ABSTRACT

The doctoral thesis named " *Research regarding the etiopathogenesis, clinical-imaging and laboratory diagnosis of diseases accompanied by dysuria in dog*" has been motivated to study affections that include, in the clinical picture, dysuria syndrome in the dog. The originality of this work is given by the studies on the vertebral column and the pelvis, which offers the possibility of integrating some elements of classification from human medicine into veterinary medicine.

The theme of the doctoral thesis is a descriptive one, aiming at approaching dysuria syndrome and, especially, its mechanisms of installation, as a pathological element itself and not just as a symptom associated with other pathologies. One of the purposes of the research is to update, analyze and apply the literature data, highlighting the importance of clinical, imaging and laboratory examinations, which can provide important information that can help establish a diagnosis of certainty and prognosis, in order to the subsequent implementation of an effective treatment protocol.

The thesis consists of 176 pages and consists of two segments - one general and one own research, comprising a total of 11 chapters. The first part of the thesis is titled "The present stage of knowledge regarding the dysuria syndrome in dog" and represents the bibliographic study of the subject, being systematized in three chapters, and the second part contains the results of own researches, structured in eight chapters. The results obtained are supported by 77 images, 2 tables and 16 graphs.

Chapter I is named "Morphophysiological concepts regarding the urinary tract in dogs" and provides information on the structure of the urinary system, the vascularization and innervation, in order to facilitate the illustration of the installing mechanism of the dysuria syndrome.

Chapter II is named "The imagistic examination of the urinary tract and of the other segments (organs) involved in the dysuria syndrome in dog". In this chapter, information regarding the pathology of the urinary system, genital system, spine and pelvis that include, in the clinical presentation signs of dysuria syndrome. The techniques and possibilities offered by imaging examination methods - radiography, ultrasonography and complex methods are detailed. The structure of the chapter is aimed at rendering the aspects of imaging examination of each organ, highlighting the particular aspects of each method.

Chapter III, named *"The diagnosis of the main diseases that are accompanied by dysuria in dog; Contributory and decisive factors"*, discusses the possibilities offered and the limits imposed by the methods of examination that can be used - clinical, imaging and laboratory examination methods. The peculiarities of the data obtained by using each method, with the significance of each and the impact on the patient evaluation process were highlighted.

The second part of the thesis, entitled *"Personal research"* is comprised of eight chapters, three of which are individual studies of a particular segment of the main target

group. In this segment of the thesis the results of research carried out during the four years of doctoral studies are discussed.

Chapter IV describes the purpose and objectives of the research, along with the working hypothesis. The aim of the research is to establish a diagnostic protocol for dysuria syndrome in dogs with the identification of etiological factors, using the semiological methods of clinical examination, imaging examinations and paraclinical examination methods - blood and urine tests. For poli-traumatized patients with pelvic and spinal lesions, it was intended to identify parameters that could be used as predictive factors for the development of signs of retention or urinary incontinence, while pursuing the vital prognosis of the examined patients. Prioritization of supportive care, at the expense of additional radiological incidences beyond the initial ones, can contribute decisively to the increase in the survival time of the patient with acute post-traumatic pathology.

Clinical research methodology has imposed strict compliance with diagnostic guidelines:

- Performing the clinical examination for patients presenting with urinary symptomatology.
- Carry out the radiological examination and identify the lesional areas of the bone, urinary or genital organs.
- Performing studies with contrast solutions in the case of suspicion of the presence of lower urinary permeability disorders.
- Performing the ultrasound examination in the case of identification of changes in shape, size and / or position of the pelvic viscera.
- Taking blood and urine samples and examining them.

The final objective of the thesis was to identify the series of etiological factors involved in the onset of dysuria syndrome in dog and to evaluate the degree of their involvement in the pathology of the urinary, genital, spine and basal system.

Chapter V of the thesis, named *"Study materials and methods"* describes the institutional framework in which the doctoral research was carried out, the applied methods and the biological work material. The doctoral study was conducted over a period of four years between October 2013 and August 2017. The patients examined came from the Department of Radiology and Imaging and the Medical Clinic of the Faculty of Veterinary Medicine Iaşi, from private veterinary offices in Iaşi County, and neighboring localities. A total of 38 French Bulldogs have been studied during a research run at the Cordoba Faculty of Veterinary Medicine, Spain.

Subchapter 5.1. details the information of the study group, being entitled "Study material". 907 canine patients who had symptoms associated with dysuria syndrome were identified. Patient selection criteria included the presence of stranguria, persistent hematuria, the presence of clinical anuria, and movement disorders that may be associated with thoraco-lombo-sacral column and pelvic lesions.

Of the total study group, 554 dogs were unsterilized at the time of the consultation (61.08%) - 165 females and 389 males, and 353 were sterilized (38.92%) - 94 females and 259 males. Most dysuria-related conditions were diagnosed in patients aged 7-12 years (308 dogs - 33.96% of the total number of patients), followed by the age group of 3-7 years with

253 (27.89%) of cases, the group over the age of 12 - 192 cases (21.17%) and the juvenile patient group, aged between 2 months and 3 years - 154 patients (16.98%).

The most affected breeds were the Mixed breeds, with a group of 432 cases presented (47.62%), followed by dogs from the Pekingese breed - 128 cases (14.12%), German Shepherds, 117 cases - 12.89%, dogs from Bichon and Caniche breed, with 64 cases (7.06%), French bulldogs, 38 cases (4.19%) and dogs of other breeds, with a small number of representatives, which accounted for 7.06% of the study group. Although it represents an important percentage of the study group, the majority of the mixed breeds can not be considered an absolute predisposing factor, this element being influenced by the predilection to this segment of the canine population existing in the geographic coverage area of the study.

Subchapter 5.2., named "*Study methods*", details the examination of the cases investigated. The examination protocol used included the clinical assessment of the patient - both at a general level - with the identification and assessment of the general condition of the animal, anamnesis, eventual modifications of the aplomb, the record of the heredocolateral antecedents and the medication received prior to the examination, the functional evaluation of the urinary system, by radiography, native or contrast medium, and paraclinical examinations - of blood and / or urine.

In order to perform the clinical examination, a consultation sheet was used where the patient's identification data - name, species, race, age, weight, reproductive status, followed by anamnesis, heredocolateral history, pre-treatment medication, and clinical signs observed, on systems - urinary, genital, bone, nervous, were written.

The radiological examination was applied to all patients under study. The iodinated contrast solution was used in 28 cases, to highlight lower urinary tract permeability, to detect bladder lesions or to check the integrity of the urethral tract in post-traumatic patients.

Ultrasound evaluation of the urinary tract or prostate was recommended in cases where the clinical and radiographic examinations did not provide sufficient information to establish a clear diagnosis and were used in 106 patients. A special method of examination applied to both bladder and prostatic structural suspicion is ultrasound-guided puncture and microscopic examination of the sample taken.

Computer tomography was applied to 18 French Bulldog dogs according to the technique described by Wisner and others in 2013 and Schwarz et al. in 2011. Patients were sedated and placed in dorsal decubitus and the examination of was performed using a High Speed Dual CT (General Electric).

Chapter VI, also named *"Results and discussions"* detailed the results obtained during the examination of the patients, following each stage of the diagnostic protocol.

Clinical investigations have led to suspicion of urinary system disorders in 136 patients, genital system disorders in 154 dogs. Spine diseases were suspected in 379 patients, while 238 dogs were redirected to the imaging of the pelvis.

The imaging examination of the patients led to the diagnosis of renal lithiasis in 8 patients, urinary bladder lithiasis in 42 dogs, integrity disorders (cuts or compressions of the lower urinary tract) in 12 patients, bladder hernia in 3 dogs and 71 dogs have been redirected to the paraclinical examination to confirm the suspicion of cystitis or bladder wall neoplasia.

Genital system disorders - prostatic and uterine, have been identified in 154 patients; the presence of benign prostatic hyperplasia in 36 dogs, the presence of prostatic cystic

formations in 47 patients, bacterial prostatitis in 41 cases, prostatic neoplastic processes in 24 dogs, were suspected. The presence of the pyometra was observed radiographically and confirmed ultrasonographically in 5 patients, and dystocia accompanied by dysuria syndrome was identified in a bitch.

Radiologically identified vertebral column changes were represented by inflammatory processes located in the supravertebral orifices (156 dogs), spondylosis (92 patients), mineralized discs (36 dogs), vertebral fractures (32 patients), disc hernias (21 dogs), vertebral subluxations (19 patients), vertebral sprains (17 dogs) and destructive/proliferative lesions (in 6 patients).

Pelvic fractures were radiologically evaluated in 238 patients using radiographic examination techniques.

Using paraclinical examination methods, the presence of bladder neoplasia, cystitis, urolithiasis or prostatitis were confirmed, following the biochemical characteristics of the samples taken as well as the existing cell populations.

Subchapter 6.4. details the statistical interpretation of the results obtained. From a pathological point of view, the cases under study could be systematized into four large groups (Figure 6.2), based on the localization of the primary pathological process: urinary system disorders - 136 patients (14.99% of the study group), genital system diseases - 154 dogs (relative value 16.98%), spine disorders - 379 (41.79%) and pelvic conditions - 238 (26.24%).

The most common disorders of the urinary system were renal lithiasis (absolute value of 8 cases), urinary bladder lithiasis (42 cases), bacterial cystitis (66 patients), integrity disorders (12 dogs), positional disorders (3 cases), bladder neoplasia (5 patients).

In the case of patients with genital system diseases (154 dogs), 36 patients (23.38%) were diagnosed with benign prostatic hyperplasia, 47 patients (30.52%) with prostatic cystic formations, without identification of the type of cysts, 41 patients (26.63% 24 patients (15.59%) were diagnosed with prostatic neoplastic processes, 5 cases of pyometra (3.24%) and one case (relative value 0.64%) with dystocia by blocking of the puppy in the vaginal vestibule, inducing urinary retention by mechanical compression of the urinary tract.

The most common lesions identified in the spine, alone or in combination with other modifications, were the increased radiopacity zones in the supravertebral orifices (inflammatory disease) - which was identified in 156 cases (a percentage of 41.16% of cases with changes in the spine), followed by spondylosis/osteophytosis - 92 patients (24.27%). discal mineralizations were identified in 36 cases (9.49%), disc hernias were identified in 21 cases (5.56%), vertebral fractures - in 32 cases (8.44%), vertebral sprains - 17 cases (4.49% subluxations - in 19 dogs (5.01%), destructive/proliferative lesions - 6 dogs - 1.58% of the group of patients with spinal disorders. In many cases, inflammatory processes have evolved simultaneously with other lesions, such as spondylosis or vertebral alignment changes.

Pelvic lesions identified in patients with dysuria syndrome were, in most cases, complex - with multiple fracture lines and pelvic cavity reduction. Of the 238 patients, only 46 (19.32% of the study group) presented a single fracture line, while 192 patients had a complex lesion pattern (80.68%). The lesions most commonly identified in canine patients were fractures of the iliac blade - 248 lesions, fractures of the ischium - 172 cases, pubic detachment - 24 cases and fractures by displacement of the acetabular cavity - 48 cases.

Chapter VII, named *"Study regarding the influence of the vertebral column modifications in the dysuria syndrome in French Bulldog"*, assessed the impact of vertebral malformations on dysuria syndrome in dogs of the French Bulldog breed.

Congenital vertebral changes of the toraco-lumbar spine may have an important impact on the clinical evolution of dogs of this breed due to instability phenomena that can be developed locally. These phenomena can lead to the emergence of local inflammatory processes with compressive action on nerve threads, chronic pain with lumbar localization, limping and neurological deficits.

Through this study, we sought to identify and classify the malformed vertebrae from the thoracic and lumbar spine from the dogs of the French Bulldog breed, to identify the vertebraes with the highest prevalence of malformations, to evaluate the angle of Cobb - scoliosis angle, the angle of kyphosis and their impact on the spinal cord and to verify the possibility of correlating the type of vertebral malformation with the kyphosis and scoliosis angles and the urinary symptomatology.

The total number of vertebrae - 13 thoracic and 7 lumbar in 38 dogs, was 760, of which 248 (32.63% of the total) were identified as malformed.

The most common congenital changes identified in French Bulldog patients were the butterfly vertebra - 56 vertebrae (Figure 7.5), in 18 patients, ventral wedge-like hypoplasia (53 vertebrae), 21 dogs, lateral hemivertebra - 38 vertebrae, 12 patients (Fig. 7.3) and shortened vertebrae - 101 vertebrae in 31 patients (graph 7.1). The number of vertebraes modified in one individual varied between 0 and 9, with an average of 5 affected vertebrae per individual.

It was noted that vertebrae T4 to T10 are most affected by fusion disorders of centers of mineralization of vertebral bodies, resulting in butterfly or hemivertebral malformations, whereas vertebrae T4, T5 and T13 show the most frequent shortening of the vertebral bodies.

The T9 vertebra was most frequently identified with changes in body or vertebral arch formation - 38 cases, representing 15.35% of the total malformed vertebrae studied.

The shortening of the vertebral bodies appears as a phenomenon associated with the other types of malformations, especially in the vertebrae adjacent to the modified ones. Thus, a transition phenomenon can be observed, from the level of the normally structured vertebrae to the modified ones and backward. This phenomenon also justifies the increased presence of shortened vertebrae versus those with changes in formation.

Kyphosis and scoliosis angles allowed the mathematical evaluation of the degree of spinal tract deviation, which was subsequently correlated with the presence of dysuria syndrome. The mean value of the scoliosis angle was 5.02° (range: 0.63° - 29.31°) and the mean value of the kyphotic angle was 21.01° (range: 1.98° - 46.18°).

Although the literature mentions that scoliosis diagnosis can be applied only in the case of lateral deviations above 10°, it should be noted that in the dog, the association of an acute angle of kyphosis with lateral deflection of the spinal tract will increase the chance of occurrence of the symptoms of the medullary compression and, implicitly, of the neurogenic dysuria syndrome.

The presence of signs of dysuria in patients with vertebral malformations outside the T12-L3 and L7-S1 areas, known as the sites of urinary and defecation control centers, has been noted.

Chapter VIII, named *"Study regarding the influence of the pelvic modifications in the dysuria syndrome in dog"*, aimed to identify canine patients with pelvic traumas and to assess the mechanical stability of the fractured fragments and the degree of lesioning of the pelvic viscera. By adapting and using the classification scale for pelvic lesions from the human medicine to the veterinary medicine, it was possible to assess the type and intensity of mechanical shock and to establish a vital and functional prognosis valid for the urinary system.

Of the group of 238 patients, only 46 (19.32% of the study group) presented a single fracture line, while 192 patients had a complex lesion pattern (80.68%).

The results of the study have demonstrated the possibility of successful application of the WSES - Young-Burgess grid from human medicine to pelvic lesions in canine patients. The results of the radiological examination have led to the correlation of low intensity trauma with lesions of the first degree of severity, moderate trauma with degrees II and III of bone lesions and high impact shocks, with fourth degree pelvic lesions.

The percentage of pelvic cavity reduction can be used as an orientation factor by the examiner to check for inferior urinary tract permeability.

Chapter IX is named *"Study regarding the influence of prostatic modifications in the dysuria syndrome in dogs"* and aimed to determine the influence of prostate changes on dysuria syndrome, following radiographic, ultrasound and urine changes.

The study was conducted on a group of 148 dogs presented for consultation within the Radiology Department of FMV Iasi. They were aged between 5 and 16 years, and 53 dogs were castrated (35.81%) and 95 were whole (64.19%).

The main diseases identified in the patients examined were benign prostatic hyperplasia - 36 dogs (24.32% of the study group), prostatic cystic formations - 47 patients (relative value 31.76%), infectious prostatitis - 41 cases (relative value 27.7%) and neoplastic processes - 24 dogs (16.22% of the study group).

The symptomatology encountered in examined patients ranged from lameness due to the modification of the aplomb by attempting to protect the hyperalgic area (caudal region of the abdomen), changes in the line of the column - kyphotic walking, to dysuria or stranguria, with the alteration of the general condition of the animal. The region indicated for the radiographic exam was the abdomen and the lumbosacral column, in the lateral and ventro-dorsal incidence.

In all cases, the radiological examination noted the mass effect caused by the increased prostate size manifested by urinary retention with the cranial displacement of the intestinal mass, the dorsal deflection of the colon in the terminal portion, and the radio-transparent triangle caused by the dorsal deflection of the bladder neck.

Urinary signs included both changes in the urinary frequency and the total amount expressed, as well as changes in urine - persistent, visible or occult hematuria, clearly detectable through laboratory examinations. When the urine was visibly altered, the owners reported the presence of blood at the end of urination, either in the form of a darker urine or in the form of blood droplets noted after the micturition was complete.

The radiographic examination of the abdomen provided important information related to the size and symmetry of the prostate gland, and the use of contrast solutions indicated the

permeability of the prostatic urethra and could reveal the asymmetric volume change by lateralisation of the urethral tract from the usual position.

Chapter X - *"General discussions"*, had the purpose of debating the results obtained in the previous chapters.

For urinary disorders diagnosed in 136 patients, the most common were cystitis (48.52%), followed by bladder lithiasis (30.9%), integrity disorders (8.82%), renal lithiasis (5.88%), bladder neoplasm (3.68%) and bladder position disorder (2.2%). During the research, we noted that, as a rule, urinary system disorders present a complex evolutionary trend, with one or more lesions - urolithiasis and cystitis, for example.

In case of genital disorders, identified in 154 dogs and visually represented in graph 10.2, the most common pathologies were prostatic cystic formations (30.52%), bacterial prostatitis (26.63%), benign prostatic hyperplasia (23.38%), prostatic neoplasia processes (15.59%), pyometra (3.24%) and dystocia (0.64%). The trend of bacterial diseases to propagate upward has been noted, thus associating infectious prostatitis with cystitis or bacterial nephritis.

The graph 10.3 in this chapter highlights the prevalence of inflammatory processes associated with urinary symptomatology (41.16% of patients), followed by spondylosis (24.27%) and discolorations (9.49%). These conditions involve the existence of partial or total medullary compression, which affects the control centers of micturition and defecation.

The native radiographic examination of the spine allows for the visualization of the changes of the vertebral bodies and of the intervertebral spaces and discs, but it does not allow examination of the medullary canal. Using the myelography technique, however, the diagnosis of disc hernia was established in 21 patients, representing 5.56% of the group of dogs with diseases of the spine.

Vertebral malformations are a predisposing factor for dysuria syndrome due to the degree of instability created in the spinal tract. The tendency of the body towards the regional stabilization phenomenon, through the formation of osteophytes and the fusion of spinal cord processes, although reducing the degree of mobility of the unstable area, can lead to the occurrence of the phenomenon of medullary compression through disc degeneration and the modification of the kyphosis and scoliosis angles.

Pelvic injuries involving urinary tract damage were diagnosed in 238 patients. Unlike dogs with spine disorders, native radiological examination provided sufficient information to determine the lesions of the pelvis - but strictly from an orthopedic point of view. To verify the permeability and integrity of the urinary tract, the radiographic examination method was augmented with iodinated contrast solutions.

By applying the classification and assessment grids of pelvic lesions from the human medicine to the veterinary medicine, it was possible to establish that the integrity of the urinary system is impaired in the case of medium-to-high intensity trauma, leading to a reduction in the size of the pelvic cavity by more than 30% of the original size. Depending on the number of resulting fractures and their mobility, the possibility of urinary tract sectioning or mechanical compression can be assessed.

Chapter XI, *"General conclusions"*, completes the work with a series of general conclusions obtained during the four years of doctoral studies.

Finally, the bibliographic list of titles from the Romanian and foreign literature is presented and the list of scientific papers published and communicated.