Ultrasonographic Adrenal Gland Measurements in Clinically Normal Small Breed Dogs and Comparison with Pituitary-Dependent Hyperadrenocorticism

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(Under the heading of Internal Medicine, J. Vet. Med. Sci. 73(8): 985–989, 2011)

ABSTRACT. Ultrasonography is a sensitive and specific screening method for assessing the adrenal glands. The upper limit of the normal adrenal gland width is used as 7.5 mm. It is not known if adrenal gland width remains consistent with body weight. A reliable criterion of adrenal gland width in small breed dogs should be established. Small breed dogs with body weights of less than 10 kg were divided into two groups: 189 normal dogs and 22 dogs with pituitary-dependent hyperadrenocorticism (PDH). A retrospective study was conducted on dogs seen between January 1, 2006, and February 10, 2008. One hundred eighty-nine dogs of 14 different small breeds were enrolled in the normal adrenal gland group; the median gland width was 4.20 mm. Twenty-two dogs were in the PDH group; the median gland width was 6.30 mm. The cut-off value between normal adrenal glands and PDH was 6.0 mm. This figure gave a sensitivity and specificity of 75 and 94%, respectively, for detecting PDH. The adrenal gland appeared as a peanut shape with homogeneous hypoechoic parenchyma in normal dogs and in most dogs with PDH as well. This study was performed in a large population of small breed dogs and suggests that the normal adrenal gland size in small breed dogs is smaller than previously reported. We believe that a cut-off of 6.0 mm may be used as the criterion for differentiating a normal adrenal gland from adrenal hyperplasia.

KEY WORDS: adrenal gland size, PDH, small breed dog, ultrasonography.

Ultrasonography has been determined to be a useful primary screening modality to identify abnormal adrenal glands, such as pituitary-dependent hyperadrenocorticism (PDH), adrenal neoplasms of the cortex and medulla and hypoadrenocorticism [2, 3, 7, 9–13]. Adrenal size has been used as the principal criterion for differentiating a normal adrenal gland from adrenal hyperplasia [2]. Ultrasonographic measurement of adrenal width—the dorsoventral dimension—is more representative of gross adrenal size than is ultrasonographic measurement of length [2, 8]. In a previous study, it was suggested that an upper limit of 7.5 mm be applied to normal adrenal width [2]. However, in that study, dogs with widely ranging body weights were used. Because adrenal size is thought to be partially dependent on body weight [8, 10], evaluation of adrenal size in a large number of normal dogs of various sizes is necessary to establish a more accurate range of normal values for ultrasonographically determined adrenal size. In this study, adrenal size was evaluated in small breed dogs, and ultrasonographic characteristics of normal adrenal glands were compared with those of adrenal glands with PDH.

MATERIALS AND METHODS

In this retrospective study, we reviewed longitudinal adrenal gland images obtained from small breed dogs under 10 kg in weight seen at the Haemaru Animal Referral Hospital for routine abdominal ultrasonography between January 1, 2006, and February 10, 2008. To reduce variation in image acquisition technique among dogs, only dogs examined by the same ultrasonographer (CJH) were enrolled. Bodyweight, breed, age and sex of each dog were recorded. Dogs with any of the following were excluded from the normal group: alkaline phosphatase (ALKP) greater than 200 U/l or clinical or physical signs (polyuria, polydipsia, pendulous abdomen, hepatomegaly, dermatologic changes) of adrenal pathology. PDH was diagnosed by abnormal results on two screening tests, such as the adrenocorticotropic hormone (ACTH) stimulation test and low dose dexamethasone suppression test (LDDST), and on the basis of response to oral trilostane (Vetoryl®, Dales Pharmaceuticals, North Yorkshire, U.K.) administration, 10 mg/kg for one month. In the ACTH stimulation test, a plasma cortisol concentration greater than 20 μg/dl one hour after intravenous administration of 5 μg/kg of tetracosactrin (Synaethen inj., Dalim Biotech, Seoul, Korea), a synthetic ACTH, was considered indicative of PDH. In the LDDST test, a plasma cortisol concentration greater than 1.4 μg/dl eight hours after intravenous administration of 0.01 mg/kg of dexamethasone sodium phosphate (dexamethasone jeil inj., Jeil Pharm., Seoul, Korea) was considered indicative of PDH.

Longitudinal images of the adrenal glands were obtained with a real-time ultrasound machine (ProSound SSD-4000SV, Hitachi Aloka Medical Ltd., Tokyo, Japan). Dogs were placed in a lateral recumbent position, and abdominal ultrasonography was performed with either a 10.0 MHz linear or a 7.5 MHz convex transducer, without sedation or anesthesia. The adrenal glands were located using a standard technique, as previously described [8–10, 15]. Adrenal width was defined as the greatest dorsoventral dimension...
and was assessed by a single measurement made perpendicular to the long axis of the adrenal gland in the longitudinal plane. Measurements were obtained with the transducer in a subcostal rather than intercostal position whenever possible. Shape, echogenicity and corticomedullary architecture of the adrenal gland were evaluated subjectively.

Within normal dogs and dogs with PDH, left and right adrenal gland sizes were compared using a paired $t$-test. Body weights and ages between normal dogs and PDH dogs were compared with paired $t$-tests as well. In normal dogs, the correlation between adrenal width and body weight and the correlation between adrenal width and age were evaluated with the Pearson correlation test. Differences in normal adrenal widths with respect to breed were estimated with one-way ANOVA. Differences in adrenal width between normal dogs and PDH dogs were assessed using the Mann-Whitney U test. A $p$ value less than 0.05 was considered significant. For adrenal width, the largest measurement within the 90th percentile of dimensions obtained from normal dogs was used as the normal cut-off value. Sensitivity and specificity of ultrasonographic measurements for diagnosing PDH were calculated using standard formulae. Statistical analysis was performed with SPSS (SPSS for Windows, Release 13.0, standard version; SPSS, Inc., Chicago, IL, U.S.A.).

RESULTS

The study population consisted of 189 normal dogs and 22 PDH dogs. Dogs of 14 different breeds were enrolled. Breeds with more than one dog in the study were Yorkshire Terrier (n=46), Shih Tzu (n=27), Maltese (n=23), Miniature Schnauzer (n=14), Poodle (n=11), Pekingese (n=6) and Pomeranian (n=3). The median body weight of the normal dogs was 4.2 kg (mean, 4.36 ± 2.09 kg; range, 0.84–10 kg). The median body weights were determined for each breed with over 10 members enrolled in the study: Yorkshire Terrier 8.01 kg, Shih Tzu 5.48 kg, Maltese 3.34 kg, Miniature Schnauzer 8.01 kg and Poodle 3.82 kg. The median body weight of the normal dogs and PDH dogs was 4.48 kg (mean, 4.68 ± 1.82 kg; range, 1.75–10 kg), and there was no significant difference in body weight between the normal and PDH dogs ($P<0.05$). The median ages of the normal dogs and PDH dogs were 8.1 yr (mean, 8.39 ± 3.84 yr; range, 0.7–16 yr) and 11 yr (mean, 10.80 ± 3.37 yr; range, 4–16 yr), respectively. There were 117 females (29 spayed) and 72 males (35 castrated) in the normal group and 14 females (5 spayed) and 8 males (6 castrated) in the PDH group.

Because this study was not principally performed to investigate the adrenal glands, the glands were not always imaged bilaterally. In normal dogs, the left adrenal gland was identified in 175 dogs, and the right adrenal gland was identified in 80 dogs. In PDH dogs, the left and right adrenal gland was identified in all 22 dogs.

The median normal adrenal width was 4.20 mm (mean, 4.43 ± 1.00 mm; range, 2.2–6.65 mm). The mean left adrenal width was 4.32 ± 1.00 mm, and the mean right adrenal width was 4.21 ± 1.1 mm. A difference was not noted between the left and right adrenal gland measurements. In the small breed dogs, the normal adrenal width was not significantly different with regard to body weight ($P>0.05$) or age ($P>0.05$). The median width of normal adrenal glands for breeds in which over 10 dogs were enrolled were as follows: Yorkshire Terrier 4.3 mm, Shih Tzu 4.4 mm, Maltese 3.9 mm, Miniature Schnauzer 4.5 mm and Poodle 4.03 mm. There was no significant difference in normal adrenal gland width with respect to breed. The median adrenal gland width in PDH dogs was 6.30 mm (mean, 8.01 ± 1.46; range, 4.55–10.10 mm), significantly higher than the normal adrenal width ($P<0.001$; Fig. 1).

The adrenal glands in the normal dogs were peanut shaped, with a narrow middle region and two definite poles (Fig. 2). In most of the normal dogs (n=184), symmetric poles were observed, but in 5 dogs, the caudal pole of the gland was nearly twice as wide as the cranial pole. The contours of normal adrenal glands were smooth. In the 22 dogs with PDH, the basic peanut shape and smooth contour of the adrenal gland were the same as those described in the normal dogs, despite increased thickness (Fig. 3). The cranial and caudal poles of the adrenal gland were symmetric in 12 PDH dogs, but in 10 dogs, the caudal pole was over twice the diameter of the cranial pole. The adrenal cortex was hypoechoic to the renal cortex and adjacent fat. A homogeneous parenchyma was noted in all normal dogs and in 19 dogs with PDH. However, a heterogeneous parenchyma with focal hyperechoic regions was observed in 3 dogs with PDH. Differentiation of the adrenal cortex and medulla was possible in 73% (n=138) of the normal dogs and in 59% (n=13) of the PDH dogs.

DISCUSSION

A number of hormonal tests, as well as multiple imaging modalities—radiography, ultrasonography, CT and MRI—have been used to assess adrenal size and shape and to diagnose hyperadrenocorticism [5, 16–18]. CT and MRI enable...
visualization of the adrenal glands in dogs and may be useful in differentiating bilateral adrenal hyperplasia from unilateral adrenal gland neoplasia. However, these techniques are time consuming, require general anesthesia and are not readily available [1, 12, 17]. Ultrasonography is the most popular screening test for assessing the adrenal glands in dogs on the basis of the advanced ultrasound machines available and accumulated experience [2, 9, 10].

The ultrasonographic techniques used in this study were similar to those previously described for adrenal ultrasonography in dogs [8–10, 15]. The left adrenal gland was imaged from a subcostal position in all dogs. However, because of the more cranial position of the right adrenal gland, an intercostal approach was often needed for evaluation. In some cases, the right adrenal gland was not imaged when the abdominal pressure was elevated or when large amounts of pyloric, duodenal, or colonic gas were superimposed over it [9]. Therefore, the adrenal glands were not imaged bilaterally in all dogs, and the right adrenal gland was scanned less than half as often as the left adrenal gland. This result is compatible with a previous study in which the left adrenal gland was imaged in 182 of 193 dogs, but the right adrenal gland was imaged in only 85 of those dogs [4].

Ultrasonographic determination of the width of the adrenal gland is considered a more accurate means of evaluating adrenal gland size than adrenal length because adrenal width is more consistent through different regions of the gland, regardless of body size [2, 3]. Using a normal upper limit of 7.5 mm for adrenal width, a previous study differentiated normal dogs from PDH dogs with 81% sensitivity and 100% specificity [2]. However, that study was performed on dogs with body weights ranging from 1.8 to 70 kg [4]. Another study performed on 15 dogs with functional adrenal tumors enrolled 14 small breed dogs and 1 Rhodesian Ridgeback, and the body weights ranged from 3 to 30 kg [12]. Therefore, it is not clear that the 7.5 mm cut-off is a reliable criterion across all breeds and body weights; adrenal size may depend to some extent on body weight, and the sensitivity and specificity values assessed using the 7.5 mm cut-off may be falsely elevated [8, 10]. This suspicion has been supported by the findings of a few previous studies. One study showed the normal adrenal dorsoventral dimensions to be 3–5 mm in young adult medium-sized dogs, and

Fig. 2. Longitudinal image of the left adrenal gland in a normal dog. The adrenal gland is peanut-shaped. It is hypoechoic to the adjacent fat. The scan depth is 5 cm.

Fig. 3. Longitudinal image of the left adrenal glands in dogs with PDH. (A) In this dog, the peanut shape of the adrenal gland is maintained, with smooth contours. The adrenal gland has a narrow middle region and symmetric cranial and caudal poles. It is hypoechoic compared with the adjacent fat and homogenous. (B) The adrenal gland changed to an asymmetric shape. The caudal pole (Cau) is over twice the diameter of the cranial pole (Cr). Mixed echogenicity and a focal hyperechoic region are seen.
another study demonstrated an adrenal width of 3.5 mm in a Yorkshire Terrier and 14.3 mm in a Staffordshire Bull Terrier [7, 8]. There is limited information concerning the normal ultrasonographic size of the adrenal glands in small breed dogs, and there are no published normal adrenal measurements for each breed.

In this study, the normal adrenal width was determined to be 4.2 mm, significantly smaller than the PDH adrenal width. A normal adrenal gland cut-off value of 6.0 mm was determined, yielding a sensitivity of 75% and a specificity of 94%. Bilateral adrenal hyperplasia is a common ultrasonographic sign in PDH. However, unilateral hyperplasia or normal adrenal size may be seen in up to 20% of cases of PDH [2, 10]. When 22 dogs with confirmed PDH were evaluated with a criterion of 7.5 mm for the upper limit of adrenal width, bilateral adrenal hyperplasia was diagnosed in 3 dogs, unilateral adrenal hyperplasia was diagnosed in 3 dogs and normal adrenal size was diagnosed in 16 dogs. However, when these same 22 dogs were classified with a criterion of 6.0 mm, bilateral adrenal hyperplasia was noted in 13 dogs, unilateral adrenal hyperplasia was noted in 4 dogs and normal adrenal size was noted in 5 dogs (23%). A normal cut-off of 6.0 mm may have allowed for accurate classification of PDH dogs in this study.

There was no significant correlation between adrenal width and body weight under 10 kg, and there was no significant difference in adrenal width with respect to breed. Right adrenal width has been reported to be smaller to left adrenal width [4, 8]. However, there was no significant difference between left and right adrenal width in the small breed dogs in this study. The mean age of the normal dogs in this study was consistent with our geriatric hospital population. Because adrenal size has been found to be unrelated to age, differences in age between the groups in this study do not affect the validity of the results [2]. We investigated the correlation between adrenal width and body weight, but not between adrenal width and body surface area (BSA), because it has been previously reported that there is no significant correlation between adrenal size and BSA [4].

Normal adrenal glands are peanut-shaped with symmetrical poles, though various changes in the shape and size of the cranial and caudal poles have been reported in dogs with PDH and in normal dogs [14]. The size of the caudal pole was larger than that of the cranial pole in 5 normal dogs and in 10 dogs with PDH. The adrenal glands in most PDH dogs preserved their peanut shape with a narrow middle region [8]. A severely enlarged adrenal pole can mask a normal opposite pole. In such a situation, the overall shape of the adrenal gland can be confused as a mass, instead of an asymmetric peanut shape [3]. The adrenal cortex was hypoechogenic in comparison with the renal cortex and the surrounding fat in all the PDH dogs in this study, which is a feature seen in normal canine adrenal glands as well [8]. Most adrenal glands in the normal group showed homogeneous echogenicity. However, the adrenal glands of some dogs with PDH were found to have mixed echogenicity with focal hyperechoic regions; this finding was considered to be indicative of hyperplastic parenchyma [10]. Hyperplastic adrenal glands in dogs with PDH have been suggested to be less echogenic than normal adrenal glands [9]. However, this was not investigated in this study because the relative echogenicity between normal and hyperplastic adrenal glands depends on a lot of factors, such as mechanical settings and animal conformation. Ultrasonographic differentiation of the adrenal cortex and medulla has been accomplished in 60–70% of all normal and PDH dogs in published studies [7, 8]. Ultrasonographic characteristics such as adrenal shape, contour and echogenicity were not pathognomonic for PDH [3].

There is a limitation to the present study. Normal dogs were not selected through functional testing of the pituitary-adrenal axis, but through history, clinical index of suspicion for adrenal disease and elevation of ALKP. This is consistent with previous studies [4, 12]. However, such methodology may not exclude all dogs with PDH from the normal group. Because 25–50% of dogs with PDH fail to show suppression in an high dose dexamethasone suppression test (HDDST) and therefore these dogs would be incorrectly diagnosed as having adrenal tumors [6]. Therefore, an HDDST was not performed as hormonal screening in this study, and dogs with adrenal tumors may be included in the PDH group. However, we monitored the medication response of the PDH dogs, and this was expected to help correctly identify PDH dogs.

Ultrasonography is a useful screening test for identification and localization of adrenal lesions, even though there are no pathognomonic adrenal signs [3]. Adrenal width is the primary factor differentiating a normal adrenal gland from adrenal hyperplasia. Our results are clinically significant in that adrenal width in small breed dogs was investigated and was revealed to be smaller than data from previous studies have suggested. Moreover, this study determined the normal adrenal gland widths in specific breeds. This study appears reliable because it was conducted in a large population with a small range of body weights. An upper limit of 6 mm was determined for normal adrenal width in small breed dogs. Through further studies, we expect this criterion can be applied in clinical practice.

ACKNOWLEDGMENT. This study was supported by the Research Institute for Veterinary Science at Seoul National University.

REFERENCES


