

CONTRAST-ENHANCED COMPUTED TOMOGRAPHY AS A PREOPERATIVE INDICATOR OF VASCULAR INVASION FROM ADRENAL MASSES IN DOGS

RYAN M. SCHULTZ, ERIK R. WISNER, ERIC G. JOHNSON, JENNIFER S. MACLEOD

The purpose of this study was to determine if contrast-enhanced computed tomography (CT) accurately reflected vascular luminal invasion by adrenal masses in dogs. Medical records of 15 dogs with 17 adrenal masses that underwent preoperative CT imaging were reviewed. Presence or absence of vascular invasion was confirmed by surgery or necropsy/histology. Vascular invasion was identified correctly using contrast-enhanced CT in 11/12 dogs. The sensitivity and specificity of contrast-enhanced CT for vascular invasion compared with surgery or necropsy was 92% and 100%, respectively. The positive predictive value and negative predictive value of contrast-enhanced CT was 100% and 90%, respectively. The accuracy was 95%. In one dog, invasion of the phrenicoabdominal vein was not identified on CT images. Six of eight masses with vascular invasion where a histologic diagnosis was obtained were malignant. Four of four pheochromocytomas invaded adjacent vasculature. Contrast-enhanced CT provided accurate preoperative assessment of adrenal masses. Vascular invasion by adrenal masses in this study occurred by way of the lumen of the phrenicoabdominal vein with subsequent intraluminal extension into other veins, rather than by erosion through vessel walls. *Veterinary Radiology & Ultrasound*, Vol. 50, No. 6, 2009, pp 625–629.

Key words: adrenalectomy, canine, computed tomography, pheochromocytoma, phrenicoabdominal, tumor thrombus.

Introduction

DIAGNOSTIC IMAGING EVALUATION of adrenal masses for size and assessment of vascular invasion is commonly performed preoperatively.^{1–22} Although a significant difference in mortality between dogs with and without vascular invasion of an adrenal tumor has not been found, the statistical power of the trial was low.³ Regardless, preoperative evaluation of adrenal masses is indicated for surgical planning as the difficulty of the resection is increased with vascular invasion.³ Further, the need for concurrent nephrectomy due to invasion of an adrenal mass into the renal vein may worsen the prognosis.⁴

Ultrasonography and computed tomography (CT) are thought to be superior to radiography for staging adrenal masses.^{18,20,21} Preoperative ultrasonography has an 80% sensitivity and 90% specificity for detection of caudal vena cava invasion.³ Specific accuracy of CT for adrenal mass staging has not been reported.

The purpose of this study was to assess the utility of contrast-enhanced CT for preoperative detection of vascular invasion of adrenal masses in dogs.

Materials and Methods

Fifteen dogs with an adrenal mass (two dogs had bilateral masses) that received a preoperative CT scan within a week of surgery and subsequent confirmation of vascular invasion between January 2002 and May 2008 were identified. The median age was 12 years (range 5–14 years). There were nine neutered males six neutered females. The breed distribution was two Labrador Retrievers, but all others represented only one breed each or were of mixed breeding.

In nine dogs the adrenal masses were found incidentally. Five of the remaining six dogs had findings related to hyperadrenocorticism, such as polyuria/polydypsia, a pendulous abdomen, symmetric alopecia, and/or hyperpigmentation. One dog had ascites due to an adrenal mass that invaded the caudal vena cava and extended caudal and cranial to the liver. Definitive diagnoses were obtained by surgical reports and confirmation of vascular invasion was made by visualization, palpation, and dissection as needed with histologic correlation.

CT images were acquired on one scanner with patients under general anesthesia.* The CT images were acquired in a cranial to caudal direction during a forced breath hold following assisted hyperventilation with the patient in sternal or dorsal recumbency. The CT protocol used was at the discretion of the radiologist on duty and identical imaging parameters were not used in all patients. The mAs of the scans was typically 150 and the kVp was typically 120.

From the Veterinary Medical Teaching Hospital (Schultz) and the Department of Surgical and Radiological Sciences (Wisner, Johnson, MacLeod), School of Veterinary Medicine, University of California, Davis One Shields Ave, Davis, CA 95616-8747.

Address correspondence and reprint requests to Dr. Wisner, at the above address. E-mail: erwisner@ucdavis.edu

Received February 11, 2009; accepted for publication May 30, 2009.
doi: 10.1111/j.1740-8261.2009.01593.x

*HiSpeed FX/I; GE Medical System, Milwaukee, WI.

Both ionic and nonionic iodinated contrast medium was used, but dosage was approximately 880 mgI/kg of body weight in all patients. Vascular phase images were acquired immediately following manual intravenous bolus administration of contrast medium. Initial CT image collimation ranged from 3 to 5 mm in all dogs. Additional 1–2 mm collimated images through the adrenal mass and vasculature were acquired in 10 dogs. Delayed postcontrast CT images were acquired 5–10 min following the initial postcontrast image acquisition in eight dogs. Delayed postcontrast images were evaluated for contrast enhancement of the invasive tumor thrombus when available.

All precontrast and postcontrast CT images were reviewed by the primary author without knowledge of the surgical or necropsy/histologic findings. Images were assessed at a window and level setting optimal for the region of interest, and were manipulated for soft tissue and contrast enhanced vascular detail, which was typically at a window of 350 and a level of 75. Images reformatted in planes parallel, perpendicular, and oblique to the mass and surrounding vasculature were used in all patients. The adrenal masses were assessed for laterality, number, contrast enhancement, size, shape, attenuation, mineralization, margination, and muscular invasion. The surrounding vasculature including the caudal vena cava, aorta, and renal and phrenicoabdominal arteries and veins were assessed for luminal invasion and mural compression. Intraluminal vascular invasion of tumor thrombus was determined by identification of a mass-like void of contrast medium within a specific vessel during the angiographic phase of the CT study.

Sensitivity, specificity, positive and negative predictive values, and accuracy were calculated for CT assessment of vascular luminal invasion.

Results

Of the 17 adrenal masses, nine were left sided, four were right sided and two were bilateral. Based on gross and/or histologic findings, eight of 17 masses had invaded one or more of the following vessels: phrenicoabdominal vein ($n = 6$), caudal vena cava ($n = 5$), or renal vein ($n = 1$).

A histologic diagnosis was obtained for 12 of 17 masses; there were six cortical carcinomas, four pheochromocytomas, one cortical adenoma, and one metastatic hemangiosarcoma. Of the 12 histologically confirmed masses, six invaded surrounding vasculature and all six were malignant. These included four of four confirmed pheochromocytomas and two of six carcinomas. There were two other masses with vascular invasion without histologic confirmation. Of those masses with histologic confirmation, three were mineralized. Two of these three were carcinomas and the other was an adenoma. All four of the exclusively right-sided masses were invasive, three of nine left-sided masses were invasive, and none of the bilateral

TABLE 1. Surgical and Necropsy/Histology Diagnosis of Vascular Invasion Compared with Contrast-Enhanced Computed Tomography

Vascular Invasion	Surgical and/or Necropsy/ Histologic Conclusion	Contrast- Enhanced CT
None	9	9
Phrenicoabdominal vein	6	5
Caudal vena cava	5	5
Renal vein	1	1

There were 15 Dogs with 17 Total Adrenal Masses, but the Invasive Masses Often Involved Multiple Vessels.

masses invaded the surrounding vasculature. In one dog the bilateral masses were both cortical carcinomas, in the other histologic assessment was not performed.

All grossly identified adrenal masses were detected using CT imaging (Table 1). The sensitivity and specificity of contrast-enhanced CT for specific, i.e. phrenicoabdominal vein, caudal vena cava or renal vein, intraluminal invasion compared with surgery or necropsy was 92% and 100%, respectively. The positive predictive value and negative predictive value of contrast-enhanced CT was 100% and 90%, and accuracy was 95%. The nine noninvasive adrenal masses were all correctly identified as noninvasive (Fig. 1). All invasive adrenal masses were identified using contrast-enhanced CT with the exception of one phrenicoabdominal vein invasion that was not seen due to the 5-mm-thick image collimation used (Fig. 2).

Two dogs had phrenicoabdominal vein invasion that extended into and directly invaded the hypaxial and epaxial musculature (Fig. 3).

Compression of the phrenicoabdominal vein, renal vein, and/or caudal vena cava without intraluminal invasion was detected accurately in 10 dogs. These 10 masses, as well as five of eight with vascular invasion, distorted and displaced the renal vein or caudal vena cava without invasion. In the dog with invasion of the renal vein and in three of five dogs with caudal vena cava invasion, the invasion that appeared to extend from the phrenicoabdominal vein into the lumen of the renal vein or caudal vena cava rather than through the vessel wall. In the two remaining dogs with caudal vena cava invasion, the masses were so extensive that the phrenicoabdominal vein was obliterated and not described in the surgical report.

Adrenal masses, excluding the intraluminal component, ranged in height, width, and length from 1.5 to 5, 1.5 to 4.5, and 2 to 9 cm, respectively. Ten masses had homogeneous attenuation characteristics averaging 38 HU (range 22–52), three had heterogeneous attenuation characteristics with a cystic component and four were partially mineralized. The masses were round with smooth ($n = 11$), lobular ($n = 3$), or irregular margins ($n = 3$). The contrast enhancement was either heterogeneous ($n = 8$), peripheral ($n = 7$), or mild ($n = 2$).

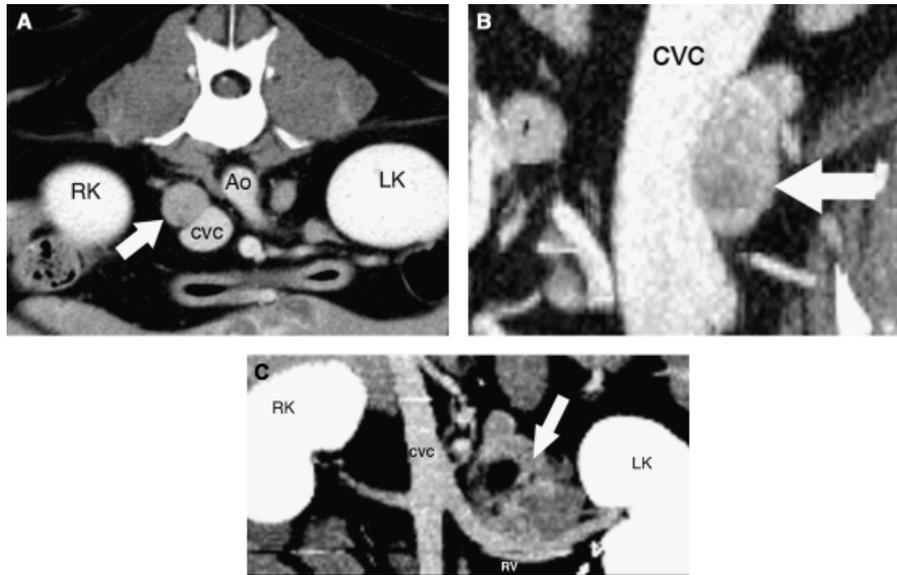


FIG. 1. Compression of adjacent vasculature by an adrenal mass, but without invasion. (A) Twelve-year-old Alaskan Malamute with a right-sided adrenal mass that invaded the right PV but not the CVC. The mass was adhered to the CVC wall. The PV is not identified on this transverse image, but the hypoattenuating adrenal mass (white arrow) is seen compressing the CVC without direct intraluminal invasion. (B) Reformatted oblique plane image from the same dog. Note the CVC compression by the adrenal mass (white arrow) without evidence of luminal invasion. (C) Reformatted dorsal plane image from an 8-year-old Beagle with a left-sided adrenal mass without vascular invasion. The heterogeneously attenuating and cystic left adrenal mass (white arrow) compressed and displaces the left RV without luminal invasion. Ao, aorta; CVC, caudal vena cava; LK, left kidney; RK, right kidney; RV, renal vein; PV, phrenicoabdominal vein.

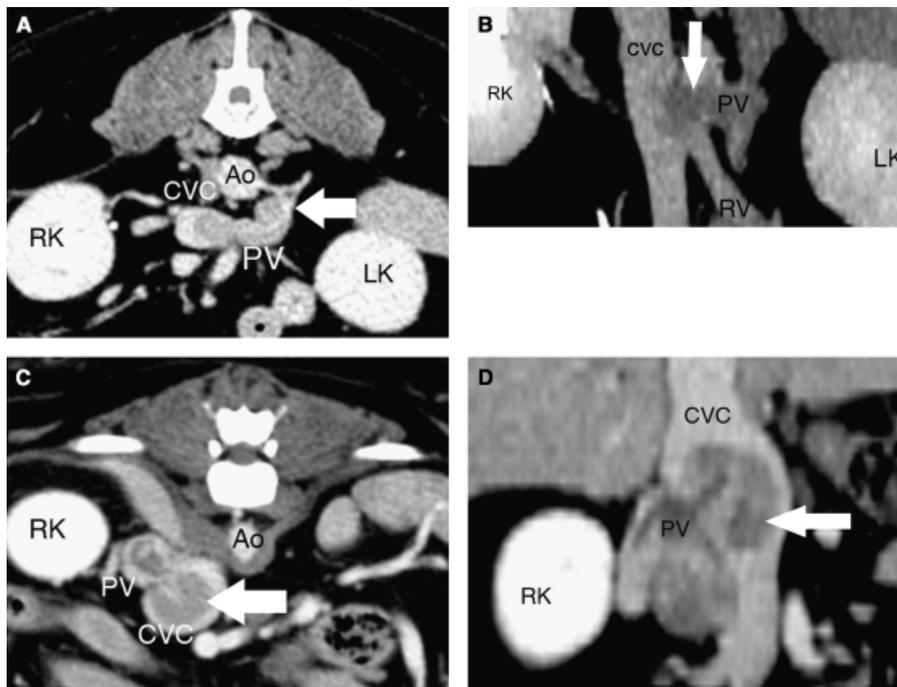


FIG. 2. Vascular invasion of adrenal masses. (A) Transverse image from a 12-year-old Shetland Sheepdog with a hypoattenuating left-sided adrenal mass (white arrow) that invaded the left phrenicoabdominal vein (PV) and extended into the caudal vena cava (CVC). (B) Reformatted dorsal plane image from the same dog. Note the invasion by a hypoattenuating mass (white arrow) into the left PV with extension into CVC. The junction of the left renal vein (RV) and the CVC is in close proximity but the mass does not extend into the RV lumen. (C) Transverse image from a 13-year-old Shih-Tzu. Note invasion of the CVC and right PV by a right-sided adrenal mass. The hypoattenuating adrenal mass (white arrow) extends from the right PV into the CVC. (D) Reformatted oblique plane image from the same dog as in (C). Note the right PV and CVC with invasion by the hypoattenuating adrenal mass (white arrow). See legend from Fig. 1 for additional abbreviations.

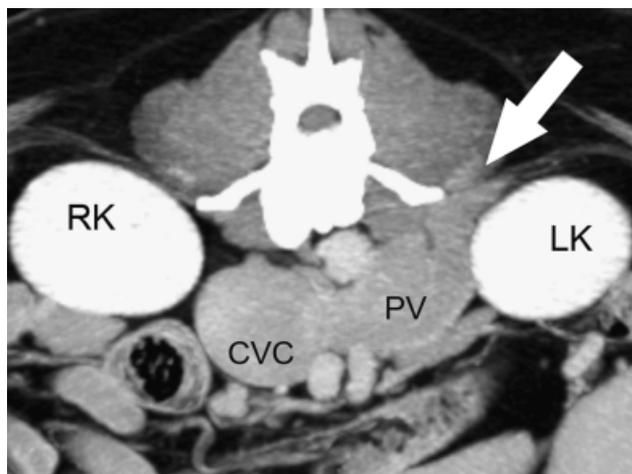


FIG. 3. Transverse image of an 11-year-old Labrador Retriever mix with distal invasion of the phrenicoabdominal vein (PV), caudal vena cava (CVC) and hypaxial and epaxial musculature by a left sided adrenal mass (white arrow). See legend from Fig. 1 for additional abbreviations.

In the eight dogs where delayed CT images were acquired, the average precontrast attenuation was 35 HU (range 22–52), the average immediate postcontrast attenuation was 83 HU (range 26–130) and average delayed postcontrast attenuation was 79 HU (range 55–109). Five of these dogs had vascular invasion, of which four had delayed contrast enhancement. Of the invasive masses the precontrast average attenuation of the tumor thrombus was 46 HU (range 40–52), the average postcontrast attenuation was 113 HU (range 50–191) and average delayed postcontrast attenuation was 83 HU (range 67–100).

Discussion

All adrenal masses in this study were identified using contrast-enhanced CT and sensitivity, specificity, positive and negative predictive values for vascular invasion were higher than those reported previously for sonography.³ Ultrasound has been reported to be 80% sensitive and 90% specific for the presence of vascular invasion by adrenal masses.³

In the dog where phrenicoabdominal invasion was not identified, relatively thick image collimation led to the false-negative finding. However, because the portion of the phrenicoabdominal vein coursing over the adrenal gland is excised during adrenalectomy, this type of error may have minimal significance when vascular invasion does not extend into the hypaxial musculature.³ However, invasion of hypaxial and epaxial muscles has a profound impact on feasibility of tumor excision.

Vascular invasion was thought to originate in the phrenicoabdominal vein, then subsequently into the caudal vena cava and then into the renal vein. This route of invasion is likely because tumor cells can migrate through small adrenal veins directly into the phrenicoabdominal vein. This

intraluminal migration scenario was considered likely in our population, although direct vascular invasion has also been reported.³ In some dogs, the adrenal veins do not drain directly into the phrenicoabdominal vein, but into the caudal vena cava or a renal vein.²³ Therefore, in these dogs invasion from an adrenal mass may extend directly to the caudal vena cava or renal vein, without phrenicoabdominal vein involvement. The presence of vascular invasion in our population was higher than reported previously and was likely attributed to the selection of patients for contrast-enhanced CT imaging when a tumor thrombus was suspected.^{1,3} No patients with direct renal parenchymal invasion or hemoabdomen were seen in this study, although this has been reported.^{4,5,24}

In this investigation, all histologically confirmed masses with vascular invasion were malignant. In addition, all four pheochromocytomas were invasive compared with only two of six carcinomas, findings comparable to those of others.^{3,5,6} The increased frequency of right-sided adrenal mass invasion in this study has been identified by others³ but a statistically significant difference between invasion from right- vs. left-sided adrenal tumors has not been found. Mineralized adrenal masses are usually carcinomas or adenomas as documented previously.⁶ The age, breed, gender, clinical signs, laboratory findings, CT characteristics of the adrenal masses, and histologic diagnoses were similar to other reports.^{1,3–8,10,12,14,15,25} Other adrenal mass parameters such as attenuation characteristics, margination, and contrast enhancement could not be analyzed for a relationship with tumor type due to the small sample size.

In humans, CT is the preferred modality to evaluate adrenal masses with the primary objective being to differentiate benign from malignant disease. Imaging features used to characterize masses include size, shape, attenuation characteristics, homogeneity of initial contrast enhancement, and contrast washout values on 10-min delayed scans. Imaging assessment of vascular invasion is a secondary consideration in humans with adrenal masses because this is relatively uncommon. Therefore, in humans, the CT protocol for assessing an adrenal mass typically consists of precontrast, immediate postcontrast, and 10-min delayed postcontrast images with 3–5 mm collimation.^{26–33} However, delayed postcontrast images acquired at least 10 min after injection of contrast medium may be useful to document the presence of contrast enhancing intraluminal tumor. Contrast enhancement suggests the presence of a neoplastic mass rather than a thrombus.^{26–28,34}

Preoperative adrenal mass assessment using a standardized contrast-enhanced CT protocol would likely further improve the accuracy of CT for detecting regional vascular invasion in dogs. Based on findings from this investigation, we recommend obtaining thinly collimated (1–2 mm) images from at least 1 cm cranial and caudal to the adrenal mass and including the phrenicoabdominal and renal

arteries and veins as well as the adjacent caudal vena cava and kidneys. Thin collimation allows for visualization of the small phrenicoabdominal veins, which may not be identified on thicker images, as seen in this study.

In conclusion, contrast-enhanced CT is a sensitive and specific preoperative indicator for the assessment of intraluminal vascular invasion of adrenal masses in dogs. Vascular

invasion occurred through the lumen of the phrenicoabdominal vein, presumably through extension from the adrenal veins, and not by direct vascular wall invasion or destruction. Masses with vascular invasion are malignant and these are most commonly pheochromocytomas. CT is indicated for evaluation of vascular invasion when extension into the hypaxial and epaxial musculature is a concern.

REFERENCES

- Anderson CR, Bitchard SJ, Powers BE, Belandria GA, Kuntz CA, Withrow SJ. Surgical treatment of adrenocortical tumors: 21 cases (1990–1996). *J Am Anim Hosp Assoc* 2001;37:93–97.
- Gilson SD, Withrow SJ, Orton EC. Surgical treatment of pheochromocytoma: technique, complications, and results in six dogs. *Vet Surg* 1994;23:195–200.
- Kyles AE, Feldman EC, DeCock HE, et al. Surgical management of adrenal gland tumors with and without associated tumor thrombi in dogs: 40 cases (1994–2001). *J Am Vet Med Assoc* 2003;223:654–662.
- Schwartz P, Kovak JR, Koprowski A, Ludwig LL, Monette S, Bergman PJ. Evaluation of prognostic factors in the surgical treatment of adrenal gland tumors in dogs: 41 cases (1999–2005). *J Am Vet Med Assoc* 2008;232:77–84.
- Barthez PY, Marks SL, Woo J, Feldman EC, Matteucci M. Pheochromocytoma in dogs: 61 cases (1984–1995). *J Vet Intern Med* 1997;11:272–278.
- Besso JG, Penninck DG, Gliatto JM. Retrospective ultrasonographic evaluation of adrenal lesions in 26 dogs. *Vet Radiol Ultrasound* 1997;38:448–455.
- Rosenstein DS. Diagnostic imaging in canine pheochromocytoma. *Vet R Ultrasound* 2000;41:499–506.
- Gilson SD, Withrow SJ, Wheeler SL, Twedt DC. Pheochromocytoma in 50 dogs. *J Vet Intern Med* 1994;8:228–232.
- Myers NC III. Adrenal incidentalomas. Diagnostic workup of the incidentally discovered adrenal mass. *Vet Clin North Am Small Anim Pract* 1997;27:381–399.
- Barthez PY, Nyland TG, Feldman EC. Ultrasonographic evaluation of the adrenal glands in dogs. *J Am Vet Med Assoc* 1995;207:1180–1183.
- Douglass JP, Berry CR, James S. Ultrasonographic adrenal gland measurements in dogs without evidence of adrenal disease. *Vet Radiol Ultrasound* 1997;38:124–130.
- Voorhout G. X-ray-computed tomography, nephrotomography, and ultrasonography of the adrenal glands of healthy dogs. *Am J Vet Res* 1990;51:625–631.
- Grooters AM, Billers DS, Theisen SK, Miyabayashi T. Ultrasonographic characteristics of the adrenal glands in dogs with pituitary-dependent hyperadrenocorticism: comparison with normal dogs. *J Vet Intern Med* 1996;10:110–115.
- Hoerauf A, Reusch C. Ultrasonographic characteristics of both adrenal glands in 15 dogs with functional adrenal tumors. *J Am Anim Hosp Assoc* 1999;35:193–199.
- Kantrowitz BM, Nyland TG, Feldman EC. Adrenal ultrasonography in the dog. Detection of tumors and hyperplasia in hyperadrenocorticism. *Vet Radiol Ultrasound* 1986;27:91–96.
- Morandi F, Mays JL, Newman SJ, Adams WH. Imaging diagnosis – bilateral adrenal adenomas and myelolipomas in a dog. *Vet Radiol Ultrasound* 2007;48:246–249.
- Bailey MQ. Use of X-ray-computed-tomography as an aid in localization of adrenal masses in the dog. *J Am Vet Med Assoc* 1986;188:1046–1049.
- Penninck DG, Feldman EC, Nyland TG. Radiographic features of canine hyperadrenocorticism caused by autonomously functioning adrenocortical tumors: 23 cases (1978–1986). *J Am Vet Med Assoc* 1988;192:1604–1608.
- Poffenbarger EM, Feeney DA, Hayden DW. Gray-scale ultrasonography in the diagnosis of adrenal neoplasia in dogs: six cases (1981–1986). *J Am Vet Med Assoc* 1988;192:228–232.
- Tidwell AS, Penninck DG, Besso JG. Imaging of adrenal gland disorders. *Vet Clin North Am Small Anim Pract* 1997;27:237–254.
- Voorhout G, Stolp R, Rijnberk A, van Waes PF. Assessment of survey radiography and comparison with X-ray computed tomography for detection of hyperfunctioning adrenocortical tumors in dogs. *J Am Vet Med Assoc* 1990;196:1799–1803.
- Bertolini G, Furlanello T, DeLorenzi D, Caldin M. Computed tomographic quantification of canine adrenal gland volume and attenuation. *Vet Radiol Ultrasound* 2006;47:444–448.
- Evans HE. *Miller's anatomy of the dog*, 3rd ed. Philadelphia: WB Saunders, 1993.
- Whittemore JC, Preston CA, Kyles AE, Hardie EM, Feldman EC. Nontraumatic rupture of an adrenal gland tumor causing intra-abdominal or retroperitoneal hemorrhage in four dogs. *J Am Vet Med Assoc* 2001;219:329–333.
- Ford SL, Feldman EC, Nelson RW. Hyperadrenocorticism caused by bilateral adrenocortical neoplasia in dogs: four cases (1983–1988). *J Am Vet Med Assoc* 1993;202:789–792.
- Mayo-Smith WW, Boland GW, Noto RB, Lee MJ. State-of-the-art adrenal imaging. *Radiographics* 2001;21:995–1012.
- Ilias I, Sahdev A, Reznick RH, Grossman AB, Pacak K. The optimal imaging of adrenal tumours: a comparison of different methods. *Endocr Relat Cancer* 2007;14:587–599.
- Peppercorn PD, Reznick RH. State-of-the-art CT and MRI of the adrenal gland. *Eur Radiol* 1997;7:822–836.
- Tassi A, Cirocchi R, Volpi G, Pacifici A, Goracci G. Preoperative evaluation of inferior vena cava involvement secondary to malignant abdominal neoplasms. *J Cardiovasc Surg (Torino)* 1993;34:241–247.
- Giuliani L, Gilberti C, Martorana G, Isotta A, Neumaier CE. Value of computerized tomography and ultrasonography in the preoperative diagnosis of renal cell carcinoma extending into the inferior vena cava. *Eur Urol* 1987;13:26–30.
- Hallscheidt PJ, Fink C, Haferkamp A, et al. Preoperative staging of renal cell carcinoma with inferior vena cava thrombus using multidetector CT and MRI: prospective study with histopathological correlation. *J Comput Assist Tomogr* 2005;29:64–68.
- Mildenberger P, Lotz R, Bierhoff E, Schmiadt W. Tumor invasion of the vena cava inferior in adrenal carcinomas. The preoperative diagnosis. *Rofo* 1987;147:160–165.
- Delis SG, Bakogiannis A, Ciancio G, Soloway M. Surgical management of large adrenal tumours: the university of Miami experience using liver transplantation techniques. *BJU Int* 2008;102:1394–1399.
- Szolar DH, Unger B, Heinz-Peer G, Preidler K, Ranner G. Differential diagnosis of space-occupying adrenal masses. *Rofo* 1999;171:269–278.