Abstract

The doctoral thesis entitled ***„Clinical and paraclinical studies on myocardial and endocardial diseases in dog”*** was motivated by the study of the most frequent cardiopathies in dogs, which involves the pathology of endocardium and myocardium. The original character of this work is given by the statistical study of electrocardiographic and echocardiographic parameters obtained by laboratory investigations of a polymorphic canine population diagnosed with mitral valve disease from an epidemiological point of view. The final study brings an original note to the thesis by identifying disturbances in the electrical activity of the heart as a result of the pathophysiology of various neuropathies.

The thesis consists of a total of 187 pages and is divided into two representative parts: the first part, the bibliographic study, representing 30% and the second, 70% of the thesis represented by personl research. The results are supported by 23 tables, 32 graphics and 25 figures.

The thesis includes two representative parts. The first part, entitled *„The current state of knowledge”* represents a brief bibliographical study of the cardiopathies which involve the endocardium and myocardium in dogs. This part is divided into five chapters describing the myocardial and endocardial diseases diagnosed and described in dogs, the heart failure syndrome from a physiopathological and and clinical point of view, the laboratory methods of investigation in canine cardiology and therapeutical aspects in canine cardiovascular diseases. The informations obtained after this study were further used in elaborating, interpreting and comparing the results obtained in the personal researches.

The first chapter entitled *„Myocardial diseases of the dog”*, takes a brief incursion into canine primary genetic cardiomyopathies and secondary myocardial diseases which can occur with systemic pathologies or with cardiovascular diseases involving other cardiac structures (myocardial remodelling).

The second chapter named *„Epidemiological and lesional aspects in endocardial diseases of dogs”* describes the current state of knowledge of valvular degenerative pathology, which has a high incidence in the canine population, and of inflammatory conditions of the endocardium.

Chapter 3 describes the *„Heart failure syndrome”* from a physiopathological and clinical point of view in dogs to facilitate the understanding of the evolution of cardiopathies and

the interpretation of the results of laboratory investigations. This chapter also includes the diagrams for the classification and stadialisation of heart failure syndrome in various cadiopathies.

Chapter 4 entitled „*Clinical and paraclinical methods of examination used in canine cardiology*" divides investigation techniques into two sub-chapters: the clinical examination of the cardiac dog and paraclinical methods of investigation which include echocardiography, cardiothoracic radiology, electrocardiography and advanced imaging techniques (angiography, computer tomography and magnetic resonance). The description of laboratory methods includes standard examination and interpretation techniques currently recomended in scientific literature.

Chapter 5 describes the therapeutics of veterinary cardiology, its title being „*Therapeutic principles used in heart failure syndrome"*. In the first chapter, the main therapeutical classes approved for veterinary medicine are briefly described from a pharmacological and pharmacodynamical point of view, and the next subchapter is aimed at therapeutical strategies used in heart failure.

Part II, Personal contributions, is made up of 7 chapters presenting and discussing the results of the researches undertaken.

"Epidemiological characteristics of the canine population diagnosed with mitral valve endocardiosis" is the title of the 6th chapter which observed the epidemiological characteristics of a polymorphous population of dogs diagnosed with valvular endocardiosis during the study period between 2006 and 2012. At the same time, we tried to identify the typology of individuals predisposed to develop this pathology. From the point of view of breeds diagnosed with MVD, 80.9% were small size dogs, the largest share being Cavalier King Charles Spaniel mixes. The group of large size dogs was poorly represented, 19.1%, with a high variability of breeds. Of the population investigated, 42,4% (n= 28) were females and 57,6 % (n=38) were males, with a mean age of 11,08 ± 3.63 years (with limits between 1-20 years). The clinical examination and laboratory investigations allowed the assignment of the dogs to stages of heart failure as follows: 10.6% (7/66) in stage A, 27.3% (18/66) in stage B, 48.5% (32/66) in stage C and 13.6% (9/66) in stage D. We notice that the highest share was that of dogs classified in clinical stages. From the point of view of age and sex, the poplation studied is predominantly old, 81.7% of the dogs being older than 10 years, and is dominated by males, in which this pathology develops 1.5 times more often than in females. Examining the mean age of identification and manifestation of clinical signs in the two subgroups, we notice the chronic evolution of MVD in small breed dogs, highlighted by statistically significant differences between the ages of dogs in different stages of heart failure ($p = 0.003$). Large breed dogs had closer mean ages for each stage of evolution of the pathology, without

statistical differences, which suggests a more accelerated progression of MVD from the identification of the lesions to the manifestation of clinical signs. The descriptive epidemiology of the population studied is similar to that described in literature on much larger groups of dogs. These common points allow us to state that small breed male dogs over 10 years of age are predisposed to developing heart failure secondary to valvular degeneration.

Chapter 7 follows the *„Clinical signs of heart failure syndrome secondary to mitral regurgitation as a consquence of mitral valve endocardiosis"* based on clinical cardiological examination and drawing the clinical examination chart for each patient. The clinical signs observed in this group of dogs were represented by bouts of chronic coughing in 75.8 % (50/66) of the dogs, reduced physical activity and moderate effort intolerance in 69,7% (46/66), episodes of sycope in 18.2% (12/66), ascites, associate with pleural and pericardial effusions in 10.6% (7/66) and rear limb oedema in 4.5% (3/66). The left apical systolic murmur, one of the criteria of inclusion in the study was present in all the patients in stages B,C and D (89,3 %). Statistical analysis of the clinical data base showed the folowing aspects: decompensated MVD is characterised clinically by signs of left heart failure and in advanced stages of the disease, the complex clinical manifestation of global heart failure is installed. The main reason of presentation for consultation of patients with MVD is the association of bouts of coughing with reduced physical activity. The complex clinical manifestations, noticed on the first consultation is predominant in larg breed dogs who have a more accelerated evolution of the decompensated stage, compared to small breed dogs. Syncope, a negative prognosis symptome, appears in advanced stages of the pathology and is associated with a decrease in cardiac output in large breed dogs. Polycavitary effusions indicate a decompensation of the right heart, either as a result of right atrioventricular regurgitation secondary to the process of degeneration of tricuspid leaflets, or as a result of an increase in intrapulmonary pressure.

The objective of chapter 8 is the echographic study of degenerative valvular lesions and the ultrasonographic characteristics of the consequences of mitral regurgitation. The descriptive study entitled *„Echocardiographical aspects of valvular degenerative lesions and consequences of mitral insufficiency in dogs diagnosed with mitral valve endocardiosis***"** has shown through the echographic technique the standard sections recommended for cardiac examination, degenerative valvular lesions were characterised by a thickened, hyperechogenous, irregular aspect with the presence of nodular formations on their tip. The chordae tendineae appear irregular, intensely hyperechogenous and thickened at their insertion area and may have an ondulated aspect. Valvular prolapse which appears when the chordae tendinae is identified in bidimensional echography by the passing towards the left atrium of mitral foils during systole. The main consequences of mitral

regurgitation identified through bidimensional echocardiography are represented by: atrial dilation, ventricular dilation, pulmonary trunk dilation, polycavitary effusions. The clinical consequences of pulmonary hypertension were identified in the advanced stages of heart failure.

Chapter 9 is also an echographical study but it analyses the echocardiographical parameters indicating cardiac remodelling. The title of the chapter is *„Echocardiographical evaluation of cardiac remodelling and of systolic function in the evolution of heart failure secondary to valvular endocardiosis in dogs”* and it regards the statistical analysis of the atrial and ventricular systolic and diastolic diameters, excentric hypertrophy and systolic function throughout all the phases of evolution of the heart failure syndrome secondary to mitral regurgitation. At the same time, it describes the evolution of this pathology in large breed dogs compared to small breed ones. The results of the study were supported by the statistical analysis of these parameters on evolution stages and by comparing the groups. Atrial remodeling, defined by the As/Ao ratio represents the first reaction of the heart to the increase in the volume of intracavitary blood and the correlation to the evolutive stage of the pathology defines it as a marker of this pathology. The inconsistency noticed between ventricular dilation and myocardial thickening defines excentric hypertrophy as a reaction of ventricular remodelling in the cronic increase of intracavitary blood. The high values for the shortening fraction and the ejection fraction define a hyperdinamic state of the left heart in valvular endocardiosis. The decrease of these values in the final stage was associated to the increase in the volume of systolic blood and it proves the alteration of systolic function in this pathology .

Chapter 10 addresses another common laboratory method of investigation in veterinary and human cardiology- electrocardiography. The objective of the study is revealed in the title of this chapter – "*Study of electrocardiographic changes in dogs with mitral valve endocardiosis and analysis of the correlations between electrocardiographic parameters and the echocardiographical indexes of cardiac remodelling”* This study aimed to characterize the rhythm and conduction disorders and the incidence of arrhythmias seen in dogs with MVD, without treatment, in different stages of evolution of the pathology. It also evaluated the relationship between changes in volume observed by echocardiography and their electrocardiographic signs. The results revealed an increased frequency of appearance of arrhythmias in advanced stages of development of heart failure secondary to valvular endocardiosis. The most common rhythm disorders diagnosed were sinus tachycardia, atrial fibrillation and ventricular abnormalities. Increased P wave duration was not associated with left atrial dilation, assessed by echocardiography, but was associated with the development of heart failure. R-wave amplitude did

not correlate with left ventricular diameter or thickness of the ventricular wall, and was above the normal reference value only in 5 dogs. Electrocardiography is not a method sensitive to changes in volume, but by analyzing the length and character of waves of atrial and ventricular depolarization and repolarization we may identify structure abnormalities which can alter the conduction patways of the electrical impulse. MVD is a chronic pathology in continuous dynamic involving primary endocardial lesions and secondary alteration of the myocardium by ventricular remodeling and circulatory disorders. Myocardial lesions are identified echocardiographically by assessing its thickness and kinetics in systole and diastole, and electrocardiographically by identifying abnormal conduction in the ventricular network.

Chapter 11 addresses the therapies used in mitral valve endocardiosis, and in this direction was created the study of *"Assessment of therapeutic efficiency of benazepril – furosemide bimedication from a clinical and echocardiographical point of view in dogs with mitral valve endocardiosis"*. This study included dogs diagnosed with valvular endocardiosis by clinical and paraclinical examination, which had not received any medication prior to consultation which allowed assessment of therapeutic efficacy of only this combination. Dogs were re-evaluated, both clinical and by laboratory tests, at an interval of 2 weeks and 2 months. The results showed the benazepril - furosemide bimedication to be effective in the resolution of clinical signs and increasing the quality of life in a short time and for a long period, reaching its main therapeutic purpose.

The topic addressed in Chapter 12 is outside the field of primary cardiac pathology and highlights the electrocardiographic changes that are known to be specific to primary cardiac pathologies, but produced by another mechanism. The pilot study "*Electrocardiographic changes induces by various neuropathies in dogs"* revealed in the 27 dogs diagnosed with various central and peripheral neuropathies the presence of arrhythmias and conduction disturbances with severe implications on body homeostasis. Through simultaneous study of heart rate variability we observed alterations of the autonomic neurovegetative system that explain the changes observed. This study launches the premise of autonomic imbalance in neuropathies with impact on the cardiovascular system in dogs, but further studies are needed to analyze these phenomena on categories of neuropathologies and possible cardiovascular therapeutic interventions in dogs. Following the cardiac electrophysiological changes observed, we consider cardiovascular evaluation is required in the diagnostic protocol of neurological disorders, both central and peripheral, in dogs.

The thesis concludes with the 13th chapter which presents general conclusions and recommendations of the thesis. The paper concludes with the presentation used during the research journal literature (227 titles from national and international literature) and appendices.