Urodynamic and morphometric characteristics of the lower urogenital tract of male Beagle littermates from four months to two years of age

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OBJECTIVE
To describe functional and anatomic changes of the lower urogenital tract of healthy male dogs during the sexually immature period and up to 2 years of age by urodynamic and morphometric assessment.

ANIMALS
6 sexually intact male Beagle littermates.

PROCEDURES
Dogs underwent electromyography-coupled urodynamic tests, CT-assisted retrograde urethrography, prostatic washes, and blood sampling monthly from 4 through 12 months of age and then at 3-month intervals. Urodynamic and morphometric variables and serum canine prostate–specific esterase concentrations were analyzed by statistical methods.

RESULTS
Integrated pressure of the urethra was significantly increased beginning at 8 months of age, compared with earlier time points. Urethral pressure peak amplitudes varied among anatomic regions. During bladder filling, few electromyographic signals were concurrent with urethral pressure peaks; these were most commonly detected in the penile portion of the urethra. Urethral length and prostate gland volume were significantly greater from 7 to 24 months of age than at younger ages. Urethral length was approximately 26 to 27 cm after 9 months, and prostate gland volume was approximately 11 to 12 cm^3 after 11 months of age. Serum canine prostate–specific esterase concentrations correlated with prostate gland volume. Urinary bladder threshold volume was significantly increased at 6 months of age, compared with that at 4 months, with a maximum of 197.7 mL at 24 months.

CONCLUSIONS AND CLINICAL RELEVANCE
Urethral resistance was acquired at approximately 8 months of age, when growth of the lower urinary tract was incomplete. Electromyographic and integrated pressure measurement results and the distribution and amplitude of urethral pressure peaks highlighted the potential role of the prostate gland and possibly the bulbocavernosus muscles in control of continence. (*Am J Vet Res* 2021;82:144–151)

Functional characteristics of the lower urogenital tract have been studied in children and immature female Beagles. In children, control of micturition is enabled during the first 3 years of age by increased urinary bladder capacity and improved coordination of the bladder and urethral sphincter.[1] In immature female Beagles, control of vesicourethral function is acquired during the sexually immature period and improves during the first 2 estrous cycles.[2]

ABBREVIATIONS

APL	Anatomic profile length
CPSE	Canine prostate–specific esterase
FPL	Functional profile length
IP	Integrated pressure
IQR	Interquartile (25th to 75th percentile) range
MUCP	Maximum urethral closure pressure
MUP	Maximum urethral pressure
UPP	Urethral pressure profilometry

Previous urodynamic investigations of adult male dogs describe an initial increase in urethral pressure at the level of the prostatic portion of the urethra, followed by another plateau[3,4] or a slightly ascending pressure curve distal to this region.[5] However, to the authors' knowledge, no published studies have evaluated vesicourethral function during the sexually immature period or baseline urodynamic values for healthy sexually immature and mature male dogs, which makes the interpretation of urodynamic data difficult for male dogs with signs of vesicourethral dysfunction. Morphometric characteristics of the lower urogenital tract in immature female Beagles have been described,[2] but to the authors' knowledge, similar data have not been reported for immature male dogs. In male dogs, 3 urethral regions are described: the prostatic, membranous (corresponding to the postprostatic region up to the bulb of the penis), and penile regions.[6] In people, morphometric

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characteristics of the urethra can be assessed with CT-assisted retrograde urethrography.[7,8] This technique has been partially described for use in dogs[9]; however, the lower urogenital tract in dogs is usually investigated by use of ultrasonography to approximate prostate gland volume,[10,11] coupled with radiography or conventional CT for measurement of urethral length.[12–14]

The prostate gland may have a role in urinary continence for males. In dogs, the severity of incontinence after prostatectomy is thought to be related to the prostatic disease that necessitates the procedure and previous urethral dysfunction.[15–18] In men, low preoperative MUCP is a prognostic factor for persistent incontinence after radical prostatectomy.[19] In healthy adult dogs, prostate gland volume assessed by CT is more strongly correlated with the length and width than with the height of the prostate gland.[18] To the authors' knowledge, prostate gland assessment in immature dogs by CT-assisted retrograde urethrography has not been described.

The objective of the study reported here was to compare urodynamic and morphometric variable measurements of the lower urogenital tract in healthy sexually intact male Beagles at predetermined time points during the sexually immature period (with sexual maturity determined by the presence of spermatozoids in prostatic wash fluid or urine samples) and up to 2 years of age. We aimed to determine normal functional and anatomic changes that develop in maturing male Beagles and to report the results found for these healthy dogs as a basis for further urodynamic or morphological investigations. We hypothesized that the main morphological changes of the lower urogenital tract would precede the functional changes and, specifically, that prostate gland development would be associated with evidence of the maturation of urethral function.

Materials and Methods

Dogs

Six sexually intact male Beagle littermates were included in the study. The dogs were 4 months old at the beginning of the study and 24 months old at the end of the study; they were born and housed at local animal facilities. Animal housing and care at the Faculty of Veterinary Medicine of the University of Liège and experimental procedures were approved by the Ethical Committee of Animal Use at the University of Liège (reference No. 1730; December 2015). Prior to each experiment, each dog was weighed, a complete physical examination was performed, and a urine sample was obtained via cystocentesis. Urinalysis was performed by 1 author (MMP) and included a dipstick test (to determine pH and concentrations of blood, protein, bilirubin, and glucose),[a] specific gravity measurement with a manual refractometer,[b] and cytologic examination. A prostatic wash was also performed. Urine samples and prostatic wash fluid samples were submitted to a commercial laboratory[c] for bacteriologic culture if infection was suspected on the basis of bacteriuria with evidence of phagocytosis by polymorphonuclear neutrophils on cytologic evaluation. Jugular venous blood samples (5 mL) were collected for each dog at 4, 12, and 24 months of age, and a CBC[d] and serum biochemical analyses[e] were performed in the authors' research laboratory.

Study design

Each dog underwent testing at 4 months of age; tests were repeated monthly until the dog was 12 months of age and then every 3 months until the dog was 24 months of age. At each time point, serum CPSE concentration was measured with an ELISA kit.[f] Anesthesia was induced with a bolus of propofol (6 mg/kg, IV) and maintained with a continuous rate IV infusion of propofol (maximum dose, 20 mg/kg/h). A light depth of anesthesia characterized by a central eye position and presence of a palpebral reflex and jaw tone without movement was maintained during testing. Three successive UPP measurements followed by retrograde filling cystometry[g] (once) were performed as previously described,[2,20] and the mean of the 3 measurements was reported for each variable. Urodynamic tests were coupled with electromyography of the external anal sphincter. Two surface electrodes were applied on the lateral aspects of the anus, with the reference electrode at the level of the shoulder joint. After the urodynamic testing, each dog received buprenorphine (15 µg/kg, IV). A cuffed endotracheal tube was placed, and anesthesia was maintained with isoflurane in oxygen for image acquisition with a 16-slice CT-scanner[h] during unenhanced and contrast-enhanced[i] retrograde urethrography.[j] After a single acquisition of unenhanced images, 2 acquisitions were performed at 50% (craniocaudal acquisition) and 90% (caudocranial acquisition) of the volume of fluid infused into the urinary bladder, which was calculated as 5 mL/kg or the bladder threshold volume determined by cystometry (whichever was smaller). Diagnostic imaging procedures were performed by an individual certified by the European College of Veterinary Diagnostic Imaging as a specialist in veterinary diagnostic imaging (GEB) who was not blinded to the cystometry results. Dogs were monitored throughout experiments by 1 investigator (VL) who assessed oxygen saturation and pulse rate with a pulse oximeter.[k] During recovery from anesthesia, dogs were routinely monitored until their body temperature reached 37°C. Micturition behavior was monitored for 2 days after the experiments by 1 individual (MMP).

Data interpretation

The following variables were measured by UPP: MUP, MUCP (calculated as the difference between MUP and urinary bladder pressure), APL (distance be-

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tween the point in the urethra where urethral pressure exceeded bladder pressure and the point where urethral pressure decreased to atmospheric pressure), and FPL (length of the urethra along which the urethral pressure exceeded bladder pressure). The IP was calculated as the area under the urethral functional profile (ie, the area under the urethral pressure curve spanning the entire FPL).[21] The IP of the entire urethral profile, as well as IPs of the prostatic, membranous, and penile portions of the urethra, were calculated. For each pressure increase > 5 cm H_2O, the peak amplitude and its location in 1 of 5 urethral anatomic regions (the prostatic portion, membranous portion [from the distal aspect of the prostate gland to the bulb of the penis], penile portion [from the bulb of the penis to the proximal limit of the os penis], portion within the os penis, and the free extremity of the urethra [from the distal limit of the os penis to the external urinary meatus]) as defined on CT-assisted retrograde urethrography were recorded **(Figure 1)**. The presence of signals on the electromyography recording was also noted.

Threshold pressure (urinary bladder pressure at the time of micturition reflex) and threshold volume (volume of fluid collected from the bladder at the time of micturition reflex) were determined from the

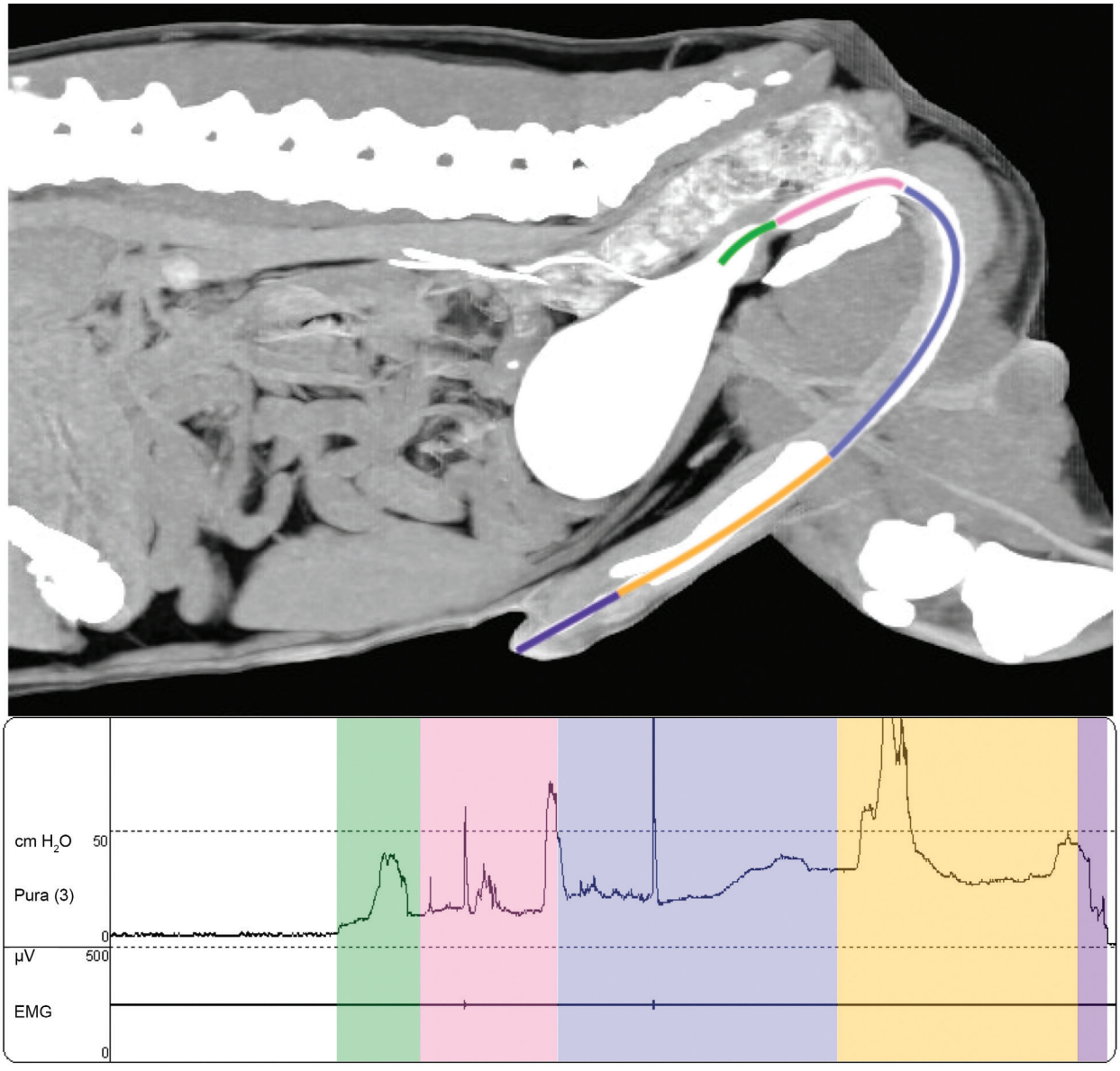

Figure 1—Reconstructed sagittal plane maximum-intensity projection image obtained during contrast-enhanced, CT-assisted retrograde urethrography of a healthy 8-month-old sexually intact male Beagle (top) and an electromyogram-coupled UPP recording for the same dog (bottom). The 5 anatomic regions assessed with electromyogram-coupled UPP are depicted with matching colors on the CT image, which is viewed in a soft tissue window. The prostatic (green), membranous (pink), penile (light purple), os penis (yellow), and free extremity (dark purple) portions of the urethra are indicated. EMG = Electromyography. Pura = Urethral pressure.

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cystometrograms. Compliance was calculated with the following equation:

$$C = (TV - V_0)/(TP - P_0)$$

where C is the compliance; TV is threshold volume; V_0 and P_0 are urinary bladder volume and pressure at the start of the cystometry, respectively; and TP is threshold pressure. Definitions were in accordance with those of the International Continence Society.[22]

At the end of the study period, the following variables were measured on the CT-assisted retrograde urethrograms. Urethral length was measured on the reconstructed sagittal maximum intensity projection CT image from the soft tissue window and was divided into the 5 described anatomic regions. The volume of the prostate gland was calculated with a volume-of-interest function in the imaging software.[l] Limits of the prostate gland were highlighted on each transverse CT image and summed to define the volume calculated by the software. The percentage of the prostate gland length located cranial to the pubic rim was calculated on the reconstructed sagittal CT image with a bone window to define the relative position of the prostate gland to the bone.

Statistical analysis

Statistical analysis was performed with commercially available software.[m] The assumption of normal distribution for all tests was evaluated with a Kolmogorov-Smirnov test. Normally distributed data are reported as mean ± SD, and nonnormally distributed data are reported as median and IQR. Potential associations of age and body weight with urodynamic and morphometric variables and CPSE concentrations were analyzed with a mixed procedure for variables that were distributed normally. When a significant effect was observed for 1 variable, the least squares mean was estimated at each age. For variables that were not normally distributed, a Friedman test was applied. Then, Wilcoxon signed rank tests were used for pairwise comparisons between ages. The distribution of urethral pressure peaks (ie, any deflection > 5 cm H_2O) along the 5 urethral regions was analyzed with a 2-way ANOVA, with the urethral regions and age of the dogs used as independent variables. The association of the amplitude of these peaks with age was assessed with a Friedman test and Wilcoxon signed rank tests for pairwise comparisons; its association with urethral regions was assessed with a Kruskal-Wallis test and Mann-Whitney tests for pairwise comparisons. The relationship between urethral length and APL was tested with Pearson correlation analysis. Relationships between other urodynamic and morphometric variables or between these variables and serum CPSE concentrations were tested with Spearman correlation analysis. The distribution of electromyography signals along the 5 urethral regions was compared with a Fisher exact test. The relationship between age and weight was modeled with quadratic regression. False discovery rate corrections were performed with *P* values to adjust for multiple comparisons. Values of $P < 0.05$ were considered significant.

Results

Dogs

Mean ± SD body weight of the 6 dogs was 9.3 ± 1.2 kg at the start of the study and 15.4 ± 1.1 kg at the end of the study. Complete blood count and serum biochemical analysis results were within the respective reference ranges for all dogs at 4, 12, and 24 months of age. No bacteriuria or leukocyturia was detected during the study. Spermatozoids were observed for the first time in samples collected for urinalysis or in prostatic wash samples of all dogs between 8 and 10 months of age. Median serum CPSE concentration was 5.82 ng/mL (IQR, 4.86 to 7.11 ng/mL). Age was significantly ($P = 0.036$) associated with serum CPSE concentration, but comparison between ages yielded

Table 1—Urodynamic variables for 6 healthy sexually intact male Beagle littermates at predetermined time points from 4 to 24 months of age.

	Age (mo)												
Variable	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**15**	**18**	**21**	**24**
MUP (cm H_2O)	74.9 ± 12.3[a,c,d]	48.5 ± 3.8[b,c]	38.1 ± 12.2[b]	44.9 ± 9.4[b,d]	102.6 ± 13.8[a,e]	108.3 ± 44.0[a,e]	84.4 ± 19.9[e]	85.8 ± 14.8[a,e]	115.5 ± 44.5[e]	86.4 ± 19.5[a,e]	88.8 ± 25.5[a,e]	87.3 ± 23.9[a,e]	107.1 ± 20.2[a,e]
MUCP (cm H_2O)	70.4 ± 13.5[a,c,j]	45.6 ± 4.4[a,b]	30.3 ± 9.7[b,d]	35.5 ± 8.8[b,d]	95.4 ± 13.6[c,e,g,j]	103.9 ± 43.7[e,f,j,l]	74.1 ± 16.9[a,e,h,j]	80.3 ± 13.9[c,f,h,k]	108.3 ± 44.1[i,m,n]	72.6 ± 20.6[a,g,k]	59.7 ± 25.0[a,d,k,m]	69.9 ± 19.3[a,g,k]	100.0 ± 18.8[j,l,n]
FPL (cm)	21.8 ± 1.1[a,b]	21.2 ± 1.1[b,d]	21.6 ± 1.9[b,d]	24.1 ± 2.0[a,c]	24.5 ± 1.2[a,c]	25.0 ± 0.8[c,e]	25.1 ± 1.6[c,e]	25.3 ± 2.0[c,e]	25.8 ± 0.8[c]	23.1 ± 3.1[a,d,e]	20.9 ± 3.2[b]	23.4 ± 1.6[a,d,e]	26.3 ± 1.3[c]
APL (cm)	22.7 ± 1.1[a,b,d,g]	22.1 ± 1.9[a,b,g]	22.1 ± 1.9[b,h]	24.3 ± 2.0[a,c,d,g]	24.8 ± 1.3[d,e,f]	25.0 ± 0.9[d,e,f]	25.4 ± 1.5[d,e,f]	26.0 ± 0.9[c,e]	26.0 ± 0.9[c,e]	23.3 ± 3.4[a,b,f,g]	21.9 ± 2.5[g,h]	24.3 ± 1.4[a,b,d,f]	26.1 ± 1.3[d,e]
IP of the urethra (cm•cm H_2O)													
Entire profile	450.8 ± 65.7[a]	379.8 ± 30.0[a]	393.6 ± 44.7[a]	524.8 ± 37.7[a,b]	742.4 ± 65.8[c,d]	763.7 ± 89.0[c,d]	774.5 ± 129.3[c,d]	882.8 ± 239.9[d]	856.2 ± 138.4[d]	782.8 ± 149.4[c,d]	685.1 ± 123.9[b,c]	804.3 ± 120.9[c,d]	858.3 ± 55.2[d]
Prostatic portion	18.8 (16.0–21.3)	17.4 (14.7–19.3)	24.5 (22.3–28.3)	33.8 (29.7–50.3)	55.5 (26.0–57.7)	43.5 (35.7–51.7)	61.3 (53.3–67.3)	51.9 (40.7–71.7)	59.5 (53.0–60.7)	66.17 (54.3–76.3)	47.3 (45.0–59.0)	76.3 (69.0–89.3)	62.3 (48.3–73.7)
Membranous portion	84.3 (66.3–87.3)	61.8 (54.0–67.0)	53.0 (47.0–59.3)	58.5 (54.0–85.0)	84.8 (78.0–96.0)	81.5 (76.3–96.3)	92.7 (86.3–96.0)	113.7 (90.0–162.7)	127.7 (108.7–149.3)	105.3 (84.0–153.0)	72.0 (66.7–77.7)	106.2 (65.0–124.7)	122.5 (114.7–137.0)
Penile portion	155.2 (135.7–175.7)	137.1 (128.3–148.7)	143.8 (137.0–158.7)	181.0 (175.7–190.3)	287.3 (257.0–337.7)	259.2 (227.3–275.7)	223.2 (209.7–236.0)	280.8 (218.7–301.0)	268.8 (239.0–296.7)	236.8 (222.7–273.7)	241.7 (240.3–266.7)	261.5 (211.3–272.3)	278.2 (197.3–284.0)
Urinary bladder													
Threshold pressure (cm H_2O)	31.0 ± 6.0[a,b]	23.2 ± 8.5[a,b]	21.3 ± 12.2[a,b]	18.2 ± 4.4[b]	34.5 ± 9.5[a]	29.3 ± 15.2[a,b]	28.3 ± 11.2[a,b]	28.1 ± 14.5[a,b]	29.8 ± 7.8[a,b]	32.3 ± 16.6[a,b]	54.0 ± 8.1[c]	37.8 ± 9.6[a]	38.0 ± 8.3[a,c]
Threshold volume (mL)	53.4 ± 23.0[a]	90.7 ± 15.1[a,b]	116.3 ± 25.3[b,c]	94.5 ± 15.9[a,b]	95.2 ± 14.7[a,b]	119.5 ± 32.7[b,c]	114.5 ± 34.2[b,c]	123.0 ± 49.4[b,c]	140.8 ± 36.7[b,c]	156.2 ± 59.3[c,d]	151.3 ± 45.2[c,d]	158.5 ± 55.4[c,d]	197.7 ± 49.2[d]
Compliance (mL/cm H_2O)	1.7 (1.1–2.1)	4.3 (2.9–5.9)	7.7 (4.0–10.8)	5.3 (3.8–7.0)	3.3 (2.4–3.1)	4.7 (2.7–7.4)	4.5 (2.9–5.1)	3.8 (2.1–7.8)	5.1 (4.6–5.9)	5.0 (3.4–6.8)	2.8 (2.1–3.3)	4.7 (3.4–5.5)	5.7 (4.7–5.5)

Data are reported as mean ± SD or median (IQR).
[a–n]Within a row, values with different superscripted letters are significantly ($P < 0.05$) different.

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no significant differences after false recovery rate correction.

Urodynamic variables

Age was significantly ($P < 0.05$ for all comparisons) associated with all urodynamic variables. Most urethral urodynamic variables increased significantly, compared with the previous time point, at 7 (APL, $P = 0.017$; FPL, $P = 0.017$) and 8 (MUP, MUCP, and IP of the entire urethral profile: $P < 0.001$, $P < 0.001$, and $P = 0.001$, respectively) months of age. Thereafter, these values remained increased overall, although some variability was observed among time points; notably, values were significantly lower at 18 months of age for MUCP (compared with 8, 9, and 24 months [$P < 0.025$ for all comparisons]), FPL (compared with all other time points after 6 months [$P < 0.038$ for all comparisons]), APL (compared with 8, 9, 10, 11, 12, 21, and 24 months [$P < 0.016$ for all comparisons]), and IP of the entire urethral profile (compared with 11, 12, and 24 months [$P < 0.027$ for all comparisons]; **Table 1**). Subjective assessment indicated that IP of the prostatic portion of the urethra increased from 5 to 10 months of age and then remained stable; IP of the membranous portion of the urethra increased from 6 to 8 months of age, then increased again from 10 to 12 months of age; and IP of the penile portion of the urethra increased from 5 to 8 months of age and remained stable thereafter; however, these differences were nonsignificant after false discovery rate correction.

Along the urethral length, 14.35%, 18.5%, 26.35%, 34.75%, and 6.05% of pressure peaks were localized within the prostatic, membranous, penile, os penis, and free extremity portions of the urethra, respectively. The number of peaks was significantly ($P < 0.05$) different among urethral anatomic regions, except between the prostatic and membranous portions (data not shown). Beginning at 4 months of age, a single pressure peak consistently spanned the region of the UPP recordings that corresponded to the prostatic portion of the urethra. The mean amplitude of pressure peaks increased significantly ($P = 0.005$) between 6 (14.9 ± 5.8 cm H_2O) and 7 (19.6 ± 11.1 cm H_2O) months of age and remained stable thereafter. The mean amplitude of the pressure peaks varied significantly ($P = 0.002$) among urethral anatomic regions. Although amplitudes of pressure peaks observed in the prostatic and membranous portions of the urethra appeared higher than those in the penile portion, the result was not significantly different after false discovery rate correction. For all dogs, some urethral pressure peaks of similar shape were observed at the same location on 3 consecutive UPP recordings, at different ages, or both.

Threshold pressures remained fairly stable throughout the study, except for a significant ($P = 0.005$) increase at 18 months of age (Table 1). Threshold volumes were significantly ($P = 0.03$) increased at 6 months of age, compared with the result at 4 months, and were significantly ($P < 0.05$) greater than the initial measurement from 9 to 24 months of age, with a maximum mean value of 197.7 mL at 24 months. Mean urinary bladder capacity was 10 mL/kg and 12.9 mL/kg at 12 and 24 months of age, respectively. No significant difference in urinary bladder compliance was found between ages after false discovery rate correction.

Morphometric variables

Age and body weight were each significantly ($P < 0.001$ for both comparisons) associated with urethral length. All urethral length measurements from 7 to 24 months of age were significantly ($P < 0.001$ for all comparisons) greater than those at 4 to 6 months. A peak mean urethral length of 27.2 cm was detected at 10 months of age, with values remaining close to 26 or 27 cm thereafter **(Table 2)**. All prostate gland volume measurements from 7 to 24 months were significantly ($P < 0.05$ for all comparisons) greater than those at 4 to 6 months. A peak mean volume of 12.07 cm^2 was detected at 18 months of age, with values remaining close to 11 or 12 cm^3 from 11 to 24 months of age. The percentage of the prostate gland length located cranial to the pubic rim was ≤ 38.6% (peak mean value detected at 15 months of age) throughout the study.

Correlation among variables

There was a significant ($P < 0.001$) correlation ($r = 0.64$) between age and body weight. Urethral length was significantly ($P < 0.001$) correlated with APL ($r = 0.70$). The IP of the prostatic portion of the urethra was significantly correlated with the percentage of prostate gland length cranial to the pubic rim ($r_S = 0.36$; $P = 0.001$), prostate gland volume ($r_S = 0.71$; $P < 0.001$), and serum CPSE concentration ($r_S = 0.41$; $P < 0.001$). Prostate gland volume was significantly correlated with urethral length ($r_S = 0.84$; $P < 0.001$) and serum CPSE concentration ($r_S = 0.31$; $P = 0.007$).

Electromyography

Seventeen electromyography signals were recorded concomitantly with a urethral pressure peak

Table 2—Morphometric variables of the lower urogenital tract for the 6 dogs in Table 1.

	Age (mo)												
Variable	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**15**	**18**	**21**	**24**
Prostate gland volume (cm^3)	2.45[a] (1.80–2.75)	2.53[a,b] (2.30–3.45)	3.90[b] (3.54–5.13)	6.22[c] (5.83–8.50)	7.17[c] (6.79–9.08)	8.45[d] (8.22–11.99)	9.60[d,e] (9.37–11.09)	10.52[e,f] (9.26–12.81)	11.10[f,g] (10.38–12.40)	11.69[g] (10.82–15.33)	12.07[g] (10.67–14.77)	10.57[e,f] (9.56–14.60)	11.95[e,f,g] (10.42–15.79)
Urethral length (cm)	24.1 ± 1.5[a]	23.9 ± 1.5[a]	24.4 ± 1.3[a]	25.8 ± 0.9[b,e,f]	26.2 ± 1.1[b,c,e,f]	27.0 ± 1.0[d]	27.2 ± 0.8[d]	26.9 ± 0.9[c,d]	27.1 ± 0.7[c,d]	26.6 ± 1.2[b,d]	26.8 ± 1.5[d,e]	25.8 ± 0.7[b]	26.6 ± 1.0[d,f]

See Table 1 for key.

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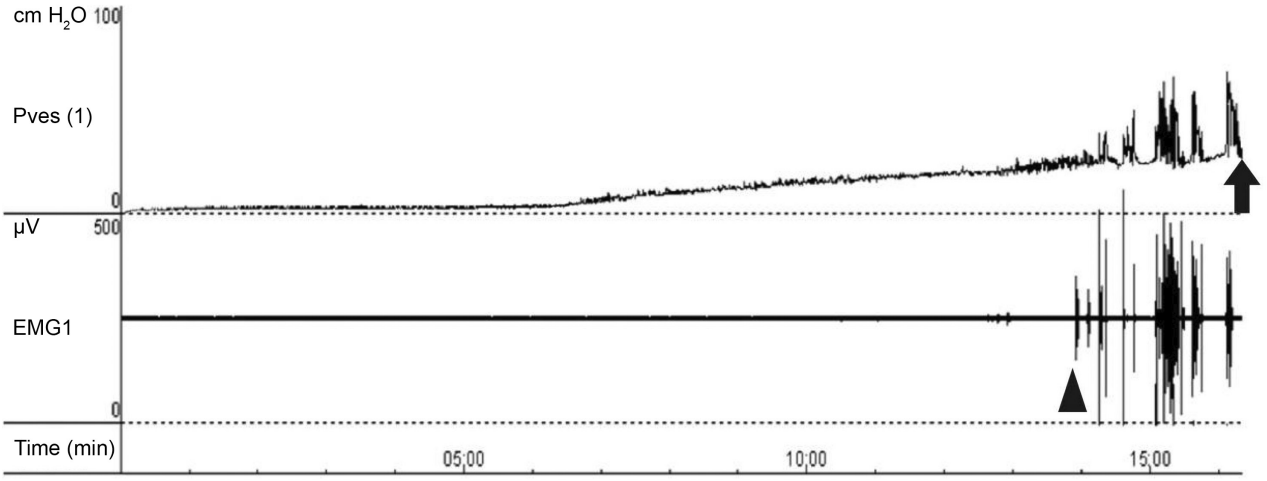

Figure 2—Electromyography-coupled cystometrogram of a healthy 18-month-old sexually intact male Beagle (1/9 procedures in which an EMG signal was detected concurrently with a bladder pressure peak). As urinary bladder pressure increases, the electromyography signal intensifies (arrowhead). Urinary bladder pressure decreases at micturition (arrow). Tic marks on the x-axis represent 1-minute increments. EMG = Electromyography. Pves = Urinary bladder (vesica) pressure.

during UPP. Twelve of these pressure peaks were observed within the penile portion, 3 within the os penis portion, and 2 within the membranous portion of the urethra. Among 78 cystometry records, only 9 showed electromyography signals synchronized with bladder pressure peaks just before micturition; an example is provided **(Figure 2)**.

Discussion

The present study investigated the evolution of urodynamic and morphometric variables of the lower urogenital tract in healthy sexually intact male Beagle littermates from 4 to 24 months of age. Our results indicated that in growing male dogs, similar to what has been observed in females,[2] urethral resistance (as assessed by IP of the entire urethral profile) increases at 8 months of age to reach values reported[23] for healthy adult male dogs. This implied that urethral competence is achieved while the lower urinary tract is still growing. Indeed, the peak mean prostate gland volume was detected at 18 months of age in the dogs of our study.

In the present study, UPP recordings started with a broad burst of pressure corresponding to the junction between the urinary bladder neck and prostatic portion of the urethra. The urethral pressure then slowly increased with a baseline slope that remained < 50 cm H_2O, whereas a plateau at approximately 50 cm H_2O has been described in conscious male dogs.[4] In the study reported here, sudden rises in urethral pressure were observed at the level of the ischiatic curvature and at the level of the os penis. One striking finding was the presence of pressure peaks of variable amplitude along the urethral profile, some of which were reproducible for the same dog throughout the study. The mean amplitude of those peaks was stable after 7 months of age and appeared higher in the prostatic and membranous portions of the urethra than in the penile portion, although this difference was not significant. The value of 5 cm H_2O was arbitrarily chosen to increase sensitivity in detecting a peak, but this may have been detrimental to specificity since sudden changes in urethral pressure were of unknown origin and may also have represented artifacts. Therefore, these results should be interpreted with caution. In people, rhythmic urethral pressure variations may be part of normal urethral physiology, as they can be observed in healthy subjects.[24]

Furthermore, urethral pressure measurements should be interpreted cautiously because they provide a description of passive pressure mechanisms detected during catheter withdrawal but do not explain continence mechanisms. Indeed, the high passive resistance of the penile portion of the urethra observed in the present study could not be sufficient to counteract increases in abdominal or urinary bladder pressure. The penile portion of the urethra opposes resistance to urine outflow because its less expandable lumen, compared with the prostatic and membranous portions of the urethra, results in a higher regional IP. Consequently, interpretation of UPP results for male dogs with pathological conditions may not be sufficient to draw conclusions, and a subtle balance between active and passive mechanisms may explain why subtotal penis amputation is not associated with urinary incontinence,[25,26] whereas prostatectomy may lead to urinary incontinence[6,9] in this species.

Urinary bladder compliance depends on threshold pressure and threshold volume. In the present study, variations of these 2 variables did not correspond with each other, which could have contributed to the absence of significant differences in bladder compliance between ages. Bladder compliance is a measurement of bladder distension aptitude during the filling phase, so it is important to compare the

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development of bladder compliance and bladder capacity.[1] In the present study, there was an apparent increase in bladder capacity from 12 to 24 months of age, but compliance did not change significantly. This suggested that, at approximately 2 years of age, the bladder has a large capacity but does not readily adapt to pressure changes. This late increase in bladder capacity might be associated with urinary marking behavior of male dogs, considering that storage of a large volume of urine may not be needed when micturition is frequent.

During CT-assisted retrograde urethrography, precise delimitation of the prostate gland and surrounding tissues before 6 months of age was hampered by the immaturity of the prostate gland. The prostate gland was localized by the slight urethral deformation observed caudal to the urinary bladder. In 1 dog, this deformation of the prostatic portion of the urethra was reinforced by a sigmoid inflection. The mean prostate gland volume stabilized at approximately 12 cm^3 at 15 months of age, and this value at 24 months was substantially smaller than the 26 cm^3 reported for 2-year-old dogs of other breeds.[15] For dogs of the present study, the main portion of the prostate gland was always localized in the pelvic canal. This finding was similar to results of a previous study[27] that showed a gradual displacement of the prostate gland toward the abdomen, with half of the gland being intra-abdominal at 4 years of age. Prostate gland volume and IP of the prostatic portion of the urethra were correlated (r_S = 0.71) for dogs in our study. In men, the prostate gland enlargement secondary to benign hyperplasia leads to an increase in FPL but not in MUCP.[28] We could therefore hypothesize that similarly in dogs, the increasing IP values observed with increasing prostatic volume would result from an increase in FPL rather than an increase in MUCP.

Some of the EMG signals observed during cystometry were synchronized with urinary bladder pressure peaks and were observed just before micturition. These signals likely evidenced contractions of the external urethral sphincter when bladder threshold volume was reached. During the urine storage phase in a healthy individual, a progressive increase of electromyography activity is expected because of the recruitment of motor units. Just before micturition, urethral muscles relax and electrical silence should be observed.[29] A limitation in the present study was the interpretation of a silent electromyogram, as this can reflect the absence of signal or an undetected signal. Unlike needle electrodes, surface electrodes record global activity from the muscle but do not record a unique motor action potential of a motor unit.[30] Surface electrodes can be difficult to attach at the proper position, so recordings are less reproducible than those obtained with needle electrodes.[30] This might also explain why urethral pressure peaks of the membranous portion of the urethra were rarely synchronized with an electromyography signal in our study. Interestingly, 12 out of 17 urethral pressure peaks that were synchronized with EMG signals were localized in the penile portion of the urethra. Such signals might correspond to a sacral reflex leading to bulbocavernosus muscle contractions after a stimulus initiated by the displacement of the urethral catheter within the penile urethra.[31,32] This hypothesis is supported by the monomorphic aspect of pressure peaks when they are observed at the same location on 3 consecutive UPP recordings. Thus, in adult male dogs, the bulbocavernosus muscles might potentially have a role in urethral resistance in addition to the striated urethral sphincter.

In the present study, serum CPSE concentration was correlated (r_S = 0.41) with prostate gland volume, in agreement with the findings in a previous study[33] of adult dogs. The influence of age on serum CPSE and on prostate gland volume was evidenced by the loss of correlation between prostate gland volume and serum CPSE when time was withdrawn from the analysis, although no significant difference between ages was found for CPSE concentrations. Serum CPSE was detected at all time points in our cohort of young dogs, although concentrations were markedly lower (median, 5.82 ng/mL) than concentrations described in 1 study[34] for castrated and sexually intact male dogs of various breeds without prostatic diseases (mean ± SD, 41.8 ± 68.5 ng/mL). However, CPSE serum concentration as low as 9.65 ng/mL has been reported for a healthy 3-year-old Weimaraner.[35]

Limitations of the study reported here included the need for general anesthesia to allow urodynamic examinations, although a standardized urodynamic protocol was used.[2,20] Surface electrodes may not be reliable enough when applied over the thin anal sphincter muscle; however, it was not possible to adapt needle electrodes to our device. Moreover, the assessment of plasma luteinizing hormone concentrations may have been useful to assess the potential role of hormonal changes in urethral pressure and lower urinary tract growth from the sexually immature stage. Finally, it must be acknowledged that the study was conducted with a single litter of Beagles. Evaluation of unrelated Beagles and dogs of other breeds is needed to confirm these findings for healthy dogs, and additional research is required to assess the consequences of pathological conditions on bladder and urethral function in male dogs.

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Footnotes

a. Urispec Plus VET 10 Plus urinalysis strips, Henry Schein Inc, Melville, NY.
b. Euromex microscopen, Arnhem, Netherlands.
c. Synlab Laboratoire Collard, Liège, Belgium.
d. Procyte Dx, Idexx Laboratories Inc, Westbrook, Me.
e. Catalyst Dx, Idexx Laboratories Inc, Westbrook, Me.
f. Odelis CPSE, Bio Veto Test, La Seyne sur Mer, France.
g. Libra+, Medical Measurement Systems, Retie, Belgium.
h. Somatom, Siemens Healthineers, Erlangen, Germany.
i. Télébrix 35, 350 mg of I/mL, Guerbet, Villepinte, France.
j. Porato M, Hamaide A, Noël S, et al. CT-assisted retrograde urethrography in male dogs (abstr), in *Proceedings*. Annu Meet Eur Vet Diagn Imag 2017;142.
k. Viamed Ltd, Keighley, England.
l. Syngo.via, Siemens Healthineers, Erlangen, Germany.
m. SAS/STAT, version 9.1, SAS Institute Inc, Cary, NC.

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