Clinical findings in dogs with incidental adrenal gland lesions determined by ultrasonography: 151 cases (2007–2010)

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Objective—To determine the prevalence of and clinical features associated with incidental adrenal gland lesions (IAGLs) discovered during abdominal ultrasonography in dogs.

Design—Retrospective case series.

Animals—151 dogs with an IAGL and 400 control dogs.

Procedures—Reports of ultrasonographic examinations of the abdomen of dogs performed during a 3.5-year period were reviewed. Adrenal glands were classified as having an IAGL if a nodule or mass was described or the width of either gland was ≥10 mm. For dogs with an IAGL, information regarding signalment, concurrent disorders, and outcome was obtained from the medical record. Findings were compared with those in a control population of 400 dogs examined during the same period.

Results—An IAGL was detected in 151 of 3,748 (4%) dogs. Dogs with an IAGL were significantly older (median age, 11.25 years) and heavier (median body weight, 21 kg [46.2 lb]) than the control population (median age, 9.5 years; median body weight, 14 kg [30.8 lb]). Malignant tumors were reported in 6 of 20 (30%) dogs that underwent adrenal glandectomy or necropsy and had a maximum IAGL dimension that ranged from 20 to 46 mm; benign lesions all had a maximum dimension <20 mm. Various coincidental conditions were reported in dogs with an IAGL, including nonadrenal gland malignant neoplasia in 43 (28.5%) dogs.

Conclusions and Clinical Relevance—IAGLs were more likely in dogs ≥9 years of age. On the basis of this small data set, malignancy should be suspected for IAGLs ≥20 mm in maximum dimension. (J Am Vet Med Assoc 2014;244:1181–1185)

The use of advanced imaging modalities (eg, ultrasonography, CT, and MRI) in human patients has led to the routine identification of incidental adrenal gland masses. These are defined as a focal enlargement of the adrenal gland in patients without prior evidence of adrenal gland disease. Lesions found in patients undergoing imaging procedures as part of the staging process for cancer are inconsistently excluded from this definition in the human medical literature.1–3 The prevalence of such masses in humans is low, affecting only 2% to 5% of patients undergoing CT, but does increase with age.1–3 Most IAGLs in human patients without concurrent malignancy are benign and nonfunctional.3 Size of the mass is not a specific indicator of malignancy in human patients, although larger lesions are more likely to be a cortical carcinoma.1,4–6 Imaging characteristics, such as noncontrast CT attenuation, appear to be more useful predictors of malignancy, with low attenuation (ie, <10 Hounsfield units) supporting a diagnosis of adenoma or hyperplasia in humans with cortical lesions.5,7

The first descriptions of the ultrasonographic appearance of normal canine adrenal glands were published in the mid-1990s.8,9 Prior to this time, the available technology did not support the routine identification of adrenal glands in healthy dogs.10,11 Since those first reports, the ability of an experienced sonographer to visualize the adrenal glands has continued to improve, and the identification, description, and measurement of both adrenal glands is now considered a standard part of an abdominal ultrasonographic examination in dogs. Therefore, IAGLs are now routinely detected in dogs, and veterinarians are faced with the challenge of defining the importance of these lesions.12–14 Advanced imaging modalities, such as CT, MRI, and positron emission tomography, may provide useful additional information but require anesthesia and incur substantial additional costs.13,16

Focal adrenal gland lesions (nodules and masses) or nonspecific enlargement may reflect one of many processes. A lesion may be a benign tumor (ie, a cortical adenoma) or a malignant tumor (ie, a cortical carcinoma, pheochromocytoma, or metastases). Alternatively, it may be a granuloma, cyst, or area of hyperplasia. Although evidence of vascular invasion indicates malignancy and is often associated with cortical carcinomas and pheochromocytomas, limited information is gained regarding biological behavior from ultrasonography alone.12,17,18

The goals of the study reported here were to determine the prevalence of IAGLs in dogs undergoing routine diagnostic abdominal ultrasonography at a veter-
nary teaching hospital, to describe the demographics of dogs with IAGLs and compare these findings with those in a control population, and to determine the diagnoses and outcome (where available) for dogs with an IAGL.

Materials and Methods

Selection of cases and controls—Dogs that underwent routine abdominal ultrasonographic examinations performed at Texas A&M Veterinary Medical Teaching Hospital between January 2007 and the end of June 2010 were considered for the study. Dogs were excluded if the entire abdomen was not examined, if abdominal ultrasonography had been performed within the previous 2 months, or if the scan was performed to evaluate a previously identified adrenal gland lesion. All scans were performed by diplomates of the American College of Veterinary Radiology or a radiology resident under direct supervision of a board-certified radiologist. Two ultrasonography systems were used during this period, and transducer type and frequency were selected on the basis of patient size. Following every examination, a written report was generated by the radiologist and included in the computerized medical record within 3 days.

From the medical records, the appearance of the adrenal glands was classified as abnormal if a distinct nodule or mass was described in either gland or if the width of either gland (ie, dorsoventral dimension, measured from a longitudinal image) was ≥10 mm. For focal lesions, the largest measurement (in any dimension) included in the written report was recorded. The adrenal gland lesion was determined to be clinical or incidental on the basis of a review of the medical record by a board-certified veterinary internist (AKC). A lesion was defined as clinical if there was an indication of pre-existing adrenal gland disease (eg, clinical signs or laboratory findings suggestive of hyperadrenocorticism or unexplained hypertension) or evidence that the adrenal gland lesion was directly related to the decision to perform imaging (eg, signs of acute abdominal pain related to a hemorrhagic adrenal gland mass). All other adrenal gland lesions were classified as incidental. Dogs with an IAGL were included in the study. For comparison of age, breed, sex, and body weight, a cohort of 400 control dogs without adrenal gland ultrasonographic lesions was randomly selected from those undergoing abdominal ultrasonography during the same time period.

Medical records review—Information regarding the age, breed, sex, and body weight of dogs with an IAGL and control dogs was obtained from the medical record. Additional features such as clinical signs, concurrent diseases, clinicopathologic information, and final diagnoses were reviewed as appropriate for dogs with an IAGL. Where available, necropsy findings and results of adrenal gland histologic examinations (on tissues obtained surgically or after death) were also recorded. For all dogs with adrenal gland histopathologic results, archived specimens were reviewed and the diagnosis was verified by a board-certified veterinary pathologist (JFE).

Statistical analysis—Statistical analysis was performed with a commercial software program. Where appropriate, data sets were tested for normality by means of the D’Agostino and Pearson omnibus normality test. Median values of selected data sets were compared by means of the Mann-Whitney test for unpaired data. A Fisher exact test was used to compare population characteristics. For all comparisons, P < 0.05 was considered significant.

Results

Review of the medical records yielded 4,150 ultrasonographic examinations performed on 3,748 dogs that met the criteria for consideration. Adrenal gland abnormalities were noted in 206 dogs. Lesions were classified as IAGLs in 151 (4%) dogs, which constituted the study population.

Dogs with an IAGL ranged in age from 3.5 to 16.9 years, with a median of 11.25 years, which was significantly (P < 0.001) different from the dogs in the control group (median age, 9.5 years; range, 2 months to 19.2 years). Only 26 (17%) dogs in the IAGL group were <9 years of age, compared with 44% of the control population (OR, 3.74; 95% confidence interval, 2.35 to 5.96; P < 0.001; Figure 1). Median body weight for the IAGL group was 21 kg (46.2 lb; range, 2 to 56 kg [4.4 to 123.2 lb]), which was significantly (P = 0.037) greater than the control group (median, 14 kg [30.8 lb]; range, 1 to 71 kg [2.2 to 156.2 lb]). Male and female dogs were equally represented in the IAGL group (49.7% female and 50.3% male) and control group (52% female and 49% male). Forty-three breeds were represented in the IAGL group, most frequently Labrador Retriever (11.3%), Miniature Dachshund (7.9%), and Golden Retriever (6.0%). Thirty-one (20.5%) mixed-breed dogs had an IAGL. Breed distributions were similar in the control group, with Labrador Retrievers (9%), Golden Retrievers (4.3%), and Dachshunds (4%) listed most often. Mixed-breed dogs comprised 16.5% of the control group.

Most IAGLs were unilateral, affecting the left adrenal gland in 74 (49%) dogs and the right in 60 (39.7%). Both adrenal glands were abnormal in 17 (11.3%) dogs. One hundred sixty-three adrenal gland nodules or masses were reported in 146 dogs. Information regard-
ings were reviewed in the cases with a definitive diagnosis of vascular invasion on ultrasonography. A pheochromocytoma was detected during ultrasonography. A pheochromocytoma histologic evaluation in a dog with a 20-mm mass depicted a 4-mm nodule in 1 gland.

Sonographic enlargement of 1 adrenal gland (width, 12 mm) revealed a 4-mm nodule in 1 dog and nonspecific ultrasonographic findings were detected in 2 dogs. Ultrasonography in these dogs revealed a 4-mm nodule in 1 dog and nonspecific ultrasonographic findings were detected in 2 dogs.

Unilateral adrenal cortical hyperplasia. Unilateral cortical adenomas were reported in 115 dogs; the maximum dimension ranged from 3 to 60 mm, with a median of 12 mm. Only 20 (17.4%) of these were ≥ 20 mm in any dimension. The other 48 lesions were described as nodules, but the size was not reported. In 5 dogs, the width of the right (n = 3) or left (2) adrenal gland was ≥ 10 mm (range, 10 to 12 mm), but a discrete lesion was not identified.

Evidence of vascular invasion was noted in 9 dogs. Information regarding the size of the adrenal gland mass was reported in all these dogs; maximum dimensions ranged from 11 to 53 mm (median, 33 mm). Histopathologic findings were available for 3 of these masses, all of which were pheochromocytomas. Adrenal glandectomy was performed in 6 dogs with an IAGL. Maximum dimension for these lesions ranged from 15 to 47 mm (median, 21 mm). Histopathologic findings included cortical adenoma (n = 2), pheochromocytoma (2), and cortical carcinoma (2). The adenomas had maximum dimensions of 15 and 17 mm. The pheochromocytomas and carcinomas were all ≥ 20 mm (20, 22, 23, 37, and 46 mm). Both pheochromocytomas had evidence of vascular invasion on ultrasonography; which was confirmed surgically.

Necropsy was performed in 14 dogs with an IAGL. In 4 dogs, the adrenal glands were reported to be grossly unremarkable and not examined further. Three of these dogs underwent necropsy within 7 days after ultrasonography, at which time unilateral nodules ranging in size from 6 to 11 mm were reported. The fourth dog was reported to have a 13-mm mineralized adrenal gland lesion during ultrasonography; this dog died 15 months later from an acute arrhythmic episode, attributed at necropsy to myocardial degeneration.

Discrete unilateral adrenal gland lesions (all < 1 cm) were noted grossly at necropsy in 3 dogs reported to have nodules (size not reported) during ultrasonography; the attending pathologists reported these to be hyperplastic changes, but the glands were not examined microscopically. One dog with a nodule in the right adrenal gland (size not reported) was euthanized 4 weeks later, during which time high doses of glucocorticoids were administered. At necropsy, bilateral adrenal gland atrophy was noted grossly.

Histologic examination of the adrenal glands was performed in 6 of the dogs submitted for necropsy. One dog with a unilateral nodule (size not reported) noted on ultrasonography had a histologic diagnosis of bilateral cortical hyperplasia. Unilateral cortical adenomas were detected in 2 dogs. Ultrasonography in these dogs revealed a 4-mm nodule in 1 dog and nonspecific ultrasonographic enlargement of 1 adrenal gland (width, 12 mm) in the other. Bilateral adenomas were reported in 1 dog; ultrasonography performed 1 week earlier indicated a 4-mm nodule in 1 gland.

A low-grade cortical carcinoma was diagnosed on histologic evaluation in a dog with a 20-mm mass detected during ultrasonography. A pheochromocytoma was reported in 1 dog; this mass was 32-mm wide, with evidence of vascular invasion on ultrasonography. Objective and descriptive ultrasonographic findings were reviewed in the cases with a definitive diagnosis (n = 12). The most consistent predictive findings included size (maximum dimension ≥ 20 mm indicated malignancy in 6/6 cases) and vascular invasion, which indicated pheochromocytoma in 3 of 3 cases. Two of the 3 carcinomas were described ultrasonographically as heterogeneous. Five of the 6 adenomas were reported to be hyperechoic in comparison to adjacent adrenal gland cortical tissue.

Concurrent malignant neoplastic diseases were documented in 43 (28.3%) dogs with an IAGL, of which the majority (29 [67.4%]) had overt evidence of abdominal involvement. Half of the 20 dogs with adrenal gland lesions ≥ 20 mm had cancer in other organs. If dogs with concurrent neoplasia were excluded from the IAGL group, overall prevalence of an IAGL in this population was 108 of 3,748 (2.9%). Numerous other concurrent disorders were reported, including gastrointestinal, renal, pulmonary, and immune-mediated disorders. A definitive diagnosis was not available for all dogs.

Twenty-six (17.2%) dogs in the IAGL group died or were euthanized within 7 days after ultrasonography. Sixty-eight (45%) dogs were discharged from the hospital but were immediately lost to follow-up. Follow-up information was available for 37 dogs without concurrent neoplasia. Actual survival data were not available for many of these, but more than half (19) were known to be alive ≥ 10 months after identification of the IAGL (contact time ranged from 1 to 66 months).

Twenty dogs had an IAGL with a maximum reported measurement ≥ 20 mm. Four dogs underwent adrenal glandectomy (2 carcinomas and 2 pheochromocytomas). Six dogs died or were euthanized due to their illness; postmortem examinations were performed on 2 and revealed a carcinoma in one and a pheochromocytoma in the other. Five dogs survived 3 to 23 months (median, 12 months). Five other dogs in this subset were lost to follow-up.

Ultrasonography was repeated in 7 dogs with an IAGL. A lesion was not identified in 3 dogs previously reported to have unilateral adrenal gland nodules (sizes, 3 mm, 8 mm, and size not reported) when examined > 4 months later. No growth was reported after > 6 months in 2 dogs with 9- and 11-mm lesions. Progressive enlargement was detected in 2 dogs. One dog had a 16-mm mass, which grew to 25 mm and invaded the vena cava within 10 months. The dog died 15 months after the mass was first detected. In the other dog, a 25-mm mass grew to 31 mm within 8 months; the dog was lost to follow-up 23 months after the initial ultrasonographic examination.

**Discussion**

The prevalence of an IAGL in dogs examined via abdominal ultrasonography at the authors’ institution was low (4%) but was similar to that reported in human patient populations undergoing abdominal CT.1-3 Similarly, IAGLs were more likely to be found in older dogs, compared with the control population, with > 80% of affected dogs at least 9 years of age. Although the median body weight for dogs with an IAGL was significantly higher than the control group, substantial overlap existed between the 2 populations, and strong inferences regarding
size could not be made. Results of this study did not suggest any breed or sex predispositions toward an IAGL.

A substantial proportion (28.5%) of the dogs with an IAGL had concurrent, nonadrenal gland malignant neoplasia. In the human literature, some patients with cancer are not regarded as having an IAGL, given that the adrenal gland lesion may be related to the primary tumor. In fact, results of 1 study indicate that > 75% of adrenal gland lesions in such patients are ultimately proven to be metastatic. Metastatic adrenal gland lesions were not identified in any of the dogs in the present study, although the number of necropsied dogs was small and the adrenal glands were not consistently evaluated. In a previous study, 21% of dogs with nonadrenal gland malignancies were found to have metastasis to 1 or both adrenal glands at necropsy. Therefore, it is possible that some or many dogs of the IAGL group with concurrent neoplasia had metastatic adrenal gland lesions. In addition, only dogs with a final diagnosis of nonadrenal gland neoplastic disease were included in the subset of dogs with concurrent neoplasia, so the true prevalence of concurrent neoplasia was likely higher than that reported because many dogs had an open or poorly defined diagnosis at the time of discharge.

A histopathologic diagnosis was available for only 12 of the 151 (8%) dogs with an IAGL. Although half of these dogs had a malignant neoplasm (cortical carcinoma [n = 3] or pheochromocytoma [3]), this finding was subject to substantial bias and should be interpreted with caution. Dogs with larger lesions or those with vascular invasion may be more likely to be treated with surgery or submitted for postmortem examination. In 5 dogs with IAGLs diagnosed by use of ultrasonography, no gross lesions were detected at necropsy. Potentially, small lesions may be overlooked if overall adrenal gland size and shape are within reference limits or if substantial concurrent disease causes the changes in the adrenal glands to be indiscernible. On postmortem evaluation in 3 dogs, gross assessment suggested a benign lesion (adenoma or hyperplasia) but was not confirmed microscopically. Only 2 of 14 dogs that were necropsied had proven malignant lesions, and only 2 of 6 IAGLs examined histologically as part of a postmortem examination were malignant. The true prevalence of adrenal gland malignancies in dogs with an IAGL is likely between these 2 values.

More than two-thirds of incidental adrenal gland masses in human patients are benign adenomas with no endocrine activity. Direct comparisons between human and canine studies regarding the risk of malignancy are difficult because of the different biological behavior of adrenal gland medullary tumors (ie, pheochromocytomas) in the 2 species. In humans, these tumors are usually benign (≥ 85%) and invasion of adjacent structures is not expected. Removal is recommended simply because of the consequences of excessive catecholamine release. In contrast, pheochromocytomas in dogs are more likely to be aggressive and vascular invasion and metastases are commonly reported.

In humans, the size of an IAGL is a useful indicator of malignancy, and the current recommendation is for the removal of any mass > 6 cm in size in any dimension. In 1 retrospective study, a cutoff size of 5 cm was 93% sensitive for malignancy. In the present study population, every mass ≥ 2 cm for which a definitive diagnosis was available was either a cortical carcinoma (n = 3) or a pheochromocytoma (3). This finding is consistent with a previous report that size of an adrenal mass is predictive of malignancy in dogs. Although firm conclusions regarding the reliability of size as a predictor of biological behavior were limited by the small data set, it seems appropriate to recommend adrenal glandectomy if an IAGL is ≥ 2 cm.

Measurements of adrenal gland lesions were based on the written ultrasonography reports and were not verified from stored images. Unfortunately, information regarding lesion size was not available for all cases and one-third were described simply as a nodule. A previous veterinary report defined a nodule as a focal increase in adrenal gland thickness without distortion of normal shape, although no guidelines regarding size were proposed. If it is assumed that most nodules are < 1 cm, the median size for an IAGL was probably smaller than the 12 mm in the present study.

Five dogs with an adrenal gland width ≥ 10 mm were included in the IAGL group, even though a discrete lesion was not reported. This was to allow for the fact that a distinct nodule or mass may not have been clearly evident to the radiologist or was not described specifically if its importance was overshadowed by other findings. One of these dogs had an adenoma on necropsy, which suggests that a distinct lesion may not be readily apparent via ultrasonography if the echogenicity of the mass is similar to that of the surrounding tissue. Adrenal gland width when viewed in a longitudinal plane in clinically normal dogs ranges from 3 to 7.4 mm. In 1 report describing dogs without hyperadrenocorticism examined at a veterinary school, a range of 1.9 to 12.4 mm was reported. The cutoff of 10 mm used in the present study was chosen to avoid inclusion of dogs with nonspecific adrenal gland hyperplasia, which has been reported in dogs with chronic or severe illness and is presumed to reflect increased adrenocortical demand in response to physiologic stress. However, it is possible that a cutoff ≥ 10 mm resulted in inappropriate classification of some dogs.

Although follow-up ultrasonography was performed in few dogs, lesions were reported to regress in 3 of 7. The lesions were all described as nodules and may have simply represented areas of hyperplasia. In the 2 dogs with documented progression of lesion size, both masses were fairly large when first identified (16 and 25 mm). Assuming these masses were spherical, tumor volume increased by > 100% in 8 to 10 months. On the basis of these findings, repeated ultrasonography within 3 to 4 months may be an appropriate method for assessment of lesion progression. It is interesting to note that the dog with the 25-mm IAGL lived ≥ 23 months, suggesting that a large mass is not necessarily an imminent cause of death.

Results of previous studies suggest that ultrasonographic findings other than size and vascular invasion have limited value for differentiation between benign and malignant lesions. Additional noninvasive diagnostic options, such as contrast-enhanced ultrasonography, aid in the differentiation of adrenal gland

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adenomas from other lesions in human patients. \textsuperscript{26} Although data regarding this imaging modality are limited in dogs, recent studies\textsuperscript{26–31} suggest that the technique is technically feasible and provide preliminary information regarding appropriate methodology in dogs. There were several limitations to this study. Although IAGLs were reported in a substantial number of dogs, a definitive diagnosis was available in < 10% of cases. In addition, dogs with larger lesions were probably more likely to undergo adrenal glandectomy or postmortem examination of adrenal gland tissue, which likely biased the histopathologic findings. It was also unfortunate that measurements were not available for many of the IAGLs, which limited the reliability of conclusions regarding lesion size. Due to the retrospective nature of this study, follow-up information was limited and survival times were undetermined for most dogs. Prospective, longitudinal studies are needed to provide more information regarding histopathologic diagnosis and outcome.

On the basis of this data set, malignancy should be strongly suspected in any mass ≥ 2 cm or with evidence of vascular invasion. Screening for excessive catecholamine release should be considered prior to removal, given that pheochromocytomas were identified in 3 of 20 dogs that underwent surgery or necropsy.\textsuperscript{12,31} Further research is needed to define appropriate criteria for additional diagnostic testing or surgical intervention in dogs with an IAGL.

\begin{itemize}
\item \textsuperscript{a} Acuson Sequoia 512, Siemens Medical Solutions USA Inc, Mountain View, Calif.
\item \textsuperscript{b} Acuson Antares, Siemens Medical Solutions USA Inc, Mountain View, Calif.
\item \textsuperscript{c} GraphPad Prism, version 5.01, GraphPad Software Inc, La Jolla, Calif.
\end{itemize}

References


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