twenty-three dogs with right atrial HSA that had undergone surgical resection of the tumor fulfilled the criteria for inclusion in the study. Dogs had been examined and treated at 10 hospitals, including the University of Pennsylvania, Michigan State University, the University of Minnesota, Cornell University, the University of Guelph, Florida State University, Iowa State University, the University of Illinois, the University of Missouri, and the Veterinary Referral Center of Little Falls, NJ.

Mean age of the dogs at the time of initial examination was 9.1 years (median, 9.1 years; range, 3.2 to 13.5 years). Seven (30%) dogs were sexually intact males, 7 (30%) were castrated males, and 9 (39%) were spayed females. There were 8 (33%) Golden Retrievers, 5 (22%) dogs of mixed breeding, 2 (9%) German Shepherd Dogs, 2 (9%) Labrador Retrievers, 2 (9%) Siberian Huskies, and 1 (4%) each of the following breeds: Bichon Frise, English Setter, Irish Setter, and Viszla.

Information regarding initial complaints was available for all 23 dogs. The most common initial complaints included acute collapse (8 [35%] dogs), anorexia or inappetence (8 [35%]), lethargy (8 [35%]), signs of respiratory difficulty (7 [30%]), and vomiting (7 [30%]).

Information on results of the initial physical examination was also available for all 23 dogs. The most common physical examination abnormalities included muffled heart sounds (12 [52%] dogs), tachycardia (7 [30%]), weak pulses (7 [30%]), pale mucous membranes (5 [22%]), signs of depression (5 [22%]), abdominal fluid wave (4 [17%]), increased respiratory effort (3 [13%]), dehydration (3 [13%]), recumbency (3 [13%]), and pulsus paradoxus (2 [9%]).

Results of an initial CBC and serum biochemical profile were available for 21 dogs. The most common hematologic abnormalities included high WBC count (12 [57%] dogs), a left shift (7 [33%]), anemia (6 [29%]), and low platelet count (5 [24%]). The most common biochemical abnormalities included high alanine aminotransferase activity (8 [38%] dogs), high BUN concentration (5 [24%]), high alkaline phosphatase activity (5 [24%]), and high aspartate aminotransferase activity (4 [19%]). Coagulation screening was performed in 16 dogs, and abnormalities were identified in 7 of the 16. Both the prothrombin time and partial thromboplastin time were prolonged in 3 dogs, the partial thromboplastin time alone was prolonged in 2 dogs, the prothrombin time alone was prolonged in 1 dog, and the activated clotting time was prolonged in 1 dog.

Results of abdominal radiography were available for 7 dogs. One dog had radiographic evidence of a possible splenic mass, and a second dog had radiographic evidence of a possible hepatic mass. Abdominal ultrasonography was performed in 18 dogs. Splenic nodules were identified in 4 dogs, a splenic mass was identified in 2 dogs, a renal mass was identified in 1 dog, enlargement of the liver and spleen were identified in 1 dog, prominent mesenteric lymph nodes were identified in 1 dog, and thickening of the stomach wall was identified in 1 dog. Results of thoracic radiography were available for 21 dogs. No evidence of pulmonary metastatic disease was seen.

Results of a cardiac examination were available for all 23 dogs. Nineteen (83%) dogs had pericardial effusion, 7 (30%) had cardiac tamponade, 5 (22%) had muffled heart sounds, 2 (9%) had cardiomegaly, and 2 (9%) had pleural effusions. In 11 (48%) dogs, cardiac masses were identified by means of echocardiography; 6 of the 11 reportedly had a right atrial mass, and 5 reportedly had a right atrial appendage mass. Reasons for surgery in the remaining 12 dogs were not readily apparent from the medical records.

Pericardiocentesis was performed in 21 dogs. Pericardiocentesis was performed 3 times in 1 (5%) dog, twice in 7 (33%) dogs, and once in 12 (57%) dogs. The remaining dog was reported to have had pericardiocentesis performed multiple times. Pericardial fluid from 5
dogs that underwent a median sternotomy and dogs that underwent a lateral thoracotomy were performed. In 10 dogs, a lateral thoracotomy was performed. The surgical approach was not described in the remaining 2 dogs. A right atrial mass was resected in 8 (35%) dogs, and a right atrial appendage mass was resected in 15 (65%). In 1 (4%) dog, metastatic pulmonary masses (multiple 3- to 5-mm-diameter masses) were identified grossly at the time of surgery. This dog did not receive chemotherapy and survived 82 days after surgery. In 1 (4%) dog, a metastatic cardiac lesion was suspected to be present but the lesion was not resected or biopsed. This dog did not receive chemotherapy and survived 135 days after surgery. Surgical margins, tumor grade, and tumor cell morphology were not routinely reported; however, pathology reports for 3 dogs indicated that surgical margins were incomplete. None of these 3 dogs received chemotherapy; survival times were 12, 56, and 68 days. A pericardectomy was performed in 21 (91%) dogs, and the pericardium was closed in 2 (9%) dogs. The 2 dogs in which the pericardium was closed did not receive chemotherapy and lived 23 and 138 days after surgery.

Mean and median survival times for the 8 dogs that underwent right atrial mass resection were 55 and 43 days, respectively (range, 1 to 147 days). Mean and median survival times for the 15 dogs that underwent right atrial appendage mass resection were 101 and 118 days, respectively (range, 0 to 229 days).

A splenectomy was performed in 3 (13%) dogs. In 2 of these 3 dogs, the splenectomy was performed at the time of right atrial mass resection, and in both, histologic examination of the spleen did not reveal any evidence of neoplastic cells. Both of these dogs received chemotherapy, and they survived 188 and 229 days. In the remaining dog, splenectomy was performed 7 days after resection of the primary tumor and histologic examination revealed that the spleen was infiltrated with HSA. This dog did not receive chemotherapy and survived 43 days.

Postoperative complications (ie, complications that developed within 7 days after surgery) were identified in 12 (52%) dogs; however, most complications were minor. Complications included signs of pain (3 [13%] dogs), cardiac arrhythmias (3 [13%]), wound dehiscence or infection (2 [9%]), hypovolemia (1 [4%]), anemia (1 [4%]), pneumonia requiring mechanical ventilation (1 [4%]), prolonged coagulation (1 [4%]), and premature removal of the chest tube (1 [4%]). None of the dogs with cardiac arrhythmias had undergone splenectomy. There was no significant difference in postoperative complication rates between dogs that underwent a median sternotomy and dogs that underwent a lateral thoracotomy. Postoperative complications occurred in 4 of the 8 dogs that received adjuvant chemotherapy and 8 of the 15 dogs that did not receive chemotherapy. Survival times for the 12 dogs that developed postoperative complications ranged from 0 to 228 days (mean, 94 days; median, 68 days).

Twenty (87%) dogs were discharged from the hospital, but the date of discharge was recorded for only 19. Mean and median times from surgery to discharge from the hospital for these 19 dogs were 3.5 and 3 days, respectively. The remaining 3 dogs died or were euthanatized without being discharged from the hospital. One of these dogs had a hemorrhagic thoracic effusion after surgery and developed disseminated intravascular coagulation. A second surgery was performed 2 hours after the first, but no cause of the bleeding could be identified, and the dog was euthanatized. The second dog had an episode of cardiac arrest while on a short walk 1 day after surgery and did not respond to cardiopulmonary resuscitation. The third dog required mechanical ventilation 80 minutes after surgery because of pneumonia and hypoxia; the dog was euthanatized later that day.

Eight (35%) dogs received adjuvant chemotherapy. Chemotherapy protocols included doxorubicin and cyclophosphamide in 3 dogs; doxorubicin alone in 3 dogs; and doxorubicin, cyclophosphamide, and vincristine in 1 dog. The chemotherapy protocol for the remaining dog was not specified in the medical record. One dog developed vomiting and diarrhea presumably associated with doxorubicin administration. Dogs receiving doxorubicin and cyclophosphamide survived 118, 162, and 228 days after surgery. The dogs receiving doxorubicin alone survived 12, 36, and 188 days after surgery. The dog receiving doxorubicin, cyclophosphamide, and vincristine survived 205 days after surgery. The mean number of cycles for the 7 dogs for which the chemotherapy protocol was specified was 3.4 cycles. Mean time to initiation of adjuvant chemotherapy in these 7 dogs was 34 days. However, 1 dog did not receive chemotherapy until evidence of tumor recurrence was apparent 104 days after surgery.

Mean time to initiation of adjuvant chemotherapy in the other 6 dogs was 23 days.

Information regarding the cause of death was available for 16 of the 20 dogs discharged from the hospital. Fifteen dogs were euthanatized, and 1 dog died. Necropsy results were available for 5 of these dogs, all of which were reported to have diffuse, multiple-organ HSA at the time of death. The presence or absence of local tumor recurrence was not routinely reported. Mean and median survival times (ie, time from surgery to death) for all dogs were 87 and 56 days, respectively (range, 0 to 229 days; Figure 1). Mean and median survival times for the 15 dogs not receiving adjuvant chemotherapy were 46 and 42 days, respectively (range, 0 to 138 days; Figure 2). Mean and median survival times for the 9 dogs not receiving adjuvant chemotherapy that did not have gross evidence of thoracic metastatic disease and did not have incomplete surgical margins reported were 43 and 42 days, respectively (range, 0 to 138 days). Mean and median survival times were 82 and 56 days, respectively (range, 0 to 228 days).
for the 8 dogs receiving adjuvant chemotherapy were 164 and 175 days, respectively (range, 36 to 229 days). Mean and median survival times for the 8 dogs not receiving adjuvant chemotherapy and surviving at least 23 days (ie, mean time to initiation of adjuvant chemotherapy) were 77 and 62 days, respectively.

Statistical analysis indicated that survival time was significantly ($P < 0.001$) longer for dogs that received adjuvant chemotherapy than for dogs that did not. No significant differences were identified between dogs that did and did not receive adjuvant chemotherapy in regards to pretreatment PCV, total solids concentration, platelet count, creatinine concentration, serum alkaline phosphatase activity, alanine aminotransferase activity, or aspartate aminotransferase activity. However, WBC count was significantly ($P = 0.021$) higher in dogs that did not receive chemotherapy (mean WBC count, $24.5 \times 10^3$ cells/µL; range, 17.2 to $37.7 \times 10^3$ cells/µL) than in dogs that did receive chemotherapy (mean, $11.0 \times 10^3$ cells/µL; range, 2.1 to $19.1 \times 10^3$ cells/µL). In addition, dogs that did not receive chemotherapy were significantly ($P = 0.016$) older (mean age, 9.9 years; range, 8 to 13.4 years) than dogs that did receive chemotherapy (mean age, 7.5 years; range, 3.2 to 11.4 years).

**Discussion**

Results of the present study suggest that in dogs with right atrial HSA, surgical resection of the tumor was associated with a low complication rate and complications that did arise typically were minor. In addition, use of adjuvant chemotherapy following resection was associated with significantly longer survival times, compared with resection alone.

As with any retrospective study, the present study had certain limitations. No control group was available, a uniform treatment protocol was not followed, and the reason surgery was pursued was often not available. It is possible that dogs in the present study were healthier overall than dogs with right atrial HSA in general. In addition, it was difficult to evaluate the effects of adjuvant chemotherapy because important information regarding tumor staging, completeness of tumor resection, and concurrent conditions for dogs receiving chemotherapy versus dogs that did not was not always readily available. Nevertheless, of the variables that could be compared between groups (PCV, total solids concentration, platelet count, creatinine concentration, serum alkaline phosphatase activity, alanine aminotransferase activity, aspartate aminotransferase activity, WBC count, and age), only WBC count and age differed significantly between dogs that received adjuvant chemotherapy and dogs that did not. It is difficult to determine retrospectively the cause of the difference in WBC count between groups and whether this difference had any effect on prognosis. There were not enough dogs with band neutrophils to perform statistical analyses. Dogs that did not receive chemotherapy were significantly older than dogs that did, but it seems unlikely that concurrent, age-related diseases contributed substantially to the shorter survival times for dogs that did not receive chemotherapy. It is possible, however, that owners of older animals were less inclined to pursue chemotherapy.

In the present study, a right atrial mass was seen ultrasonographically in only 11 of the 23 (48%) dogs. This is consistent with result of previous studies, which reported poor sensitivity of this imaging modality. In those studies, only 14% to 17% of masses were identified ultrasonographically. Pericardial fluid pH was $> 7.0$ in 5 of 6 dogs in the present study, supporting findings of a previous study in which pericardial fluid pH $\geq 7.0$ was identified in 39 of 42 (93%) animals with neoplasia.

Although dogs that underwent right atrial appendage mass resection appeared to have longer survival times than dogs that underwent right atrial mass resection in the present study, nomenclature in the surgical reports was ambiguous and could therefore not be critically evaluated. Surgical approach did not appear to have any significant impact on outcome and should therefore be left to surgeon preference.

Postoperative complications in these dogs were common; however, most were minor and not life threatening. In addition, dogs were discharged a median of 3 days after surgery. Considering these dogs had
undergone thoracotomy and cardiac surgery for tumor excision, prolonged hospitalization, pain, and potential complications should not be considered a deterrent to surgery.

Although only a small group of dogs was included in this study, sufficient numbers were available to identify a significant improvement in survival times when adjuvant chemotherapy was used. No standardized chemotherapeutic protocol was used; however, all available protocols included doxorubicin. Survival times for these dogs were similar to those reported for dogs with splenic HSA that underwent surgery and adjuvant chemotherapy.1,2 Considering the relatively short convalescent times, minimal serious complications, and more encouraging survival times, more owners might be willing to pursue surgery and chemotherapy. Contemporary imaging modalities such as cardiac-gated magnetic resonance imaging are currently being investigated to better identify cardiac neoplasia and determine preoperatively whether these tumors can be readily excised.3

References

Selected abstract for JAVMA readers from the American Journal of Veterinary Research

Glucose, lactate, and pyruvate concentrations in dogs with babesiosis

Linda S. Jacobson and Remo G. Lobetti

**Objective**—To document changes in glucose, lactate, and pyruvate concentrations in dogs with severe or complicated babesiosis; assess relationships among glucose, lactate, and pyruvate concentrations in those dogs; and compare clinical and laboratory variables in dogs with and without hypoglycemia and hyperlactatemia.

**Animals**—20 dogs with naturally developing severe or complicated babesiosis.

**Procedure**—Samples and measurements were obtained before treatment was initiated. Babesiosis was diagnosed by examination of blood smears. Arterial blood pressure measurement, parasite quantification, CBC count, serum biochemical analysis, urinalysis, venous blood gas analysis, and acid-base determination were performed. Glucose, lactate, and pyruvate concentrations were measured in samples of venous blood.

**Results**—We detected a significant negative correlation between glucose and lactate concentrations. Glucose, lactate, and pyruvate concentrations all differed significantly between dogs that died and those that survived. Three of 5 dogs that died had concurrent hypoglycemia, hyperlactatemia, and hyperpyruvatemia. Hypoglycemic dogs differed significantly from normoglycemic dogs with regard to lactate, urea, and bicarbonate concentrations; lactate-to-pyruvate ratio; percentage parasitemia; and PCO2. Dogs with hyperlactatemia differed significantly from normolactatemic dogs with regard to clinical collapse; alanine transaminase activity; concentrations of bilirubin, urea, creatinine, and bicarbonate; percentage parasitemia; and PCO2.

**Conclusions and Clinical Relevance**—Abnormal carbohydrate metabolism is commonly evident in dogs with severe or complicated babesiosis and is often associated with changes in other clinical and laboratory variables. Significant differences were found between survivors and nonsurvivors. Hypoglycemia should be assessed and aggressively treated in dogs with babesiosis. Lactate concentration can be used as an indicator of disease severity. (*Am J Vet Res* 2005;66:244–250)