Evaluation of risk factors for outcome associated with adrenal gland tumors with or without invasion of the caudal vena cava and treated via adrenalectomy in dogs: 86 cases (1993–2009)

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Objective—To evaluate risk factors for outcome for dogs with adrenal gland tumors with or without invasion of the caudal vena cava treated via adrenalectomy.

Design—Retrospective study.

Animals—86 dogs that underwent adrenalectomy for treatment of adrenal gland tumors.

Procedures—Medical records of dogs that underwent adrenalectomy for treatment of an adrenal gland tumor from 1993 to 2009 were reviewed; data collected including signalment, clinical signs, diagnostic test findings, treatments prior to surgery, findings at surgery including additional procedures performed and extent of caudal vena caval invasion (local invasion [caudal to the hepatic portion of the vena cava] or extensive invasion [cranial to the hepatic portion of the vena cava]), procedures performed during surgery, histopathologic diagnosis, perioperative complications, follow-up data, and necropsy findings.

Results—Of the 86 dogs, 14 had adenomas, 45 had adrenocortical carcinomas, and 27 had pheochromocytomas. Fourteen dogs had invasion of the caudal vena cava; of these tumors, 7 were locally invasive and 7 were extensively invasive. Risk factors for poor short-term survival (death within 14 days following surgery) were vena caval invasion, extent of invasion, pheochromocytoma, intraoperative transfusion, and postoperative factors including disseminated intravascular coagulation, pancreatitis, hypotension, hypoxemia, and renal failure. Multivariate analysis of risk factors for poor short-term survival revealed that extensive invasion was the most important factor. Regardless of extent of invasion or tumor type, long-term survival was possible.

Conclusions and Clinical Relevance—Invasion of the caudal vena cava, particularly tumor thrombus extension beyond the hepatic hilus, was associated with a higher postoperative mortality rate, but did not affect long-term prognosis in dogs undergoing adrenalectomy because of an adrenal gland tumor. (*J Am Vet Med Assoc* 2013;242:1715–1721)

Adrenal gland tumors are rare in dogs, comprising 1% to 2% of all canine tumors.[1] The most common tumor types include adrenocortical adenoma, adrenocortical carcinoma, and pheochromocytoma.[1–5] Adrenocortical tumors may or may not be cortisol secreting, which may lead to clinical signs of hyperadrenocorticism.[1,2,6] For dogs with clinical signs attributable to an adrenal gland tumor, adrenalectomy is the gold-standard treatment.[1–6]

Invasion of the caudal vena cava by adrenal gland tumors has been reported to occur in 9.5% to 46% of cases.[6] In the past, vena caval invasion was often determined to be inoperable or to be associated with a poor prognosis. However, more recent reports[7,8] indicate that tumor invasion into the caudal vena cava may not affect short-term survival rate. Kyles et al[7] reported that adrenalectomy for tumors with associated vena caval thrombi does not result in substantially higher perioperative morbidity and mortality rates, compared with surgery in dogs without inva-

ABBREVIATIONS

CI	Confidence interval
DIC	Disseminated intravascular coagulation

sion. Those data are in agreement with the prognosis in humans with adrenal gland tumors; the presence of vena caval thrombi does not lead to a poorer prognosis.[9]

The purpose of the study reported here was to evaluate risk factors associated with short-term and long-term outcome for adrenal gland tumors with or without invasion of the caudal vena cava and treated via adrenalectomy in dogs. The hypothesis was that vena caval invasion would have no association with short- or long-term survival rate of dogs surgically treated for adrenal tumors.

Materials and Methods

Case selection criteria—Medical records of dogs that were treated for an adrenal gland tumor via adrenalectomy at Colorado State University Veterinary Teaching Hospital from 1993 to 2009 were reviewed. Criteria for inclusion were adrenalectomy and histologic diagnosis of an adrenal tumor.

Medical records review—Surgical report evaluation was performed, and dogs were subsequently allocated to a no vena caval invasion group and a vena caval invasion group. Involvement of the caudal vena cava was defined as invasion into the caudal vena cava. For the vena caval invasion group, subgroups were formed on the basis of the severity of caval tumor thrombosis as tumor thrombi extending caudal to (local invasion) or cranial to (extensive invasion) the hepatic portion of the vena cava.

The following preoperative data were collected from the medical records: signalment, clinical signs, CBC, serum biochemical analyses, results of endocrine testing, radiography and abdominal ultrasonography findings, and use of phenoxybenzamine. Diagnosis of hyperadrenocorticism was made on the basis of adrenal gland function testing, including the ACTH stimulation test, low- and high-dose dexamethasone suppression tests, and measurement of endogenous serum ACTH concentrations.

Intraoperative data collected included surgical findings, including degree of invasion of the vena cava as defined, anesthetic complications, surgical complications, and additional surgical procedures performed. Postoperative data collected included complications and medications. The diagnosis of DIC was made on the basis of the presence of at least 3 of the following findings: thrombocytopenia, increased prothrombin time, increased activated partial thromboplastin time, decreased antithrombin III activity, presence of D-dimers, and increased fibrin degradation products, compared with reference ranges.[10] A diagnosis of pancreatitis was made on the basis of clinical signs plus suggestive ultrasonographic findings or high serum canine pancreatic lipase immunoreactivity.

Histopathologic specimens were reviewed by board-certified pathologists and were classified as adrenocortical adenoma, adrenocortical carcinoma, or pheochromocytoma. Histopathologic criteria for malignancy of adrenocortical tumors included evidence of invasion, as described.[11] In addition, mitotic rate, presence or absence of vascular invasion, and degree of nuclear pleomorphism were other criteria used to differentiate benign and malignant adrenocortical tumors.

Follow-up was performed by review of the medical record in combination with a telephone interview with the owner or the referring veterinarian. Short-term survival was defined as death within 14 days following surgery. Long-term survival was defined as survival > 14 days following surgery. Dogs that died from unrelated causes, were lost to follow-up, or were still alive were censored. Dogs that died or were euthanized because of their disease were not censored. Dogs that died within 14 days following surgery were not included in long-term survival rates.

Statistical analysis—Distributions of categorical data between groups were compared via χ^2 analysis, and continuous data were compared by use of ANOVA. Median survival rate and 1-, 2-, and 3-year survival rates were analyzed via actuarial Kaplan-Meier survival analysis. Cox proportional hazard univariate analysis was used to evaluate risk factors for short-term and long-term survival of dogs with different tumors as well as with and without invasion of the caudal vena cava. Factors that were significant at $P < 0.05$ following univariate analysis were entered into a proportional hazard multivariate analysis to further evaluate risk factors for short- and long-term survival. Data presented are mean ± SD values. Values of $P < 0.05$ were considered significant. Statistical software[a] was used to perform the analyses.

Results

For the period from 1993 through 2009, 86 dogs met the inclusion criteria. Fourteen dogs had an adrenocortical adenoma, 45 had an adrenocortical carcinoma, and 27 had a pheochromocytoma. Breeds represented among the dogs with an adrenocortical adenoma were mixed (n = 3), Labrador Retriever (2), Lhasa Apso (2), and 1 each of American Eskimo Dog, Beagle, Belgian Malinois, Cocker Spaniel–Poodle cross, Golden Retriever, Miniature Poodle, and Siberian Husky. Breeds represented among the dogs with adrenocortical carcinoma were Labrador Retriever (n = 8), mixed (7), German Shepherd Dog (3), Basset Hound (2), Beagle (2), Bichon Frise (2), Dachshund (2), German Shorthaired Pointer (2), Golden Retriever (2), and 1 each of Australian Cattle Dog, Boxer, Cocker Spaniel–Poodle cross, Cocker Spaniel, Collie, Corgi, Dalmatian, Keeshond, Maltese, Rhodesian Ridgeback, Saluki, Schipperke, Shih Tzu, Siberian Husky, and Standard Schnauzer. Breeds represented among dogs with pheochromocytoma were mixed (n = 6), Labrador Retriever (4), Siberian Husky (4), Rottweiler (3), and 1 each of Airdale Terrier, Australian Shepherd Dog, Beagle, Flat-Coated Retriever, Golden Retriever, Miniature Dachshund, Old English Sheepdog, Puli, Rhodesian Ridgeback, and Samoyed. Eighty dogs underwent surgery for a suspected adrenal gland tumor. Six dogs underwent surgery for other reasons, including 4 dogs with hemoabdomen, 1 dog with an abdominal mass, and 1 dog with a suspected insulinoma.

Preoperative data—Age and weight were not significantly different among dogs with the different tumor types (**Table 1**). Systolic and diastolic arterial blood pres-

Table 1—Results of univariate analysis of association of various factors with 3 adrenal gland tumor types in 86 dogs treated via adrenalectomy.

| Variable | Tumor type | | | P value |
	Pheochromocytoma	Adenoma	Carcinoma	
Age (y)	11.0 (10.1–11.8); n = 27	11.4 (10.1–12.5); n = 14	11.4 (10.8–12.1); n = 45	0.703
Weight (kg)	29.3 (24.5–34.1); n = 27	22.8 (16.1–29.5); n = 14	25.5 (21.8–29.2); n = 45	0.246
Systolic arterial blood pressure (mm Hg)	182.5 (166.1–198.9); n = 16	152.0 (105.7–198.3); n = 2	174.9 (158.5–191.2); n = 16	0.427
Mean arterial blood pressure (mm Hg)	143.4 (124.3–162.6); n = 7	—	113.6 (91.0–136.2); n = 5	0.049
Diastolic arterial blood pressure (mm Hg)	122.0 (100.8–143.2); n = 7	—	91.8 (66.7–116.9); n = 5	0.068

Values are mean (95% CI).
— = Not determined.

sures were also similar. Mean arterial blood pressure was significantly higher for dogs with pheochromocytoma than other tumor types. Fifteen dogs were treated with phenoxybenzamine for 1 to 2 weeks before surgery, including 6 dogs with pheochromocytomas and 9 dogs with adrenocortical carcinomas.[12] Three dogs with invasion of the vena cava received phenoxybenzamine.

Surgical findings—Fourteen dogs were in the vena caval invasion group, and 72 dogs were in the no vena caval invasion group. Thirteen of the 14 invasive adrenal gland tumors were pheochromocytomas, and 1 adrenocortical carcinoma was invasive ($P < 0.001$). Seven tumors were locally invasive, and 7 tumors had extensive invasion into and beyond the hepatic portion of the vena cava. Five left-sided tumors and 9 right-sided tumors invaded the caudal vena cava ($P = 0.833$).

Intraoperative complications—Seventy-one of the 86 dogs had intraoperative complications. Seven dogs died during surgery; of these, 6 had pheochromocytomas and 1 had an adrenocortical carcinoma. Five of the intraoperative deaths occurred in the vena caval invasion group; 4 of these dogs had extensive invasion. One patient with local invasion and 2 dogs in the no vena caval invasion group died during surgery. Intraoperative death was significantly ($P = 0.001$) more frequent in dogs with invasion of the vena cava (5/14) than for dogs without invasion of the vena cava (2/72). Causes for intraoperative death included persistent hemorrhage at the surgical site ($n = 2$), cardiac arrest (3), perceived lack of resectability of the tumor followed by euthanasia (1), and persistent severe hypotension unresponsive to all treatments (1). Perceived lack of resectability was determined in 1 patient because of an extensive and intravascularly adherent tumor thrombus (length, 20 cm) that extended to the level of the right atrium.

Intraoperative complications included hypotension in 53 dogs, blood loss requiring transfusion in 22 dogs, arrhythmias in 14 dogs, hypertension in 12 dogs, and hypoxia in 7 dogs. Twenty-five of 27 dogs with pheochromocytomas and 36 of 45 dogs with adrenocortical carcinomas had intraoperative complications ($P = 0.151$).

Postoperative phase—Of the 79 dogs that survived surgery, 34 had postoperative complications. Fifteen dogs died in the postoperative period. Causes of postoperative death included cardiorespiratory arrest for unknown underlying causes in 3 dogs, suspected DIC in 4, respiratory failure in 4, peritonitis in 3, and euthanasia because of renal failure in 1. Of the dogs with complications, 12 had a pheochromocytoma, 3 had an adenoma, and 19 had a carcinoma ($P = 0.132$). Complications occurred in 10 of the dogs in the vena caval invasion group and 28 of dogs in the no vena caval invasion group ($P = 0.063$). Complications encountered included vomiting or diarrhea in 18 dogs, hypotension in 13, hypoxemia in 8, DIC in 8, pancreatitis in 5, renal insufficiency in 4, and peritonitis in 4. Pancreatitis was suspected in 5 dogs in the short term, and side of surgery was not associated with the development of pancreatitis ($P = 0.113$), despite all 5 dogs that developed suspected pancreatitis having a left-sided adrenalectomy. Dogs in the vena caval invasion group were not more likely to develop pancreatitis ($P = 0.159$)

Short-term survival—Fifty-two dogs were known to have survived the short-term period; 22 dogs died in the short-term period, and 11 dogs were lost to follow-up at a median of 14 days (range, 1 to 14 days). Given that all dogs with adenomas survived and none of these were in the vena caval invasion group, they were excluded from short- and long-term survival analysis. Fourteen-day survival rates were 79% for carcinomas and 48% for pheochromocytomas ($P = 0.003$; **Figure 1**). Ten of the 22 dogs that died in the short-term period were in the vena caval invasion group. The proportion of dogs surviving at 14 days was significantly ($P < 0.001$) different (hazard ratio, 2.29) between the no vena caval invasion group (55/71 [77%]) and the vena caval invasion group (4/14; **Figure 2**). Of the 10 dogs in the vena caval invasion group that died in the short term, 7 had extensive invasion and 3 had local invasion. Short-term mortality rates were 43% for dogs with locally invasive tumors and 100% for dogs with extensively invasive tumors (**Figure 3**; hazard ratio, 4.43; $P < 0.001$).

Univariate preoperative factors associated with short-term survival (death within 14 days following surgery) included tumor type of pheochromocytoma, invasion of the caudal vena cava, and extensive invasion of the caudal vena cava (**Table 2**). Pretreatment
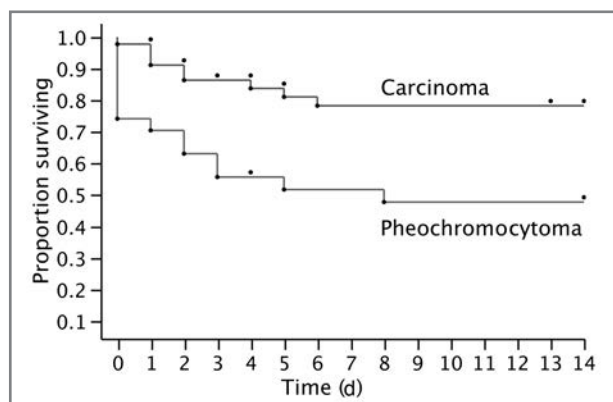

Figure 1—Kaplan-Meier survival analysis for short-term survival rate in 86 dogs treated via adrenalectomy for adrenal gland carcinoma or pheochromocytoma.
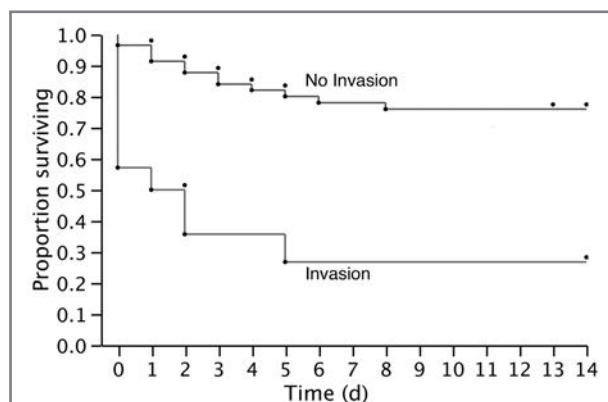

Figure 2—Kaplan-Meier survival analysis for short-term survival rate in dogs treated via adrenalectomy for adrenal gland tumors with or without invasion of the caudal vena cava.
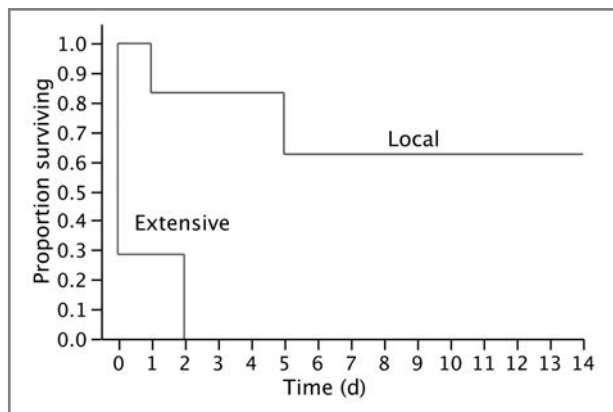
Figure 3—Kaplan-Meier survival analysis for short-term survival rate in dogs treated via adrenalectomy for adrenal gland tumors with local or extensive invasion of the caudal vena cava.
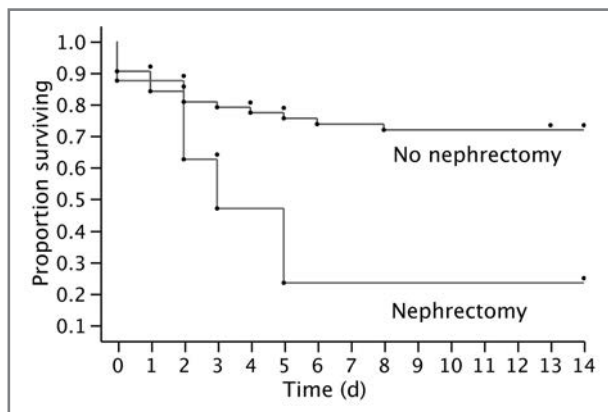

Figure 4—Kaplan-Meier survival analysis for short-term survival rate in dogs treated via adrenalectomy for adrenal gland tumors in which a nephrectomy was or was not performed.

Table 2—Results of univariate analysis of factors associated with short-term survival (death within 14 days following surgery) in dogs with adrenal gland tumors treated via adrenalectomy.

Factor	Hazard ratio	95% CI	P value
Tumor type (pheochromocytoma)	1.75	1.16–2.72	0.008
Vena caval invasion	2.29	1.48–3.48	< 0.001
Invasion extent	4.43	2.12–9.30	< 0.001
Anesthetic complications	1,300	$1.62–1.15 \times 10^{244}$	0.002
Transfusion during surgery	2.49	1.63–3.94	< 0.001
Postoperative complications	1.63	1.05–2.65	0.029
DIC after surgery	3.12	1.88–5.21	< 0.001
Pancreatitis after surgery	1.93	1.03–3.19	0.042
Hypotension after surgery	2.22	1.41–3.42	< 0.001
Hypoxemia after surgery	1.79	1.02–2.89	0.042
Renal failure after surgery	2.25	1.20–3.78	0.015

Table 3—Results of multivariate analysis of factors associated with short-term survival in dogs with adrenal gland tumors treated via adrenalectomy.

Factor	P value
Caval invasion and tumor type	0.003
Caval invasion	0.012
Tumor type (pheochromocytoma)	0.409
Extent of invasion and tumor type	0.001
Extent of invasion	< 0.001
Tumor type (pheochromocytoma)	0.192
Caval invasion and extent of invasion	0.001
Caval invasion	1.000
Extent of invasion	0.016

with phenoxybenzamine did not make a significant difference in short-term survival for adrenalectomies overall (*P* = 0.441) or for pheochromocytomas alone (hazard ratio, 1.42; *P* = 0.322). Univariate intraoperative factors associated with short-term survival included transfusion and blood loss.

Univariate postoperative factors associated with short-term survival were DIC, pancreatitis, hypoxemia, renal failure, and hypotension. Nephrectomy was not identified as a significant risk factor for decreased rate of survival for > 14 days (hazard ratio, 1.65, 95% CI, 0.95 to 2.63). However, the median survival time was significantly (*P* = 0.009) associated with nephrectomy (**Figure 4**). Nephrectomy was significantly (*P* = 0.001) associated with subsequent development of renal failure. Dogs with pheochromocytomas were significantly (*P* = 0.014) more likely to have DIC after surgery, compared with dogs with adrenocortical carcinomas. Additionally, dogs that received intraoperative transfusions with blood products were significantly (*P* = 0.003) more likely to develop postoperative DIC. The rate of hypoxemia was not significantly different among tumor types (*P* = 0.678) or between the vena caval invasion and no vena caval invasion groups (*P* = 0.057). Twenty-seven dogs in the study, including 3 dogs with adenomas, 5 dogs with pheochromocytomas, and 19 dogs with adrenocortical carcinomas, were treated with heparin during or after surgery. Administration of heparin was not associated with short-term survival rate (*P* = 0.847).

Multivariate analysis was performed to evaluate the effect of identified significant univariate factors on the outcome for dogs in the vena caval invasion and no vena caval invasion groups. When the vena caval invasion group was evaluated on the basis of adrenocortical adenocarcinoma versus pheochromocytoma tumor type, invasion of the vena cava remained significant but tumor type was no longer a significant risk factor (**Table 3**). When the extent of vena caval invasion was evaluated on the basis of adrenocortical adenocarcinoma versus pheochromocytoma tumor type, extent of the tumor thrombus was still significant but the tumor type was no longer a significant risk factor. When the vena caval invasion group was evaluated by the extent of the tumor thrombus, extent of the tumor thrombus remained significant but invasion of the vena cava was no longer a significant risk factor.

Long-term survival—Fifty-two dogs survived > 14 days. Of these, 10 were lost to follow-up at a median of 6.1 months (range, 0.6 to 49.2 months). For those not lost to follow-up, median follow-up time was 16.9 months (range, 0.5 to 54.5 months). The median survival time for dogs with adrenocortical carcinomas was 48 months (95% CI, 38.1 to 54.5 months) and was not reached for dogs with pheochromocytomas (*P* = 0.003; **Figure 5**). One-, 2-, and 3-year survival rates were 88% for carcinomas and 83%, 60%, and 60%, respectively, for pheochromocytomas.

For dogs with adrenocortical adenomas, median follow-up time was 26.3 months (range, 0.56 to 49.2
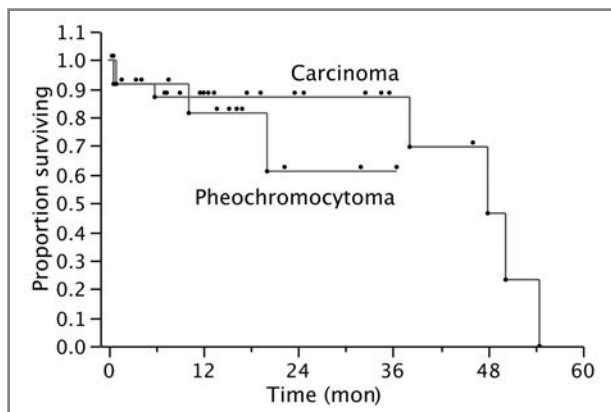
Figure 5—Kaplan-Meier survival analysis for long-term survival rate in dogs treated via adrenalectomy for adrenal gland carcinoma or pheochromocytoma.
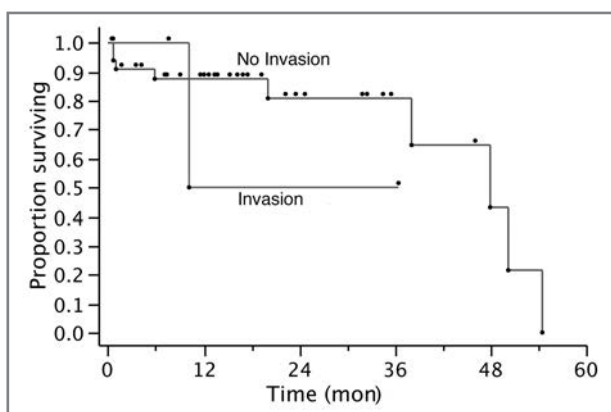

Figure 6—Kaplan-Meier survival analysis for long-term survival rate in dogs treated via adrenalectomy for adrenal gland tumors with or without invasion of the caudal vena cava.

months). Four dogs were lost to follow-up at 0.5, 0.9, 5, and 49 months after surgery. All but 1 dog had long-term resolution of clinical signs, and this dog had recurrence of polyuria and polydipsia and was euthanized; necropsy revealed growth of an adrenocortical carcinoma in the previous tumor site.

For dogs with adrenocortical carcinomas, median follow-up time was 12.7 months (range, 0.5 to 54.5 months). Six dogs were lost to follow-up at a median of 7.1 months (range, 0.7 to 24.7 months). Nineteen dogs had long-term resolution of clinical signs, and 8 had recurrence of signs. Metastasis was suspected in 6 of these dogs on the basis of clinical signs and imaging findings but not confirmed with histopathologic findings in any patient. Confirmed metastasis in the long-term period was found in 3 dogs with adrenocortical carcinoma to the liver (2 dogs) and small intestines (1 dog). Metastasis to the liver or lungs was suspected in an additional 7 dogs with adrenocortical carcinoma.

For dogs with pheochromocytomas, median follow-up time was 15.8 months (range, 1.0 to 36.5 months). Twelve of these 13 dogs had resolution of their clinical signs. One dog developed weakness, anorexia, and suspected lung metastasis 10 months after surgery and was euthanized. Necropsy revealed vertebral metastasis with pulmonary adenocarcinoma and disseminated plasma cell tumor; it was not clear which tumor was secondary.

Confirmed metastasis in the long-term period was found in 3 dogs with a pheochromocytoma to the vertebrae, lungs, and liver. Metastasis to the lungs was suspected in an additional 2 dogs with pheochromocytoma.

Three of the 52 dogs that survived into the long-term period were in the vena caval invasion group and all had pheochromocytomas. No significant (P = 0.4544) difference was seen in long-term survival rate between dogs with and without vena caval invasion (**Figure 6**). Median survival time for dogs without vena caval invasion was 48 months (95% CI, 38.1 to 54.5 months) and was not reached for dogs with vena caval invasion. No factors were significant for long-term survival rate as determined via univariate analysis.

Discussion

Adrenalectomy for tumors that invade the caudal vena cava was associated with a higher perioperative mortality rate, particularly if invasion was extensive, compared with tumors that did not invade the caudal vena cava in the present study. Because invasion of the caudal vena cava is much more common in dogs with pheochromocytoma, their short-term prognosis is affected. However, after correcting for invasion of the vena cava, the short-term prognosis for dogs with pheochromocytoma was not different than for dogs with adrenocortical adenocarcinoma. Long-term survival rate in dogs that survived the perioperative period was not associated with invasion of the vena cava at the time of surgery. The population of dogs in the study was similar in signalment, body weight, history, and clinical signs to populations in previous studies.[7,8,13] Age, body weight, sex, and breed were not significantly different among dogs with various tumor types and between the vena caval invasion and no vena caval invasion groups. A significant difference in the mean arterial blood pressure of dogs with pheochromocytomas was not detected, compared with other tumor types, which can be explained by catecholamine surges in patients with pheochromocytoma. In a study on adrenalectomy with and without vena caval thrombi, Kyles et al[7] found a similar distribution of invasion of the vena cava as in the population of the present study. Schwartz et al[13] reported a population with less invasion of the vena cava than in the population of the present study. In the present study, 50% of the cases of invasion of the vena cava were classified as extensive (extending to the hepatic vena cava or beyond), whereas it was 20%[7] or none[14] in other studies. In dogs that survived long term, metastasis was histologically confirmed in 11% of dogs with pheochromocytomas and in 6% of dogs with adrenocortical carcinoma. Although this rate is lower than in previous studies,[14–16] it likely reflected the low number of necropsies performed in long-term surviving dogs. Metastasis was suspected on the basis of clinical signs and diagnostic testing (thoracic radiography and abdominal ultrasonography) in an additional number of dogs. If these were included, metastatic rate would be 18% in dogs with pheochromocytomas and 22% in dogs with adrenocortical carcinomas.

Invasion of the caudal vena cava and extent of the tumor thrombus were risk factors for death in the short term in the population reported here. However, caval

invasion was not a risk factor for death in the long term. Dogs with caval thrombi extending cranial to the hepatic hilus were > 4 times as likely to die during the short-term period as were dogs with thrombi that did not extend past the hilus. Pheochromocytomas were significantly more likely to invade the caudal vena cava, compared with other tumor types, and all of the extensively invasive tumors were pheochromocytomas. Previous studies[7,8,12–15] have also identified the prevalence of pheochromocytomas for local vascular invasion at a rate ranging from 15% to 55%. This is in comparison to an invasion rate for adrenocortical carcinomas of 11% to 21.5%.[6,7,11,12,14] Invasion in the present study was a significant perioperative risk factor because half of these cases were extensively invasive. Surgical treatment for extensive invasion involves a greater degree of surgical invasiveness and cardiovascular compromise: inflow occlusion must be complete (vs partial occlusion options for small locally invasive tumors) and may require a greater duration of inflow occlusion and more manipulation of the pheochromocytoma, resulting in the release of catecholamines and increased risk of anesthetic instability.

Intraoperative mortality rate was 8%, and the short-term mortality rate was 25%. This finding is similar to results described in the most recent reports[12–14,17] on adrenalectomy. Only 48% of dogs with pheochromocytomas in the present study survived the short-term period, in comparison to 81% reported by Kyles et al.[7] This difference was likely attributable to the fact that 7 of the dogs with pheochromocytomas had tumor thrombi that extended into the hepatic vena cava (extensive invasion). After adjusting for presence of a tumor thrombus or the extent of the tumor thrombus in the vena cava, pheochromocytomas did not have a worse prognosis than did adenocarcinomas. All 7 of these dogs died in the perioperative period, and they accounted for more than one-quarter of the dogs with pheochromocytoma. The short-term mortality rate for adrenal tumors invading the caudal vena cava was 72%. Kyles et al[7] reported a 30% perioperative (between surgery and time of discharge) mortality rate for dogs with vena caval thrombi; those data are favorable, compared with our data, but the difference is likely reflective of the extent of the thrombi. When invasion of the vena cava was adjusted for the extent of the tumor, invasion of the vena cava was no longer a risk factor for death in the short term, which is in agreement with the findings of Kyles et al.[7] Kyles et al[7] reported 8 of 10 invasive tumors as locally invasive and 2 of 10 as extensively invasive, compared with our series, in which 7 of dogs with invasive tumors had local invasion and 7 had extensive invasion.

Nephrectomy was not directly identified as a risk factor in the present study. However, median survival time was negatively affected because it was associated with development of renal failure, and renal failure was identified as a risk factor for death in the short term. Nephrectomy was identified as a negative prognostic factor by Schwartz et al,[13] with a hazard ratio of 142; however, nephrectomy was not identified as a direct risk factor for decreased survival rate in the present study. Nephrectomy was performed if the tumor was

invading the kidney or renal vein or wrapping around the renal vein. Although presurgical renal values may have been within reference range in these dogs, many of them were older dogs that could have had subclinical renal insufficiency or sustained or paroxysmal hypertension, which would mask renal insufficiency. Because the dogs with unilateral nephrectomy were more at risk for renal failure after surgery and because renal failure was identified as a significant risk factor for decreased short-term survival rate, we recommend diagnostic evaluation for adrenal gland tumor involvement of the kidney or renal vasculature and measurement of glomerular filtration rate if nephrectomy may be needed.

Similar to the study by Schwartz et al,[13] the present study identified development of postoperative pancreatitis as a significant risk factor for decreased short-term survival rate. Manipulation of the pancreas and episodes of hypotension during surgery are factors that can induce development of pancreatitis. However, in the present study, pancreatitis was not more common in dogs with vena caval invasion, even though vena caval invasion is associated with hypotension. Also, pancreatitis was not more common in dogs with right-sided adrenalectomy, which requires greater manipulation of the pancreas. This finding was also in agreement with those of Schwartz et al.[13]

Disseminated intravascular coagulation was a significant risk factor for decreased short-term survival rate and was significantly more likely to occur in dogs with pheochromocytoma and dogs receiving intraoperative transfusions of blood or blood products. Because DIC was not significantly more likely in dogs with vena caval thrombi, the finding was not likely confounded by the number of cases of pheochromocytoma with caval invasion. Pheochromocytoma could contribute to postoperative DIC via catecholamine surges occurring during surgery.[18] Transfusion could contribute to increased risk of DIC either because the dog was entering DIC during surgery and required transfusion or because coagulation factors administered via plasma could contribute to entering the early, hypercoagulable state of DIC.[10] Additionally, massive transfusion (replacement of entire blood volume) could contribute to development of DIC via depletion of fibrinogen and coagulation factors.[19]

Hypoxemia was identified as a significant risk factor for death in the short term in the present study. Possible causes for hypoxemia in dogs with postoperative adrenalectomy include pulmonary thromboembolism, hypoventilation, aspiration pneumonia, atelectasis, and unrelated underlying pulmonary pathological changes. Because this was a retrospective study, we could not differentiate among the different causes of hypoxemia. Pulmonary thromboembolism may be tentatively diagnosed on the basis of hypoxemia, increased alveolar-to-arterial oxygen tension gradient, and the response to oxygen administration.[20] Thoracic radiographs may or may not reveal changes such as wedge-shaped, pleural-based densities.[20] Computed tomographic angiography is currently the gold-standard diagnostic test in human medicine.[20] We were unable to identify a significant association between tumor type and postoperative development of hypoxemia or between invasion status

and postoperative hypoxemia. The protective effect of heparin against development of pulmonary thromboembolism could not be evaluated in this study owing to its retrospective nature. Heparin was administered mostly to support dogs in DIC, and different dosages and routes of administration were used. If the goal is to protect against pulmonary thromboembolism, it may be more appropriate to treat with heparin at the beginning of surgery with a constant rate infusion with the intent to increase activated partial thromboplastin time by 1.5 times the baseline value.[10]

Phenoxybenzamine did not have a protective effect in the present study. Herrera et al[12] reported on the protective effect of phenoxybenzamine pretreatment in dogs with pheochromocytomas, with a reduction in perioperative mortality rate from 48% to 13% in dogs pretreated for a mean of 20 days. Seventeen percent of the dogs in the present study received phenoxybenzamine before surgery, and only 3 cases of pheochromocytoma invading the caudal vena cava were treated. Therefore, it was not possible to identify a significant effect of phenoxybenzamine on short-term survival rate.

Although vena caval invasion, extent of invasion, and tumor type were risk factors for death in the short term, no risk factors were identified that were significantly associated with long-term survival rate. Regardless of these factors, if a dog survived beyond the 14-day postoperative period, long-term survival was possible. Median survival time was 48 months for dogs with adrenocortical carcinomas and was not reached for dogs with pheochromocytomas; median survival time for the 3 dogs with vena caval invasion that survived to the long-term period was not reached. These results compare favorably with survival times described in reports of previous studies.[2,13,14,16]

Limitations in the present study were primarily related to its retrospective nature, particularly in regard to follow-up data and incomplete clinical information. Necropsies were rarely performed, particularly in dogs that did not die in the short term. Additionally, 4 dogs that were euthanized during surgery were included in the study because the decision to euthanize was primarily related to a perceived decreased quality of life related to the disease process.

It appears that the most important risk factor for decreased survival time in this population was an extensive tumor thrombus in the caudal venal cava. Risk factors for survival in the short term included anesthetic complications, intraoperative transfusion, and postoperative DIC, pancreatitis, hypotension, renal failure, and hypoxemia. In dogs that survived the short-term period, long-term survival was possible regardless of invasion status or tumor type. Careful planning with imaging to determine extent of tumor invasion may

be warranted for owner and clinician decision making prior to surgery.

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a.   JMP, version 8.0.2, SAS Institute Inc, Cary, NC.

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