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Postgraduate School of Veterinary Science

**New data and diagnostic possibilities in the cardiologic  
examination of the dog**

**Ph.D. Thesis**

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## **Introduction and goals of the study**

In the last decades veterinary cardiology has achieved a great progress. This can be explained by the increased demands on effective and professional animal health-care. On the other hand, the diagnostic capabilities have improved by the application of the more accurate imaging methods.

The clinician need to be familiar with the importance and significance of the different heart diseases. In Hungary, no retrospective studies have been previously made on the prevalence, incidence, age and sex distribution of the different cardiac diseases in dogs. Our first aim was to characterize the cardiac abnormalities according to these aspects in the canine population in Hungary.

To asses the morphological condition of the heart, echocardiography is the most applicable method, which is a non-invasive, cheap, accurate and exact diagnostic tool. The development of the ultrasonographic techniques requires more precise morphological description of the heart and more efficacious measurement points for the standardization. Our second purpose was to establish a new measurement point at the diameter of the left atrium just above the mitral annulus in healthy dogs.

In order to evaluate the severity of the cardiac insufficiency, the functional state of the heart needs to be established. Two-dimensional echocardiographic measurements allow the calculation of the volume of the left ventricle by mathematical models. The disadvantage of this technique is that the calculation is based on one diameter obtained from the frozen image of a two-dimensional picture of the heart, (this may result in inaccurate results.). Radionuclide ventriculography assess the ventricular function on the basis of several hundred heart cycles, producing more accurate calculation. However, the later mentioned method is expensive, requires anesthesia, and radioactive technique. Our third aim was to compare the diagnostic value of the echocardiography and radionuclide ventriculography in the measuring of left ventricular systolic functional parameters in healthy dogs.

According to the latest results, the oxidative stress plays an important role in the pathogenesis and progression of the cardiac insufficiency both humans and in animals. However, the biologic significance of the free radicals and oxidative stress in naturally

occurring cardiac diseases is unknown. Our fourth purpose was to evaluate the plasma antioxidant capacity in healthy dogs and compare it with dogs suffering from spontaneous dilated cardiomyopathy or mitral endocardiosis.

### **Occurrence of canine cardiological diseases in Hungary between 1997-2000**

In this retrospective survey, we analyzed the prevalence, age and sex distribution of canine cardiological diseases in Hungary between 1997-2000, based on the examination results performed at the Department and Clinic of Internal Medicine, Faculty of Veterinary Science, Szent István University. The breed prevalence and sex data were calculated by comparing the data of the cardiological cases with the data of the university's dog population (42191 dogs) during the same time period. In order to check whether the university dog population was a good indicator of Hungary's breed composition, the Budapest rabies control list of the year 2000 was also compared with the university's data.

The incidence of heart disease in the examined dog population was 4,4 % (1085 dogs). The most common acquired disorders were endocardiosis of the atrioventricular valves and dilated cardiomyopathy, followed by primer arrhythmias (arrhythmias of unknown cause) and haemopericardium. The incidence of congenital heart defects was 0,34% in the population; stenoses of the aorta and the main pulmonary artery being the most common congenital diseases, followed by tricuspid valve dysplasia and patent ductus arteriosus.

Although, the breed predisposition was similar to formerly published survey data from other countries, we have observed some notable differences. English (and to a lesser degree also Irish) setters were found to be at higher risk to develop cardiac disorders than expected from earlier literature data, in contrast some small breeds (eg. yorkshire and west highland white terriers), and rottweilers were in a better position than in other countries. The risk of congenital heart disease was highest among boxers in the examined time period in Hungary due to the high prevalence of aortic and pulmonis stenosis in this breed. Age and sex distribution of the disease groups did not differ significantly from earlier published international data.

## **Comparison of two-dimensional echocardiographic measurements of the left atrium in healthy dogs**

The aim of this study was to establish normal echocardiographic values of the left atrium just above the mitral annulus ( $LA_{ama}$ ) in healthy dogs as a new measurement technique, not published earlier, and to compare our results to formerly reported other methods. In the first part of the study 20 dogs of various breeds were examined. The diameter of the left atrium just above the mitral annulus ( $LA_{ama}$ ) was compared to the linear (left to right) dimension of the left atrium ( $LA_{r-l}$ ) as published earlier. There was a linear relationship between  $LA_{r-l}$  and the body weight ( $LA_{r-l} = 0,5061 \text{ BW (kg)} + 22,206$ ;  $R^2 = 0,81$ ), but the proportion of  $LA_{r-l}/LA_{ama}$  was independent from the body weight ( $LA_{r-l}/LA_{ama} = 0,0004 \text{ BW (kg)} + 1,0833$ ;  $R^2 = 0,01$ ).

In the second part of the study, the left atrial diameter just above the mitral annulus ( $LA_{ama}$ ) was measured in 121 dogs of various breeds. There was a positive linear relationship ( $R^2 = 0,697$ ;  $p < 0,001$ ) between body weight and  $LA_{ama}$  ( $LA_{ama} = 0,54 \text{ BW (kg)} + 18,502 \pm 4,76$ ), but there were no significant correlations between the age of animals and  $LA_{ama}$  ( $p = 0,45$ ) as well as between the gender of animals and  $LA_{ama}$  ( $p = 0,78$ ). 2DE determination of  $LA_{ama}$  as described in the present study can be suggested in those dogs where measurement of  $LA_{r-l}$  arise technical difficulties. In these cases  $LA_{r-l}$  can be calculated from  $LA_{ama}$  by using the given formula:  $LA_{r-l}/LA_{ama} = 0,0004 \text{ BW (kg)} + 1,0833$  worked out in the first experiment.

## **Comparison of echocardiography and gated equilibrium radionuclide ventriculography in the measurements of left ventricular systolic function parameters in healthy dogs**

In this study, left ventricular systolic function was assessed in 12 healthy dogs with echocardiography and equilibrium radionuclide ventriculography and their diagnostic value and accuracy were compared. Two-dimensional real time (2D) echocardiographic images of the heart were obtained using a 5 MHz phased-array sector scanner. Imaging was performed from a right parasternal position at the fourth to fifth intercostal space. Standard 2D-real time measurements were obtained from long-axis images of the left ventricle immediately below the atrioventricular valve. The measurements included left ventricular internal dimension at

the time of end-diastole and end-systole. Left ventricular volume measurements were then calculated by the *Teichholz method*:  $EDV=7 \times LVID_d^3/2.4 + LVID_d$ ;  $ESV=7 \times LVID_s^3/2.4 + LVID_s$ , where EDV is the end-diastolic volume and ESV is the end-systolic volume. LVID means the left ventricular internal dimension at the time of end-diastole and end-systole. The ejection fraction (EF) was calculated by the following formula:  $EF=(EDV-ESV)/EDV \times 100$ .

Following echocardiographic measurements, the dogs were placed in right lateral recumbency under a gamma camera. Low Energy High Resolution (LEHR) collimator was fitted with 18.9 cm x 18.9 cm detector mask. An in vivo method of labeling red blood cells was used. At first, 10 mg of pyrophosphate (PYP) was injected intravenously followed by the injection of 740 MBq of  $^{99m}\text{TcO}_4^-$  15 minutes later. Continuous ECG-gating was done for the imaging. Sixteen frames were formed in a 64x64x16-matrix array. The “region of interest” (ROI) method was used for the image analysis. The left ventricular contour was pointed at the end-systolic and the end-diastolic frames. Background ROI was drawn as a small square around the top of the heart and lungs. The EF was determined from the same formula that was used during echocardiography. EDV and ESV were calculated from the ventricular ROI of end-diastolic and end-systolic frames by the computer.

Left ventricular internal dimensions and volume were measured at the time of end-systole and end-diastole. Ejection fraction - one of the most informative parameters of cardiac function - was calculated in each animal. Values (e.g.: EDD, ESD, EDV, ESV) measured by the scintigraphic method were significantly (Student T-test,  $p < 0.05$ ) higher, than the data obtained by echocardiography. Ejection fraction (EF) was the only parameter that did not differ significantly when compared the two imaging techniques. The difference between the results of parallel measurements was in inverse ratio to the size of the heart.

## **Plasma antioxidant capacity in dogs with naturally occurring heart diseases**

The aim of this study was to compare the plasma levels of antioxidants by measuring total antioxidant activity (TAS) and ferric reducing ability of the plasma (FRAP) in healthy dogs and compare it with the same parameters in dogs suffering from spontaneous DCM or from mitral endocardiosis (ME).

Blood samples were collected from dogs that underwent cardiological examination. Dogs with echocardiographically diagnosed mitral endocardiosis (10 dogs) and with a dilated left atrium (at least 2:1 left atrium to aorta ratio in short axis view) as well as dogs with dilated cardiomyopathy (DCM and sinus rhythm group consisted of 8 dogs, DCM and atrial fibrillation group consisted of 15 animals) (based on enlarged end diastolic and end systolic cardiac chamber dimensions, reduced fractional shortening value of less than 25% and without other detectable cardiac disease) were sampled. Dogs with other cardiac problems or with detectable noncardiac diseases (based on the clinical and laboratory data) were excluded from the study. Control animals without any sign of cardiac or systemic disease based on the history, clinical examination and laboratory work up were also chosen from the university's dog population. All dogs, having received medications (cardiac or non-cardiac) were excluded; however data on the included dogs' diet or additional vitamin intake was not collected. Briefly, the study populations consisted of healthy control dogs and dogs with ME or DCM without any treatment at the time of sample collection.

Blood samples were collected from a peripheral vein into a tube containing EDTA. TAS measurement was performed as described by Miller et al. (1993). The method to measure the ferric reducing ability of the plasma (FRAP) was described in detail by Benzie and Strain (1996). The TAS and FRAP values and heart rates were compared by using two samples Student T-test.

Although we did not determine the exact stage of congestive heart failure of these animals, all of the sampled dogs had clinically apparent disease (at least NYH class II). Most probably, the DCM and atrial fibrillation (DCM-AF) groups represented the patients with the most severe heart failure, which were also reflected by the mean heart rates in the different groups. All of the groups with cardiac diseases had significantly higher mean heart rates when

compared to the control animals, moreover DCM and DCM-AF dogs also had significantly higher mean heart rate compared to the other disease groups.

The different groups were not age, sex or breed matched because of the difference in the age and breeds where this two spontaneous disease occur and due to technical reasons in case of the control group. However, the two DCM groups were similar in age, breed and sex composition, having the same untreated disease with similar fractional shortening (FS) values. This enabled us to separately asses, whether the severity of the cardiac failure reflected by increased heart rate and by a rhythm disorder, can cause any difference in the antioxidant status of these animals.

We found that the total antioxidant levels measured by the TAS assay did not differ significantly between the cardiac patients and the control group. Our normal TAS values were similar to the findings of Nemeč et al. (2000) made on healthy beagles.

Ferric reducing ability of the plasma in all groups with cardiac disease were higher than in the control animals, which reached significant level in cases of the ME, DCM and DCM-AF groups compared to the control animals and between the DCM-AF and ME groups. Moreover, there were significantly higher antioxidant levels in the DCM-AF group compared to the DCM and sinus rhythm (DCM-SR) group as demonstrated by both antioxidant (TAS and FRAP) tests. The difference between the findings of the two antioxidant tests may be explained by methodological reasons or by the different reactivity of the two assays to the various antioxidants.



## New scientific results

- Considering a four year period (1997-2000) of canine cardiological examinations (3373 dogs), we concluded that the incidence of heart disease in the examined dog population was 4,4 % (1085 dogs) in Hungary, as compared to the literature where heart disease in similar populations was about 11%.
- Although, the breed predisposition was similar to formerly published survey data from other countries, we have observed some notable differences. English setter, puli, Hungarian vizsla, Dalmatian and bobtail were found to be at higher risk to develop cardiac disorders than expected from earlier literature data, in contrast with some small breeds (eg. Yorkshire and west highland white terriers) and rottweiler, which were in a better position in Hungary than in other countries.
- We have established a new method to measure the normal echocardiographic values of the left atrium just above the mitral annulus ( $LA_{ama}$ ) in healthy dogs. The proportion of  $LA_{r-l}/LA_{ama}$  was independent from the body weight ( $LA_{r-l}/LA_{ama} = 0,0004 \text{ BW (kg)} + 1,0833$ ;  $R^2 = 0,01$ ). As a very strong relationship was found between  $LA_{r-l}$  and  $LA_{ama}$ , it can be concluded, that in healthy dogs  $LA_{r-l}$  might be substituted with  $LA_{ama}$ .
- There was a positive correlation ( $R^2 = 0,697$ ;  $p < 0,001$ ) between body weight and  $LA_{ama}$  of 121 dogs ( $LA_{ama} = 0,54 \text{ BW (kg)} + 18,502 \pm 4,76$ ). We established the normal reference range of the  $LA_{ama}$  in healthy dogs based on the data of 121 dogs.
- There was no significant correlations between the age of animals and  $LA_{ama}$  ( $p = 0,45$ ) or between the gender of animals and  $LA_{ama}$  ( $p = 0,78$ ).
- It was concluded that ejection fraction (EF) was the only parameter that did not differ significantly when echocardiography and radionuclide ventriculography, as two imaging techniques were compared.

- The difference between the results of parallel measurements by echocardiography and radionuclide ventriculography was in inverse ratio to the size of the heart. In addition, the differences between the two types of measurements were in inverse ratio to the diameter of the left ventricle.
- We concluded that there is increased antioxidant reactivity detected by the FRAP but not by the TAS assay in the blood of dogs with naturally occurring cardiac disorders (dilated cardiomyopathy and endocardiosis).
- It was concluded that the magnitude of the elevation of the FRAP level seems to be more affected by the heart failure severity and/or by the heart rate and/or by the rhythm disorder than by the underlying cardiac disease itself.

### **Publications related to the dissertation**

**Cs. Hetey**- L. Balogh- G. Andócs- K. Vörös- Gy. A. Jánoki: Comparison of echocardiography and gated equilibrium radionuclide ventriculography in the measurements of left ventricular systolic function parameters in healthy dogs. *Acta Veterinaria Hungarica*, 2002. *50*. 21-29.

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**Hetyey Cs.**- Vörös K.: Az echokardiográfia elve és gyakorlata a kutyák kardiológiai vizsgálata során. *Magyar Állatorvosok Lapja*, 2004. *126*. 48-57.

**Cs. Hetey**- K. Vörös- J. Reiczigel: Comparison of two-dimensional echocardiographic measurements of the left atrium in healthy dogs. *Acta Veterinaria Hungarica*, 2005. *53*. 23-33.