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REVISED

ASSESSMENT OF THE AGE FOR A PREVENTIVE ULTRASONOGRAPHIC EXAMINATION OF THE PROSTATE IN THE DOG.

G. Mantziaras[1], S. Alonge[2], M. Faustini[3], and G.C. Luvoni[2*]

[1]Veterinary Department, Medical Directorate of Hellenic Airforce General Staff, Athens, Greece;

[2]Dip. Scienze Veterinarie per la Salute, la Produzione Animale e la Sicurezza Alimentare; [3]Dip. Medicina Veterinaria; Università degli Studi di Milano, Italy

*Corresponding Author
Gaia Cecilia Luvoni
Dipartimento di Scienze Veterinarie per la Salute, la Produzione Animale e la Sicurezza Alimentare;
Università degli Studi di Milano, Via Celoria, 10 – 20133 Milano, Italy
Phone +39 02.503.18147
Fax +39 02.503.18148
e-mail cecilia.luvoni@unimi.it

SUMMARY

The prostate commonly develops benign prostatic hyperplasia (BPH) in dogs over 5 years, while in aged dogs other pathological findings might be revealed by ultrasonographic exam. The aim of the present study was to estimate the most suitable age for a preventive ultrasonographic examination of the prostate in the dog. The prostate of 1003 intact male dogs of 64 different breeds, of different ages (1-18 years) and bodyweights (2-55 kg) was evaluated with ultrasound, irrespective of the reason for clinical examination. The age of each dog was expressed as the ratio between the actual age and the maximum longevity expected for the breed. Dogs were divided in two groups based on breeds' life expectancy as short life (SL) and long life (LL). The size of the prostate (normal, enlarged or small) and the presence of abnormal sonographic findings were recorded for each dog. The results of the present study indicate that the most suitable age for a preventive ultrasonographic exam of the prostate in the dog is approximately at 40% of its expected longevity, both in short and long life breeds, because at this age there is a strong possibility to be able to detect abnormal prostatic findings. In 47.5% of the dogs at least one abnormal finding of the prostate was revealed by ultrasonographic exam, while dogs with long life expectancy showed a significantly higher prevalence of abnormalities, than dogs with short life expectancy. The most frequent findings were the increase of prostatic size (33.5%) and the presence of at least one cyst (33.6%), with no difference between SL and LL dogs.

In conclusion, a preventive examination of the prostate starting at 40% of expected longevity in dogs of short and long life breeds is strongly recommended for early detection of abnormalities, for scheduling specific follow up and for suggesting effective therapeutic protocols.

Key words: canine, prostate gland, echography, prevention

1. INTRODUCTION

Age related changes of the prostate in dogs have already been documented in the literature [1-5]. It is well known that the prostate gland commonly develops benign prostatic hyperplasia (BPH) in intact male dogs over 5 years [6], and that signs suggestive of prostatic disease are commonly found in dogs older than 6 years [7].

The incidence of prostatic diseases has risen steadily over the past years because dog's life expectancy has increased: the overall median age of death is 11 years approximately and, according to the literature, there is a tendency to continue to increase [8-10]. This can be attributed to different factors, including better management and nutrition, owner education and improved veterinary care and prevention.

The author's opinion is that a non-invasive screening of the prostate status and health would be advisable as a part of a preventive medicine program of geriatric diseases in dogs. The most common prostatic diseases such as BPH, and cysts are generally asymptomatic at their onset and their early detection would allow the clinician to plan specific follow up and to recommend effective therapeutic protocols. The debate on the management and therapy of prostatic diseases in dogs is still in progress, but the current availability of medical treatments prompts development of a screening program, with the aim of avoiding the potential invasive option, i.e. orchiectomy, with the end of reproductive career of the stud.

The physio-pathological process of ageing of the prostate gland has been well studied [11], but no information is available about at what age, how often and even whether a screening program of the prostate health should be recommended in dogs. To define a screening program, the age when the examination should begin, is the first decision to be made. Due to different breed's expected longevity, a dog of a certain age might be considered as geriatric in large breeds, and not geriatric in small breeds [8,10,12]. For instance, small-breed dogs become geriatric at about 11 years, whereas

giant-breed dogs at 7 years. Longevity in crossbred dogs exceeds that of purebred dogs by 1.2 years and increasing bodyweight is negatively correlated with life expectancy [10].

Thus, the age for the early detection of abnormalities in the prostate could vary in dogs of different breeds.

The aim of the present study was the estimation of the recommended age for a preventive ultrasonographic examination of the prostate in the dog. To achieve normalization between dogs breeds with different life expectancy, the ratio between the actual age and the maximum longevity, rather than the number of years, was considered.

2. MATERIALS AND METHODS

2.1 Animals

In intact male dogs presented to the hospital for the first time, prostate gland was examined by ultrasonography, irrespective of the reason of the clinical examination. All dogs that were not previously treated for genital or urinary disorders were included in the study. In all cases, informed owner consent was obtained.

Dogs (n. 1003) belonged to different pure breeds (n. 63) and to crossbreeds (Table 1) and were divided in two groups based on breeds' life expectancy [8,10,12,13] as short life (SL n. 356) and long life (LL n. 647).

2.2 Ultrasonographic examination

All dogs were examined by the same operator in standing position or in lateral recumbency and no sedation was needed. Clipping of hair was not always necessary. Acoustic gel was applied in order to obtain adequate skin contact with the transducer that was positioned on the caudal abdominal wall, to one side of the prepuce and just cranial to the pubic bone [14]. The prostate was examined with a

102 microconvex probe (variable frequency of 6-10 MHz) and a linear probe (variable frequency of 5–13
103 MHz) using a Logiq F8 General Electric (GE) ultrasound machine (GE, Jiangsu, China).
104
105 For each dog, sagittal and transverse images of the prostate gland were obtained. True sagittal position
106 was confirmed by the observation of the hypoechoic urethral tract, which was used as a landmark.
107 Length and height were measured on the sagittal images. Length was defined as the maximum
108 diameter of the gland parallel to the urethral axis. Height was defined as the maximum diameter
109 orthogonal to the axis of the length. The transducer was then rotated 90 degrees to obtain a transverse
110 image of the gland. On transverse scans, height was defined as the diameter of the prostate across
111 median septum that separates left and right lobes of the gland, and width as the maximum diameter
112 orthogonal to the axis of the height.
113 At least three separate sagittal and transverse images were obtained and the mean measurement for
114 each dimension was recorded. Prostatic volume was estimated using the ellipsoid formula L x W x H
115 x 0.523 where the average of the height measured on sagittal and transverse images was used. The
116 prostate was classified as normal, enlarged or small [2].
117
118 Ultrasonographic evaluation of the prostate also included the record of the presence of specific
119 abnormal sonographic findings such as: endoprostatic cysts (smaller or larger than 0.5 cm),
120 paraprostatic cysts, asymmetry of the lobes, mineralization, and other focal lesions [15]. Prostates
121 that had a normal size and no other findings were considered as normal.
122
123 *2.3 Statistical analysis*
124 Mean age ± SD of the SL and LL groups were analyzed by Student t-test.
125 The age of each dog was expressed as the ratio between the actual age and the expected maximum
126 longevity and not as the number of years, in order to achieve normalization between dogs of different
127 expected longevity [8,10]. An 8 years old German Spitz for example that has a maximum life

128 expectancy of approximately 16 years [8], is at a 0.5 (50%) ratio of his expected life. On the other
129 hand, an 8 years old Grand Bleu de Gascogne that has a maximum life expectancy of approximately
130 10 years [8], is at a 0.8 (80%) ratio of his expected life.
131
132 The proportions of dogs with and without abnormal sonographic findings, different size of the
133 prostate and specific abnormal findings in SL and LL groups were analyzed by Chi-square test. A
134 level of significance was set at $P \leq 0.05$.
135
136 The cutoff age ratio with the best balance between sensitivity and specificity (maximum proportion
137 of true positives and negatives) in order to detect an abnormal finding in the prostate was determined
138 by a receiving-operating characteristic curve (ROC) in both groups (SL and LL) and in the overall
139 dog sample. The area under the curve was calculated, and a z-test was performed to determine the
140 significance of the area (H_0- area>0.5).
141
142 Sensitivity (Se), specificity (Sp), positive and negative predictive values (PPV and NPV, respectively)
143 were calculated for the cutoff age ratio in both groups and in the overall dog sample.
144
145 3. RESULTS
146 Mean age of dogs in short and long life group was 7.1 ± 1.99 and 8.6 ± 4, respectively
147 ($p<0.000000005$).
148 The prevalence of abnormal findings of the prostate in 1003 dogs was 47.5%. Dogs with long life
149 expectancy (LL) showed a significantly higher prevalence of abnormal findings of the prostate, than
150 dogs with short life expectancy (SL; Table 2).
151 The enlarged prostate was the most commonly observed abnormality of the gland (Table 3). Among
152 specific abnormalities the presence of cysts (small and large) accounted for 33.6%.

Enlargement of the prostate combined with other abnormalities was imaged in 82.7% (278/336) of the dogs, with cysts in 74.3% (253/336), whereas only an enlarged prostate was observed in 17.3% (58/336).

The prevalence of specific abnormal findings in the two groups of dogs was similar with no significant difference (Table 4).

The AUC (area under curve) for the ROC curve on all dogs was 0.78 ($p<0.001$). The prevalence of findings was 47%, with an age cutoff of 0.41, i.e. the best balance between sensitivity and specificity was at 41% of the maximum expected age.

The PPV was 0.69, while the PPV was sensibly higher (0.79), making the test a negative, rather than a positive prediction test.

For the dogs of group SL, the AUC accounted for about 80% ($p<0.001$). The age cutoff was 0.44.

The PPV for this group was 0.62, but there was a remarkable NPV (0.83), making the test a better negativity, rather than a positivity prediction test.

Group LL was characterized by a ROC curve with AUC of 0.77, quite similar to that of the dogs of both groups (SL+LL). Also in this case, the AUC was highly significant ($p<0.001$) and the age cutoff was 0.41. PPV in group LL was 0.72 and NPV was 0.74.

In table 5, ROC derived parameters are summarized. No statistical significant differences were noticed between ROC derived parameters of group SL, LL and the overall dog sample (SL+LL).

DISCUSSION

Present results indicate that the most suitable age for a preventive ultrasonographic exam of the prostate in the dog is approximately at 40% of its expected longevity, both in short and long life breeds, because at this age there is a strong probability to detect prostatic abnormal findings.

Several authors reported the age at which is more common to detect prostatic abnormalities in dogs, without considering the expected longevity of the specific breed [2,4,7,16].

For instance, Krawiec and Heflin [16] have indicated that the mean age at the onset of prostatic disease was 8.9 years. According to the present study, a preventive screening at this age might be of clinical value only in dogs of breeds living longer. Polisca et al. [17] suggested that prostatic ultrasound should be performed at the 5th year of age in breeding dogs and at 6th to 7th year in non-breeding ones, but even in this case the age might be not adequate for different breeds.

Therefore, the use of the age ratio on expected longevity, rather than the number of years, is the most accurate way to express the stage of life/aging process in dogs of different breeds.

High accuracy of the obtained results, both in short and long life breeds, is indicated by the high positive and negative predictive value (PPV: 0.62-0.72; NPV: 0.76-0.83, respectively) of overall abnormal findings. These values represent the probability to have true positive or negative results at the age ratio suggested by the ROC curve. This is also confirmed by the high NPV of each abnormal finding. On the other hand, low PPV of specific findings, such as paraprostatic cysts and mineralization, is influenced by their low prevalence and in clinical practice these uncommon prostatic abnormalities have poor relevance for a preventive screening.

Concerning the prevalence of prostatic abnormalities in the overall population examined in this study, present data show that routine ultrasonographic evaluation, irrespective of the reason for the veterinary consultation, revealed in 47.5% of the dogs at least one abnormal finding and the prevalence was higher in dogs with long life expectancy than in those with short life expectancy. This high rate cannot be compared with data reported in the literature. To the authors knowledge, this is the only study in a general, intact large sample of dogs, whereas other studies have included relatively smaller samples of dogs, or pruned samples based on different inclusion criteria: intact and castrated dogs, or only dogs with clinical symptoms or suspected to be affected by prostatic disorders [16-19]. The most frequent abnormal finding (33.5%) was an increase in the size of the prostate. This increase could be the result of different disorders, such as BPH, presence of cysts, prostatitis, abscesses or

even neoplasia, although less prevalent in entire dogs [7,18]. Among these disorders, BPH is considered the most common alteration of the gland and according to other authors it accounts for over 50% of cases of prostatic disease in dogs [16,18,20].

Benign prostatic hyperplasia, as a consequence of both an increase in cell number (hyperplasia) and an increase in cell size (hypertrophy) [16,21], has a progressive course that starts without symptoms, before becoming clinically evident and requiring therapy [6,7,11]. Most dogs do not exhibit clinical signs of hyperplastic growth, because of the outward expansion of the gland into the abdominal and pelvic cavities [22], in contrast to the inward nodular growth causing early compression of the urethra in men [23]. Therefore, a non-invasive screening program of the prostate gland is advisable to early detect BPH in asymptomatic dogs.

The analysis of the specific ultrasonographic abnormal findings, demonstrate that 337 dogs out of 1003 had prostatic cyst (33.6%), with no difference between SL and LL dogs. This is a high prevalence compared to previous studies, in which the presence of cysts was low (3-15%) although the dogs examined in these studies were only those with a history and/or physical signs of prostatic disease [16,18,19].

As far as the authors know, only one study was performed in dogs with problems unrelated to the prostate gland. The results showed that 14% of male dogs were affected by cysts [24]. According to our results the prevalence of prostatic cysts in intact dogs is much higher and a possible explanation could be the improvement in quality of ultrasound machines in the last ten years.

Furthermore, it is interesting to note that in 82.7% of dogs the enlargement of the prostate coexisted with other findings. Among these, the concurrent presence of cysts was evident in 74.3% of dogs and this association is in agreement with other epidemiological studies that documented the more common

231 prostatic diseases which may sooner or later threaten the well-being of a dog [5,11]. This suggests
232 that in clinical practice when an enlarged prostate is diagnosed, a more detailed exam of the organ
233 should be performed.
234 The digital rectal examination (DRE) of the prostate gland was considered the most convenient
235 method for prostatic disease detection. Some authors suggested that DRE has a high specificity and
236 high PPV, but a low sensitivity and NPV, which limits the usefulness in clinical practice [25]. In
237 addition, the potential association of the increase in size of the gland with other abnormalities cannot
238 be revealed by DRE. For this reason, B-mode ultrasound is the method of choice for the examination
239 of the gland and can represent the gold standard for a non-invasive screening program [19,26,27].
240 Practitioners are encouraged to inform the owners about the potential effects of ageing on the prostate
241 gland. As in bitches, cystic endometrial hyperplasia (CEH) has similar epidemiological and
242 etiological features to BPH [28-32], because is age-related, under hormonal control, and symptomless
243 before it evolves into pyometra, BPH can be complicated by infection of glandular cysts resulting in
244 prostatitis. Asymptomatic male dogs should start to be screened to prevent complications which may
245 become life-threatening. Nevertheless, suggested screening intervals and clinical studies to assess the
246 effectiveness of the screening program in the reduction of morbidity of prostatic disease in dogs
247 deserve further investigations. For instance, a multi-centric study with a larger sample of dogs
248 enrolled in different countries would greatly contributed to this aim.
249 In conclusion, the preventive examination of the prostate starting at 40% of expected longevity in
250 dogs of short and long life breeds is strongly recommended for an early detection of abnormalities.
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Author contributions.

GM collected the data and drafted the paper. SA and GCL contributed to analyse the data and drafted the paper. MF performed statistical analysis. All authors have approved the final version.

Conflict of interest.

None of the authors of this article has a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of the paper.

331 Table 1. Number of dogs of different breeds of short life (SL) and long life (LL) expectancy included
332 in the study.
333

Short life		Long life	
Breed	**Dogs n.**	**Breed**	**Dogs n.**
Airedale Terrier	1	Basset hound	3
Akita	3	Beagle	15
Alaskan Malamute	1	Belgian Griffon	17
American Cocker Spaniel	1	Belgian Malinois	13
Black Russian Terrier	1	Bichon Frise	1
Borzoi	1	Cairn Terrier	1
Boxer	35	Chihuahua	15
Brittany Spaniel	8	Dachshund	4
Bulldog	2	Dalmatian	5
Bull Terrier	4	Doberman Pincher	8
Cane Corso	2	English Pointer	6
Caucasian Shepherd	5	English Setter	9
Cavalier King Charles Spaniel	10	English Springer Spaniel	4
Chow Chow	10	Fox Terrier	4
Dogo Argentino	4	German Spitz	4
Dogue de Bordeaux	2	German Wirehaired Pointer	2
English Cocker Spaniel	29	Golden Retriever	17
French Bulldog	9	Irish Red Setter	6
German Shepherd	153	Jack Russell Terrier	9
Grand Bleu de Gascogne	2	Labrador Retriever	35

Great Dane	3	Maltese	33
Kuvasz	2	Miniature Pincher	13
Mastiff	1	Miniature Poodle	10
Pomeranian	9	Miniature Schnauzer	2
Pug	13	Mixed breed	279
Pyrenean Mountain Dog	2	Papillon	1
Rottweiler	17	Pekingese	13
Shar Pei	7	Samoyed	2
Staffordshire Bull Terrier	19	Siberian Husky	5
		Shetland Sheepdog	3
		Shih Tzu	12
		Standard Poodle	25
		Weimaraner	1
		West Highland White Terrier	30
		Yorkshire Terrier	40

334

335

Table 2: Prevalence of ultrasonographic abnormal findings in the prostate of dogs of short life (SL) and long life (LL) expectancy.

Prostate	**Number of cases (%)**		
	SL	**LL**	***SL+LL***
	n. 356	**n. 647**	***n. 1003***
Normal	216 (60.7)[a]	311 (48.1)[b]	*527 (52.5)*
With abnormal finding(s) (≥ 1)	140 (39.3)[a]	336 (51.9)[b]	*476 (47.5)*

ab: different superscripts within rows (SL vs LL) denote significant differences (P<0.0005)

343 Table 3: Prevalence of normal, enlarged or small size of the prostate of dogs of short life (SL) and
344 long life (LL) expectancy.
345
346

Prostatic size	**Number of cases (%)**		
	SL	**LL**	***SL+LL***
	n. 356	**n. 647**	***n. 1003***
Normal	252 (70.8)[a]	365 (56.4)[b]	*617 (61.5)*
Enlarged	88 (24.7)[a]	248 (38.3)[b]	*336 (33.5)*
Small	16 (4.5)	34 (5.3)	*50 (5.0)*

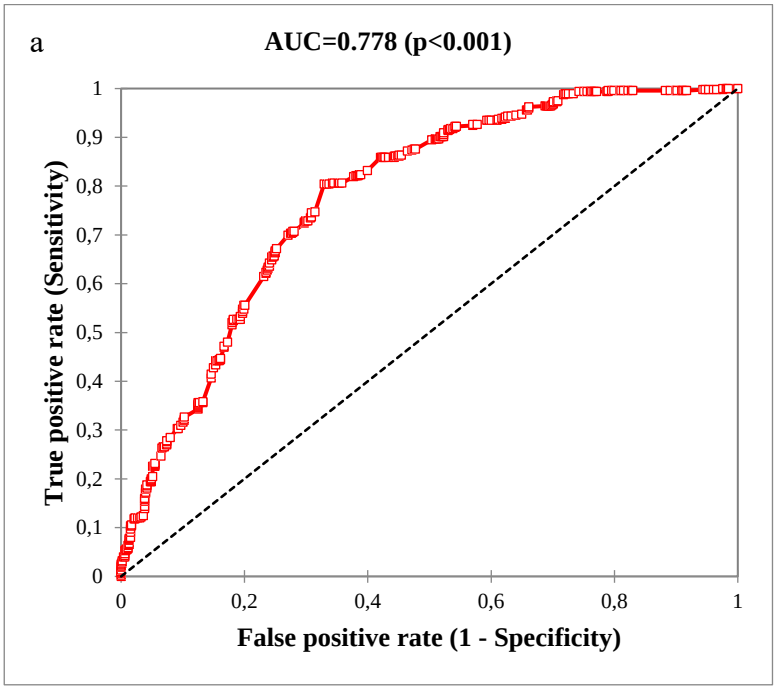
347
348 ab: different superscripts within rows (SL vs LL) denote significant differences (P<0.00005)
349

Table 4: Prevalence of specific ultrasonographic abnormal findings in the prostate of dogs of short life (SL) and long life (LL) expectancy.

Abnormal findings	**Number of cases (%)**		
	SL	**LL**	***SL+LL***
	n. 356	**n. 647**	***n. 1003***
Cysts <0.5 cm	39 (11.0)	98 (15.1)	*137 (13.7)*
Cysts ≥0.5 cm	69 (19.4)	131 (20.2)	*200 (19.9)*
Paraprostatic cysts	6 (1.7)	10 (1.5)	*16 (1.6)*
Asymmetrical lobes	11 (3.1)	16 (2.5)	*27 (2.7)*
Other focal lesions	15 (4.2)	30 (4.6)	*45 (4.5)*
Mineralization	2 (0.6)	5 (0.8)	*7 (0.7)*

No significant differences within rows (SL vs LL) ($P>0.05$).

Figure 1. ROC curve (a) and predicting values (b) of findings in the prostate of all dogs of short life and long life (SL+LL) expectancy (AUC: area under curve; PPV: positive predicting value; NPV negative predicting value).



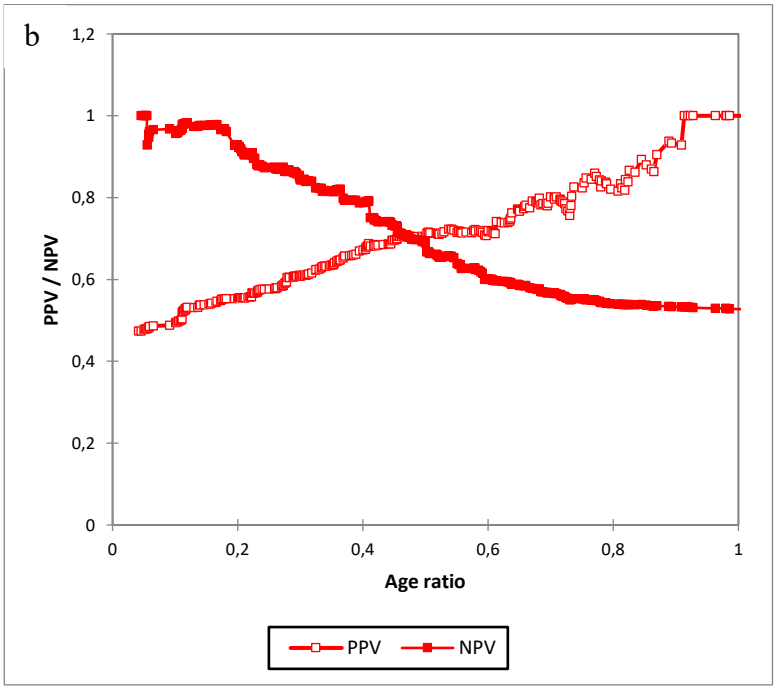
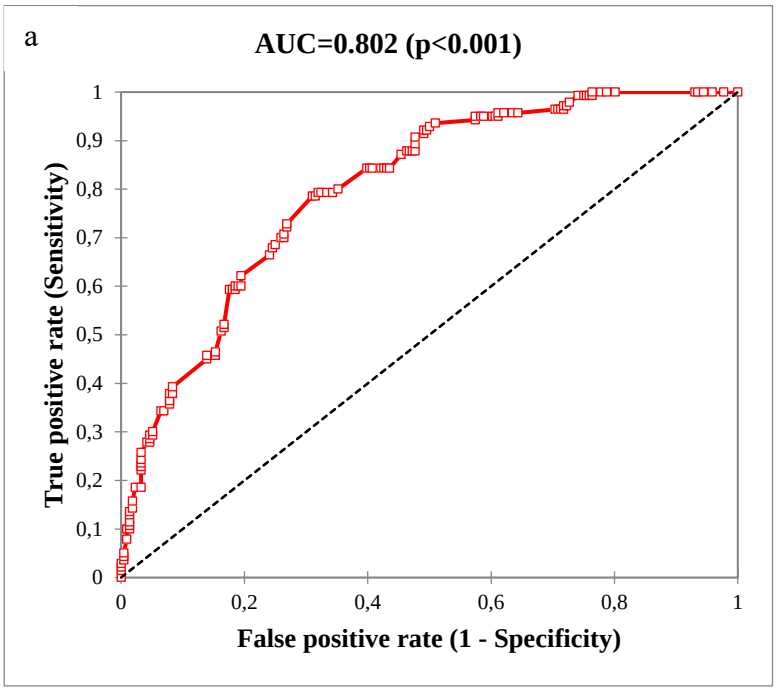
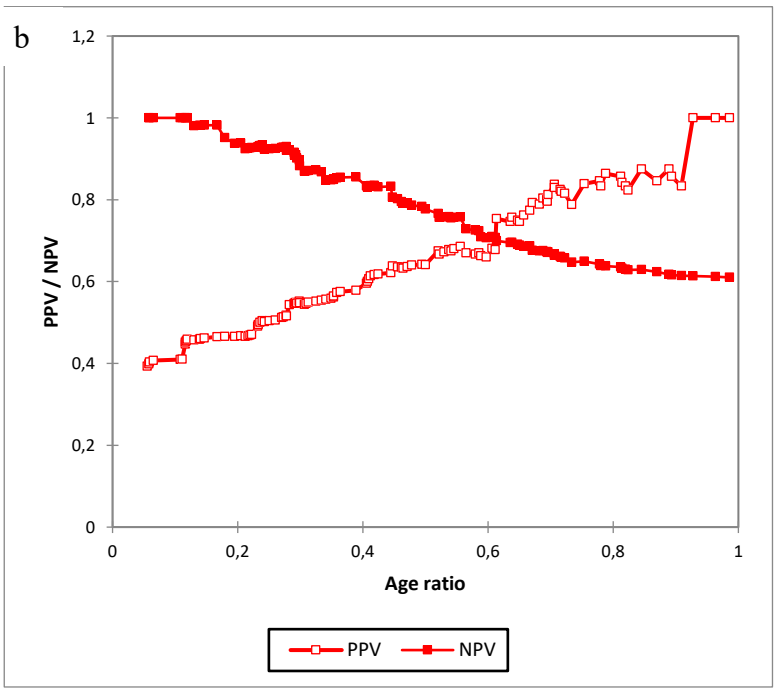


Figure 2. ROC curve (a) and predicting values (b) of findings in the prostate of all dogs of short life (SL) expectancy (AUC: area under curve; PPV: positive predicting value; NPV negative predicting value).





373 Figure 3. ROC curve (a) and predicting values (b) of findings in the prostate of all dogs of long life
374 (LL) expectancy (AUC: area under curve; PPV: positive predicting value; NPV negative predicting
375 value).
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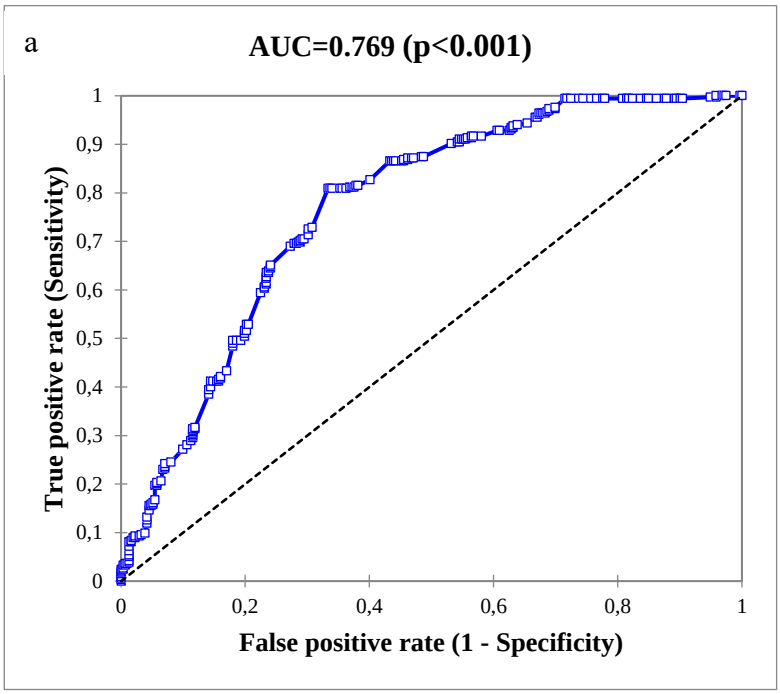

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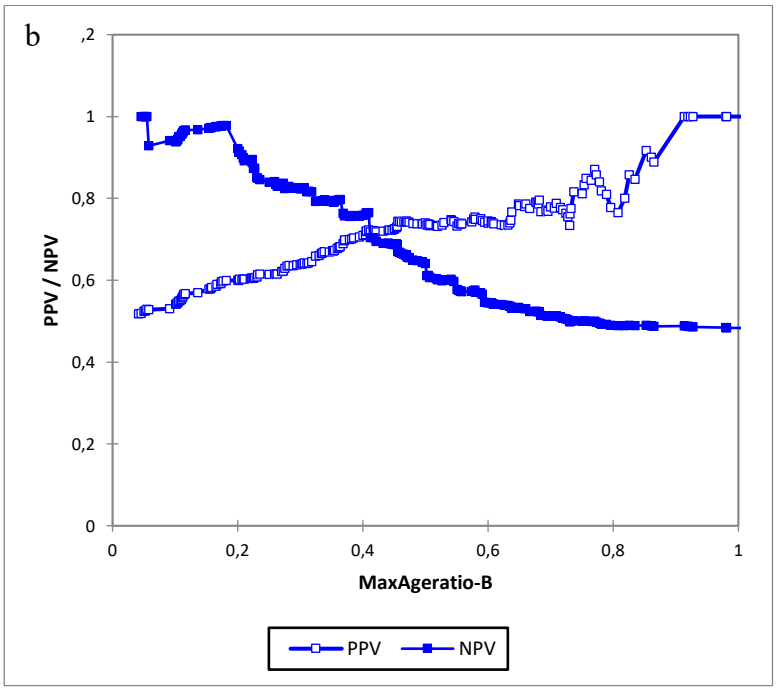
378



379
380

Table 5. ROC derived parameters for all dogs of short life (SL) and long life (LL) expectancy.

Dogs	Age ratio	Sensitivity	Specificity	PPV	NPV	Accuracy
SL + LL	**0.41**	0.80	0.67	0.69	0.79	0.73
SL	**0.44**	0.79	0.69	0.62	0.83	0.73
LL	**0.41**	0.81	0.67	0.72	0.76	0.74

No significant differences within columns.