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TITOLO TESI Nefropatie giovanili nel Boxer Studio su una popolazione di cani Boxer di un anno di età

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THESIS TITLE Nephropathy youth in Boxer Study in a population of dogs Boxer of one year of age

INTRODUCTION

Renal dysplasia

The renal dysplasia is defined as a development disorganized parenchymal failure caused by abnormal differentiation of the various parts of the nephron. The diagnosis ultimately is performed by an appropriate histological evaluation showed that an abnormal development of the kidney structures. The histopathological lesions more frequent bands consist of radial parenchyma containing immature glomeruli and tubules, adjacent to structures developed (asynchrony in differentiation nephrons) (Picut, 1987). Other elements indicate the persistence of immature mesenchymal tissue, learned metanefrici, atypical tubular epithelial proliferation and, rarely, disontogenica metaplasia. Secondary changes include hypertrophy and hyperplasia of the glomeruli and tubules, interstitial nephritis, tubule, pyelonephritis, dystrophic mineralization, glomerular cystic atrophy, cystic micro tubules, and lipidosis glomerular.

The renal dysplasia was first reported in the Lhasa Apso and the ShihTzu (Bovée, 1984). In other races have also been demonstrated that renal impairment bring to renal dysplasia (Table 1). In addition, young people with kidney disease characteristics of renal dysplasia have been reported in many races and seems likely that the problem can occur sporadically in all races (Lees, 2010). To date, scientific evidence that documents the validity of genetic tests for renal dysplasia on the various races has not been documented, though, was recently published work that suggested that renal dysplasia in the dog is related to mutations of the gene COX-2 as well as in mice (Whiteley, 2011). However, currently there are doubts about the reliability of the Scientific research and how processing of such.

Chronic renal failure is the most common clinical syndrome in these patients onset varying periods of life, from 3 months to 3 years with peaks to the first year in individuals with renal dysplasia or primary glomerular diseases. However many nephropathy family often determine the onset of symptoms later in life. Symptoms reproduces the classic development of CKD (Chronic Kidney Disease) with poor growth, weight loss, dull coat, appearance of polyuria / polydipsia (PU / PD), and subsequently or simultaneously, alterations of the examination of urine, blood parameters with increased levels of urea, creatinine, phosphorus, electrolyte abnormalities, anemia. Diagnostic imaging, ultrasound in particular highlights kidneys of abnormal morphology with altered cortical architecture and bone marrow, small size and possible expansion of the renal pelvis.

Therapies that are adopted in these cases are basically pointed to support the patient and contain the evolution of the disease that is not curable. Chronic kidney disease (CKD) is normally associated with old age in dogs with an incidence of about 20% of the diseases that afflict dogs. The etiology often it is unknown because the disease tends to evolve in a slow and devious, usually asymptomatic, especially in the early stages of the disease. In areas with endemic infectious diseases (eg leishmaniasis) CKD covers high percentage of the dog population suffers with involvement of the parenchyma

Renal extremely variable.

Causes congenital (present at birth), hereditary (genetically derived), or Family (a trait present in a group of dogs unrelated) can lead to evolution of CKD and some breeds may be particularly affected. In young animals, kidney disease is often regarded as congenital lack clinical evaluations in the long term, however, the development of lesions, consistent with the state of end-stage renal disease (end-stage kidney). It can develop already in puppies 60 days (Finco, 1995).

Nephropathy in the young has been described in over 20 dog breeds, the majority of hereditary or familial. The hereditary nephritis are mostly characterized by proteinuria, hematuria and renal glomerular damage progressive (Vaden, 2004). The renal dysplasia has been identified in at least 23 breeds of dogs and may or may not have a family-based (Vaden, 2004).

Congenital kidney diseases are, by definition, present at birth, and pathologies. They are hereditary congenital (the gene linked to the anomaly is present at birth), even in case of diagnosis in advanced stage of life. It should also be pointed out that the congenital abnormalities are not necessarily hereditary in nature, in fact the normal development of an organ can undergo deviations during gestation or the first phase of neonatal development in various ways, however, that not have a cause of hereditary. Nevertheless congenital kidney disease the most important of these pathological conditions recognized to be genetic or suspected to have a hereditary nature as the recurrence of the problem is closely related to morphologies typical of family or race (Lees, 2010).

Renal dysplasia
Lhasa Apso
Shih Tzu
Standard Poodle
Soft Coated Wheaten Terrier
Chow Chow
Alaskan Malamute
Miniature Schnauzer
Dog Kooiker Dutch (Dutch Decoy)

Primary glomerulopathies
Samoyed blood relatives and relatives Navasota (chromosome X-associated)
English Cocker Spaniel (autosomal recessive)
Bull terrier (autosomal dominant)
Dalmatian (autosomal dominant)
Doberman
Bullmastiff
Newfoundland
Rottweiler
Pembroke Welsh Corgi
Beagle

Polycystic kidney disease
Bull terrier (autosomal dominant)
Cairn Terrier and West Highland White Terrier (autosomal recessive)

Amyloidosis
Shar-Pej
English Foxhound
Beagle

Immuno-mediated glomerulonephritis
Soft Coated Wheaten Terrier
Bernese Mountain Dog (suspected autosomal recessive)
Brittany Spaniel (autosomal recessive)

Miscellanious
Boxer - reflux nephropathy with segmental hypoplasia
Basenji - Fanconi syndrome
German Shepherd - adenocarcinoma cystic (autosomal dominant)
Pembroke Welsh Corgi - telangiectasia.

Table No. 1. Nephropathies family dog listed in the standard categories of illness, breeds affected, and way of inheritance, if known (Lees, 2010).

Nephropathy in juvenile Boxer
Evaluating the literature, in purebred dogs Boxer was documented the presence of juvenile nephropathy associated with histopathological features of renal dysplasia in a case (Peeters et al, 2000) and two puppies in the same litter (Hoppe, Karlstam, 2000). As it regards recent works are only two significant studies, retrospective. In the first work (Chandler et al, 2007) retrospectively reviewed the medical records of 37 Boxers, with less than five years of age who have expressed azotemia (elevated values of urea and creatinine) hyperphosphatemia, anemia, Isosthenuria and proteinuria. Ultrasound investigations have revealed hyperechoic cortical, loss of distinction of the cortico-medullary junction, bacinetti dilated kidney and kidney-looking small and irregular margins.
Histopathological investigations always made in this group were characterized by pericapsular and interstitial fibrosis, inflammatory cell infiltration, tubular dilated glomeruli sclerotic and dystrophic calcification.
The second paper (Kolbjørnsen et al, 2008) were evaluated retrospectively, from a morphological point of view, 7 young Boxer with end-stage renal lesions compatible with chronic pyelonephritis with severe cortical atrophy and fibrosis associated with varying degrees of chronic inflammation tubule interstitial. On the basis of these morphological evaluations has been suggested by the authors that the cause of kidney damage in end-stage was related injury in chronic pyelonephritis, atrophic and not obstructive, most likely (Kidney Ask-Upmark). This type of assessment has led to interpret the tubular epithelium atypical cells of the collecting ducts in the form of adenomatous proliferation, not to metanephric development disorganized, but a lesion compensatory acquired, precisely due to kidney damage consequent to reflux during the period of development the organ (eg during gestation up to three weeks of age).
In our series (ANUBI® Hospital for Companion Animals, Moncalieri) the kidney disease youth have been identified mainly in purebred dogs Boxer. In Specifically, in the period 2005-2010, of 326 Boxer evaluated, 14 were underwent renal biopsy because had signs of suffering renal They could be associated with family pathology /congenital. Its results are described in Table No. 2 due to vesicoureteral reflux, with a picture similar to "reflux nephropathy with Segmental hypoplasia of man"

Table No. 2: Details regarding 14 Boxers that underwent renal biopsy.

no	name	age	date	symptoms diseases	concomitant	therapy	outcome
1	Brutus	11y	18/09/09	CKD da Leishmaniosi , HP P	Leishmaniosi	and hemodialysis therapy for leishmaniasis	Membranoproliferative glomerulonephritis; global sclerosis (30%); interstitial fibrosis (20%), nephritis lympho - plasma. Injury not differentiable.
2	Dux	2y8 m	18/05/10	CKD	no	symptomatic	**Dysplastic lesions: nephropathy Juvenile Boxer (JKD)**
3	Baiggio	6y	07/03/09	CKD IRIS 4		Fluids	Glomerulopathy mesangioproliferativa;

				HP NP			glomerulosclerosis by segmental to global; serious pericapsular and interstitial fibrosis diffuse (65% -75%); nephritis interstizaile chronic. injury dysplastic: mainly medullary
4	Pablo	7y	02/02/10	CKD	no		Round cell tumor. In differential diagnosis should consider lymphoma renal
5	Tequila	10y	13/03/08	anorexia slimming. CKD, IRIS Class 4, P, BH, positivity Leishmania	no	no	Blood material associated with fibrillar material necrotic It may be suggestive of a hematoma in phase organization
6	Omer	4y		CKD	no		Glomerulosclerosis diffuse fibrosis diffuse interstitial nephritis intetrstiziale chronic moderate multifocal associated with atrophy tubular widespread. injury **dysplastic: nephropathy Juvenile Boxer (JKD)**
7	Foreman	1y4m	28/05/11	no	no	no	Slight and diffuse hypercellularity mesangial; moderate mesangiosclerosi widespread and thickening of the capsule Bowman. lesion **differentiable with nephropathy youth**
8	Rambo	5y	16/10/06	CKD was uremic advanced	pyelonephritis and prostitis cystic	symptomatic	Tubulointerstitial nephritis widespread moderate and proteinuria. injury dysplastic: **nephropathy Boxer youth. (JKD)**
9	Lucky	1y1m		CKD IRIS 4 HP P	CKD		Glomerular cystic atrophy; glomerulosclerosis (33%), fibrosis interstitial (50-60%); paintings compatible with a pathology family / hereditary. **injury dysplastic: nephropathy youth Boxer (JKD)**
10	zoe	1y		CKD	kidney polycystic		Chronic interstitial nephritis associated with multifocal sclerosis focal. **Dysplastic lesions: nephropathy youth Boxer. (JKD)**
11	ohara	8y		CKD			Glomerulosclerosis and diffuse nephritis with severe interstitial fibrosis interstitial. **Dysplastic lesions: nephropathy Boxer's youth. (JKD)**
12	alba	6y		CKD IRIS 2	cardiopathy		Glomerulonephropathy membranoproliferative; glomerulosclerosis Global (5/11); nefirte interstitial lymphocyte; interstitial fibrosis (40%). **Dysplastic lesions: nephropathy youth Boxer (JKD)**
13	sebastion	8y		Anemia, ITU, CKD			chronic glomerulonephritis moderate multifocal fibrosing
14	achille	4y		CKD			Glomerulonephritis crescentica; severe diffuse interstitial fibrosis- (60-70%); tubular atrophy and severe chronic interstitial nephritis. **Dysplastic lesions: nephropathy Boxer's youth. (JKD)**

Nine biopsies (64%) of 14 cases were indicative of dysplastic lesions associated with juvenile nephropathy, the average age was 3years and 9 months with a prevalence on Boxer estimated population, equal to 3.76%.
Biopsies were performed in order eco-assisted patients maintained in intravenous anesthesia.
After clinical evaluation an intravenous catheter (20G) was placed in the vein left or right cephalic and connected to an infusion line, for fluid therapy (normal saline solution, 0.9% NaCl at the rate of 10ml / kg / hr) and for induction of anesthesia. Anesthesia was performed by injecting propofol, at a dose of 2mg / kg, bolus slow, i.v. The dog was placed in right lateral decubitus and the biopsy performed on caudal pole of the left kidney, after shearing accurate coat and the skin of area prepared aseptically.
All biopsies were performed percutaneously under ultrasound guidance, using disposable needles Biopsy, Tru-Cut 18G, operated by device automatic spring (Magnum ™ - Baxter). Two biopsy specimens were taken
the renal cortex of the left caudal pole. To avoid the formation of blood clots in the renal pelvis, the fluid therapy was maintained for about 30 minutes after each biopsy, until complete awakening of the dog, while the femoral pulse and time capillary refill (TRC) were constantly monitored. Before the end the procedure, each patient was checked by ultrasound to detect any signs of bleeding in the kidney biopsy site.

For the management of biopsy specimens was followed a standard procedure for the optical microscopy, fixing them in buffered formalin (10%), included in paraffin, and tissue slices cut at 3 microns thick. Serial sections were then stained with: hematoxylin eosin, periodic acid-Schiff (PAS), magenta and acid orange G (AFOG), Masson trichrome, hematoxylin methanamine Acid (PTAH) and elastin Miller. All renal biopsies were evaluated by the same pathologist (Dr. Luke Aresu), at the Department of Public Health, Comparative Pathology and Hygiene Veterinary - Section of Pathology, University of Padova.

Diagrams
Fig. A
Boxer dog m. about three years (Dux, No. 2 of the tab she) evaluated the first time at the age of one year and 10 months for PU / PD, IRIS stage 3 CKD, proteinuria (PU / CU = 1.7), slightly hypertensive (Sist.158 mm / Hg, oscillometric method). Re-evaluated after 10 months, the conditions were severely deteriorated and was subjected to euthanasia, the left kidney removed and evaluated by histological examination.
Fig.a: highlighting the image of the dog was significant weight loss;
Fig. B: section autopsy kidney, showed reduction in thickness of the cortex, large areas of sclerosis and renal pelvis greatly expanded

Histological images (Fig. c, d, e)
They observed three sections, obtained from renal sample sent, characterized by large areas corticomidollari, occasionally corresponding to areas of capsular hemorrhagic and proliferative with abundant fibrous stroma fibroblasts and prominent. In association they observed numerous glomeruli sclerotic and tubular structures severely dilated, often irregular or aspects proliferativoiperplastici epithelial and proteinaceous material containing abundant, eosinophilic, multifocal. in addition there has been a moderate multifocal lymphoplasmacytic interstitial infiltrate. You also note mild atrophy glomerular cystic fibrosis periglomerulare mild to moderate and multifocal mineralization. We note finally granular brownish intraepithelial tubular, refers to pigment and occasional vascular dysplasia.
Diagnosis: injury compatible with nephropathy youth Boxer

Table No. 3.
Details and examples of a case of Boxer suffering from disease renal youth / family.
PURPOSE OF THE STUDY
Based on these elements we wanted to investigate a population of young Boxers age of about 12 months, evaluated in the period from 2009 to 2010, and from the same kennel. In the terminal phase of the study there was the

possibility of investigate a limited number of boxer (five), the same age, but of different blood lines. In these subjects we were analyzed some basic parameters and easy execution, in any environment veterinarian, to assess whether they were sufficient to define the possible positive predictive index of the investigation, with the aim of early identification of individuals with renal disease or congenital family (Nephropathy youth).
They have been identified 120 cases of which were carried out clinical examinations, blood base (performed after at least eight hours of fasting) and the first morning urine, in Specifically: hematology, blood chemistry (creatinine, urea, total protein) and examination urine exam (physical-chemical, sediment and proteinuria assessed by map / dipstick and relationship with the PU / CU) performed in the hospital laboratory veterinarian ANUBI®.
Of these are eliminated 36 as non-homogeneous in the documentation.
The remaining 84 cases were subjected to evaluations and statistical surveys.

MATERIALS AND METHODS

For the blood test has been used an instrument CELL-DYN®3700 (Abbott) which uses four independent measurement methods.
1) The optical counting of leukocytes.
2) The impedance measurement of leukocytes, which is carried out in a channel electrical impedance.
3) Data from erythrocytes and platelets are measured in a second channel of electrical impedance.
4) The hemoglobin is measured channel spectrophotometer. During each cycle of the instrument sample blood is drawn, diluted and mixed, and measurements are made of each parameter.
White blood cells are analyzed in two separate channels:
a) the optical channel (WOC = optical counting of leukocytes) where, on the chamber reading, is a focused laser beam; when the flow of the sample intersects the laser beam, the light scatter, caused by the cells, it is measured at four different angular intervals.
b) The impedance measurement of leukocytes (WIC) to count the leukocytes that pass through the orifice.
The electrical impedance is also used to count the erythrocytes and platelets.

Blood chemistry

Performed by the system of Clinical Chemistry ILab 300 Plus (Instrumentation Laboratory SpA Viale Monza 338, 20129 Milan), subjected to quality control According to the "good laboratory practice".
Creatinine: fixed time analysis method based on the reaction of creatinine with picric acid in an alkaline environment. Reference ranges: 0.6-1.4 mg / dl, according to the directions IRIS (Elliott 2009).
Urea: analysis fixed time.
Method urease / GLDH2
Total protein: analysis endpoint. Biuret modified method based on the reaction of peptide bonds with Cu ++ ions in alkaline solution with development of a complex coloured. The increase in absorbance (performed at 546 nm), due to the formation of the coloured complex, is proportional to the concentration of the proteins in the sample.
Urinalysis. Chemical-physical: using a semiquantitative system maps (dipstick) with assessment pH, glucose, bilirubin, ketones, blood, hemoglobin, proteins. Maps change colour depending on the various specific reagents for each value considered (Fry, 2011).
The specific gravity was assessed by refractometer. The sediment urinary, analyzed after centrifugation of an aliquot of 5ml of urine to 1500gpm for 5 ', and elimination of the supernatant, was coloured with Kowa Stain (Hycor Biomedical Inc. Garden Grove, CA USA) and a drop placed in a special room on windows of cells to urine (urinary sediment Pentasquare for 10 seats. ROLL sas Pieve di Sacco, Italy) and evaluated under a microscope at 20X and 40X. The presence of active sediment (presence of red blood cells or leukocytes> 5 to 40X) was considered element of exclusion from the study, because any proteinuria was not of pure renal origin.
Proteinuria was also assessed by creatinine ratio urinary incontinence / urinary proteins (PU / CU) in which the creatinine in urine was quantified with the same methodology blood creatinine diluting the sample 1 to 2, while the proteinuria was quantified by colorimetric determination direct Pyrogallol with Red of the total protein in the urine. Benchmark normal: ratio PU / CU <0.5 with specific weight> 1012 (Lees et al, 2005).

Blood tests and urine tests were performed the same day of collection, performed by cephalic vein for blood and cystocentesis, urethral catheterization or spontaneous urination for urine. The sampling method of the urine was not considered influential in that the parameters analyzed, in particular, were the specific gravity and the proteinuria.

Statistical evaluation of data

The data blood and urine were subjected to statistical analysis through the use of software SIGMA STAT 3.5 through the measurement of variance (ANOVA) in order to evaluate the effect of specific gravity on the parameters considered. Finally, within each class of a specific gravity have been calculated correlation coefficients Pearson between all blood parameters and urinary considered. Details of the specific values are shown in Appendix 2.

RESULTS

The results are shown with diagrams to distribution in which the vertical axis expresses the scanned value, while the horizontal axis indicates the number of Boxers examined. In If different classification details are described in the figure legends specifications. The ellipses drawn indicate the cases in which the parameters are superior results or below the limits of the reference range. Among the haematological values, they were taken into account in particular leukocytes and the value of hematocrit (HCT)

Blood chemistry

As already mentioned, the serum chemistry values taken into considerations are limited to total protein, creatinine and urea, to use the available parameters in any Private medical and veterinary, even in normal surgeries.

Group of purebred dogs not Boxer

Extrapolated from the database of 'hospital ANUBI®, We have also been analyzed values total proteins, creatinine and urea in the serum of 30 dogs, of about 12 months of age, belonging to different races and crossings, with various diseases but not engaging the upper and lower urinary tract.

Urine tests

The urine tests were taken particularly into account values protein, derived from measuring semiquantitative via dipstick, and through protein / creatinine ratio urine - PU / PC, after the urinary sediment resulted inactive (microscopic examination of the sediment), and the value of the measured specific gravity by refractometer.
A case without measuring PU / PC.

USG

The urine samples were divided into three classes, depending on the specific weight (Osborne, 1995).
1. PS: <1012 (ipostenuriche or urine osmolality <in the serum) N: 11
2. PS: 1012-1025 (isostenuriche urine or serum osmolality = that) N: 26
3. PS:> 1025 (iperstenuriche or urine osmolality> in the serum) N: 47

The haematological, biochemical and urine were taken into account then compared to these three classes and analyzed with Anova sitema one-way, considering mean, standard deviation and standard error of average. It was also highlighted the parameters in which there is a significance statistics ($P < 0.05$). The results were shown in tables 5-6-7 below:

DISCUSSION

Whereas the classification of the causes of renal diseases listed in Table No. 1, that of the boxer is defined as reflux nephropathy with segmental hypoplasia. The opinion of the author according to what the Dr. Luke Aresu, pathologist Section of Pathology, University of Padova, does not exclude the possibility of other etiologies, considered also the fact that the article of Kolbjørnsen (2008) is based on only 7 cases. Therefore, in this study, we keep talking of renal disease in young Boxers.

As regards the evaluation of laboratory data performed on our 84 cases, as already mentioned, the values were classified according to the division into three groups, differentiated value of the urine specific gravity (hyposthenurici, isosthenurici, hypersthenurici). We have found the following.

Hematology and biochemistry

1. Leukocytes - WBC (reference range: 6.000-17.000µl). With the exception of 4 cases (n ° 15, 21, 32, 34) showing leukocytosis without particular symptomatology or clinical signs related to systemic infections or urinary tract, the values are remained within normal reference limits. The difference in the three groups showed statistical significance (P = 0.003).
2. The value of hematocrit (HCT, reference range: 37-55%) was selected as the estimate direct value of red blood cells and as an element in assessing possible anemic. Only 6 cases (# 3, 13, 99, 100, 101, 119) presented parameters referable to the lower limits of the range. There were no differences among the three groups statistically significant (P = 0.439).
3. As regards instead the values relative to total protein we find a number significant proportion of individuals in which the values are below the minimum limits of reference (Reference range 5.5-7.6 g / dl); in particular cases N ° 5, 6, 8, 23, 30, 34, 54, 55, 62, 70, 71, 72, 74,79 to 14 cases, accounting for 11.6% -. The explanation may be refers to food conditions are not optimal, since some of these individuals had a value of body scoring (BS) slightly less than optimal (4-5/9. Remillard, 2005). The data was not statistically significant (P = 0.480).
4. The values of serum creatinine (reference range of 0.68 - 1.40 mg / dl) indicate a good situation with only two cases in excess of the limits shortly (cases n ° 53, 80), these two cases have normal values of urea. The majority of cases are below the value of 1 mg / dl. A good average, given the fact that the breed Boxer is characterized by a good development of muscle mass, and therefore can present, in normal conditions, the normal values of creatinine (a metabolite of muscle creatine) to the high limits of the reference standard. Also for creatinine has no statistical significance (P = 0.395).
5. The values of the urea are in an average slightly greater than the reference (8.0-31.0mg / dl), with values in some cases relatively high. These parameters should not be related only to renal function but also the type power. In particular, since the observed population of age around 12 months, it is to assume that they were fed with high-protein diets. However, this observation is not in complete harmony with the parameters concerning the total protein. Values of urea are very influenced by the state hydration, the time between blood collection and away from meals and the presence or absence of intestinal blood (eg. from intestinal parasites) (Stockham, 2002), these variables that have not been all considered in the development of this study. No statistical significance also in this group of values (P = 0.393).

Group of dog breed not Boxer

In this group analyzed for comparison, given the availability of information, it is Interestingly, the data, although widely distributed, remain in the range and reference values for creatinine, urea and total protein are enough similar to the group of the Boxer, to emphasize a certain homogeneity of renal function in various races, when you rely on these parameters and under age similar. As previously mentioned, the muscle mass affects the creatinine value (Elliott, 2009), in fact, a value close to the maximum limit of range, eg 1.4mg / dl, leads to different clinical considerations if the value belongs a purebred dog toy or a bulldog. However, in our study, precisely for avoid that variable, we investigated on dogs with body size much standardized.

Urine tests

Data on urine, divided into three groups based osmolality, are quite homogeneous and in particular were found statistical significance in the three groups. As regards the specific weight and the ratio PU / CU, between Group A and Group C (P = <0.001). Also dependent on the pH has significance between Group A and Group C (P = 0.029), but this aspect is less important in our study, as the pH urine is affected by many factors that are beyond the disease under investigation (for as the type of feed).

Two dogs (n ° 120 and 93 - Fig. No. 10 and 11 - the study), were performed examinations repeated urine because initially showed low values of density associated a strong cylindruria (cylinders grainy). However, further evaluations

It highlighted that other measurements showed normal values of density and cylindruria was not present. In these two dogs proteinuria was associated with sediment slightly active, so there is no consideration the PU / CU. Not we are able to explain, on the basis of the available data the cause of this cylindruria alternating.
So it should be emphasized that, among all the evaluated data, countries that are elements of statistical significance were the specific weight and proteinuria assessed through ratio PU / CU.
The low urinary specific spent and the presence of proteinuria of renal origin are parameters which allow to highlight in an early and before any other laboratory examination the presence of kidney disease. Indeed, the presence of values blood levels of urea and creatinine, which indicate the so-called uremic state, is they occur when the kidney damage exceeded 75% of the volume of the two organs.
These concepts and the following discussion are related to the so-called damage primary renal, excluding the causes of pre-renal azotemia (for example: severe state of dehydration from various causes) or post-kidney (for example, obstruction of urinary tract lower urinary) and also the origin of proteinuria pre- and post-renal (For example Bence Jones proteinuria or infection of the lower urinary tract). In fact these two types of damage, pre- and post-renal, are often reversible if properly diagnosed and treated or cured. Speaking of kidney youth It is defining a primary chronic kidney disease or CKD (Chronic Kidney Disease) classified according to the scheme IRIS (Appendix 1). Returning to urine specific gravity, it is closely related to the ability of renal tubules to retain water by:
a) the mechanisms of passive absorption in bill of proximal convoluted tubule, more than 60% (Verlander, 2007),
b) concentration against the current, at the level of Henle's loop,
c) of response to the hormone antidiuretic, at the level of the collecting ducts.
Functional alterations of these mechanisms or structural renal tubules, resulting in a decreased ability to retain the 'water the production of more dilute urine. The persistence of low specific weight, that is, urine or isostenuriche hypostenuriche is an important diagnostic element, relatively early capable of detecting the presence of suffering kidney. The loss of water by the kidneys - polyuria - and the resulting dehydration of the subject, is normally compensated by a stimulus on osmoreceptors hypothalamic that automatically trigger a reflection of thirst. From here the symptom defined polyuria-polydipsia. In the very early stages of the problem can also polydipsia go unnoticed, or at least underestimated. Therefore the systematic examination urine of patients at risk becomes extremely important. In the studio is among the first to appear in the case of CKD, when blood tests are still normal, but kidney damage reaches almost 2/3 of its total volume.
It is known that hypostenuria and / or Isosthenuria should be re-evaluated in time
Subsequent to confirm the persistence. However, in our study, we have, for need, use withdrawals made once on dogs whose owners participated voluntarily in the survey, so it would be very difficult to repeat the exam given the varied and wide geographical distribution of these individuals. In our study there we are based, for this group of boxer, on a single sampling is performed in the morning without that dogs had urinated previously (for this reason, the levy is was performed in different ways: spontaneous urination, and catheterization cystocentesis). It 'well known that the first morning urine are the most significant from a diagnostically.
Another very important aspect that showed statistical significance in the groups is proteinuria was evaluated with relationship Urinary Protein / Creatinine Urinary (PU / CU). It is scientifically clear that the primary renal proteinuria is a diagnostic element, the functionality of the nephron, extremely important (Grauer, 2009).
Renal proteinuria may be the source glomerular, tubular or interstitial, but the fraction glomerular is undoubtedly the most important from a pathological point of view, at least in the light of currently available information. The glomerulus is organized to filter the blood, preventing the passage to molecules of PM greater than 69000 Daltons; this is via specific glomerular capillary endothelium fenestration and the negative electrical charge on board such fenestration (Osborne, 1995). In case of glomerular damage these characteristics are less and proteins, albumin in particular, are eliminated in the urine. The causes that lead to this type of alteration are basically two: the immune-mediated diseases, associated with third type hypersensitivity (Tizard, 2004) which cause accumulation immunocomplexes between endothelium and podocytes, in various ways, relative to the type of injury; They alter these immune structures with glomerular resulting in inability to retain proteins.

The other major cause is systemic hypertension that progressively causes glomerular fibrous structures, with similar results (Brown, 1990). Proteinuria may induce fibrosis via the activation of transcription factors such as NF-kB and the dysregulation of genes pro-inflammatory and pro-fibrotic (Abbate, 2006).
Another consequence is the differentiation of tubular epithelial cells in myofibroblasts, mediated by increased TGF-β (Tissue Growht Factor- β) that causes the increase in extracellular matrix and consequently fibrosis (Yang and Liu, 2001). Therefore, the proteinuria is considered a marker that can allow diagnosis of renal damage very early, hence the need to carry out controls on urine in patients considered at risk of developing kidney disease, whatever etiology.
Proteinuria can be diagnosed by several methods:
1) map or dipstick - semiquantitative method - containing a reagent It acts closely with albumin, but does not react with some globulins (eg: Bence Jones proteins) and can give false positives in urine alkaline,
2) test of precipitation with sulfosalicylic acid (SSA), semiquantitative method, that does not offer many advantages over maps / dipstick,
3) through urine electrophoresis agarose gel sodiododecyl sulfate. Method quality that allows the differentiation between proteins glomerular, tubular and interstitial. Has higher costs and execution times longer (Zini, 2004),
4) evaluation of microalbuminuria, using quantitative ELISA test It allows the assessment of albumin in an amount much lower than through map / dipstick (Grauer, 2004),
5) ratio Urinary Protein / Creatinine Urinary (PU / CU). Assessment quantitative protein and creatinine in urine, using the same unit of measure (mg / dl) (Grauer, 2009). The examination is performed on a sample extemporaneous urine.
6) relationship Albumins Urinary / Creatinine Urinary. Assessment similar to using previous values of albumin and creatinine in the urine. The report / UC in urine was found to be the method that combines reliability, simplicity and low cost, so it is the most popular method and recommended (Elliott 2009) for the assessment of proteinuria. The borderline value indicated (Appendix 1) is <0.5. But the value becomes much more significant when combined with low gravity (Lees, 2005)

CONCLUSIONS
The data available to us, chosen according to the working hypothesis for this thesis, not have allowed the identification of elements indicative of nephropathy youth Boxer, the group analyzed by us. However, there are some explanations. The number of cases analyzed it is not particularly high and the dogs derive from the same breeding with bloodlines homogeneous. This appearance is due to the fact we encountered considerable difficulty in seeking the cooperation of other breeders, in order to investigate different blood lines.
We're not prepared culturally to face this kind of selection still new to them, Unlike what is already the case for other diseases (for example, hips and elbow dysplasia). It should also be assumed that the age chosen for the control is too early in time and greatly limits the possibility to select sick individuals. The same concept can be seen from our documentation on renal biopsies performed, where the average age, the 14 boxers examined, is 3 years and 9 months.
However there were some interesting elements, such as the homogeneity and reproducibility of the data analyzed. It should also be assumed that for this type of research pathology requires other methods of investigation, such as ultrasound and renal biopsy in particular, which could allow the highlighting of structural alterations, even in the absence of blood parameters and urinary pathological. But propose biopsies kidney in clinically normal individuals, when it is not practically feasible. Specific genetic testing may be very helpful, but studies are still targeted be carried out in order to improve and make scientifically reliable this technique. The diagnosis of renal disease in the young , remains a topic very charming for those who deal with nephrology and substantial scarcity and uneven Information on this is an incentive to continue on this path.

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