# Evaluation of the functional capacity in dogs with naturally acquired heart disease

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**ABSTRACT**: Functional capacity is the physical ability to perform a defined task. In humans it can be evaluated by using exercise testing, for instance sub-maximal exercise tests. Walking tests are widely used variations of sub-maximal exercise tests and in human medicine are considered to be realistically related to daily physical activity and prognosis in patients with heart failure. The aim of this study was to assess a sub-maximal exercise test in dogs with varying degrees of heart disease. The 6-minute walking test was used to test the functional capacity in healthy dogs and dogs with heart disease (degenerative mitral valve disease). Three groups of untrained owned dogs were compared. Two groups were dogs had mild and moderate degenerative mitral valve disease (ME-1 and ME-2, respectively) and the third group comprised healthy dogs with the same age and size conditions. Both groups of dogs with mitral valve disease walked shorter distances during 6 min (control 448.92 m; ME-1: 406.89 m; ME-2: 350.04 m). The influence of the test on the heart rate, electrocardiography and blood pressure was also evaluated. Although the 6-minute walking test has already been tested in healthy dogs, dogs with chronic pulmonary disease and dogs with artificially induced heart disease, this is the first time that this test has been validated in elderly dogs with naturally acquired heart disease. Thus, we demonstrate here that this test can be used reliably for assessing functional capacity in dogs with heart disease.

**Keywords**: 6-minute walking test; sub-maximal exercise test; heart disease; dogs

**List of abbreviations**

**ACVIM** = American College of Veterinary Internal Medicine, **BP** = blood pressure, **CDCD-VFU** = Clinic of Dog and Cat Diseases at University of Veterinary and Pharmaceutical Sciences Brno, **DMVD** = degenerative mitral valve disease, **ECG** = electrocardiography, **FC** = functional capacity, **HR** = heart rate, **ME-1** = first target group, **ME-2** = second target group, **6-MWT** = 6-minute walking test

There has been a significant increase in the population of companion dogs in the last decades and as in human beings several chronic conditions, for instance cardiovascular or respiratory diseases, can also afflict aged canine patients. Diseases like ischaemic heart disease, valvular disease, myocardial disease, chronic bronchitis, tracheal collapse and others have been long recognised in canine geriatric medicine and there have also been enormous advances in their diagnosis and treatment. However, the ability to recognise the onset of early clinical signs represents a gap in diagnostics. The vast majority of cases are presented with overt disease and thus the survival time is consequently reduced. One of the earliest and most significant consequences for both human and veterinary patients with chronic respiratory or cardiac disease is the reduced ability to perform normal daily activities, also known as the functional capacity (FC) (O'Keeffe et al. 1998; Singh 2007). In general,

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evaluation of the FC includes measuring the cardiovascular, pulmonary and metabolic responses at rest and during exercise. A very common method is exercise testing, where determinants of the FC like oxygen consumption, anaerobic threshold, heart rate (HR), blood pressure (BP) and ventilation among others can be measured. Maximal exercise tests gradually increase the level of exertion until physical exhaustion, a target HR, or the onset of clinical signs is reached (i.e., dyspnea) or electrocardiographical changes (i.e., arrhythmia). Another variation is called the submaximal test in which only a pre-determined level of exercise is applied; because of its safety, this test is mostly indicated for patients with known cardiovascular or respiratory disease (Lear et al. 1999). Walking tests are a common modality of submaximal tests and allow evaluation of the patient's life quality because the test in fact, is an apparent normal daily activity, is safe, easy to perform and could be a simple predictor of morbidity and mortality in human patients with heart failure (O'Keeffe et al. 1998; Opasich et al. 2001). To date, the 6-minute walking test (6-MWT) has not been investigated in dogs with naturally acquired heart disease. The aim of this study was to assess the FC in owned untrained dogs with heart disease under controlled conditions.

## MATERIAL AND METHODS

### Study design and animals

The study was designed as a prospective randomised clinical trial. Patients were chosen from the canine patient population, who visited the Clinic of Dog and Cat Diseases at the University of Veterinary and Pharmaceutical Sciences Brno (CDCD-VFU), Czech Republic. Signed consent was obtained from the owners and all procedures were approved by the Animal Care and Use Committee of the University of Veterinary and Pharmaceutical Sciences, Brno, Czech Republic.

The studied population included patients diagnosed with degenerative mitral valve disease (DMVD) confirmed by clinical examination, electrocardiography (ECG), radiography and echocardiography and a control group comprised of healthy dogs in the same age and size range. Patients with heart disease were subsequently divided into two different groups. The first group (ME-1) belonged to the disease category B2 of disease (evidence of cardiac remodelation) established by the ACVIM (American College of Veterinary Internal Medicine) (Atkins et al. 2009). The other ME group (ME-2) were categorised as level C2 of disease (past clinical signs of heart failure). The members of both groups were already receiving medication. All dogs underwent a full clinical and cardiac investigation before enrolling in the study (history, physical examination, arterial blood pressure measurement, full haematology, routine serum biochemistry, urianalysis, electrocardiography, thoracic radiographs and echocardiography) carried out at the CDCD-VFU to confirm health status and rule out any other concomitant condition.

Thirty eight dogs were recruited for this study. Fifteen dogs were classified as ME-1, nine were ME-2 and 14 were control subjects. All dogs successfully finished the test and there were no complications. Overall, the mean age and weight of patients were 11.07 years and 8.6 kg, respectively. Seventeen patients were male and there were 21 females. Mongrels, Daschunds and French Poodles were over-represented (ten Mongrels, nine Daschunds, eight French Poodles, two German Spitz, two Japanese Chin, two King Charles Cavalier Spaniel, two West Highland White Terriers, two Czech Terrier, and one Pekinese). Average time from diagnosis for DMVD patients was 207 days.

In the ME-1 group the mean age of patients was 11.5 ± 2 years. The average weight was 8.1 ± 3 kg, and six were male and nine were females. There were several breeds of dogs (four French Poodles, three Daschunds, three mongrels, two German Spitz, two Japanese Chins, and one Pekinese). These patients were receiving a combination of an ACE inhibitor and spirinolactone. In the ME-2 group the average age and weight was 12.5 years and 7.2 kg, respectively. Seven patients were males and two were females. The dogs were comprised of four Daschunds, two Mongrels, two French Poodles, and one Czech Terrier. These patients were receiving in addition to ME-1 furosemide and pimobendan. Patients in the control group had an average age of 9.6 ± 1.4 years. The average weight was 10.4 ± 1.1 kg, and four were males and 10 females. The distribution of the breeds was, five mongrels, two King Charles Cavalier Spaniels, two French Poodles, two Daschund, two West Highland White Terriers, and one Czech Terrier.

### Blood pressure measurement and recordings and definition of ECG variables

Once the subject was calm, ECG and blood pressure were determined. A conventional oscillometric blood pressure system (Vetmon 2200, version 1.16, Czech Republic) using insuflable cuffs (determined by ~40% of the circumference of the measured area of the limb) was applied either to the forelimb medioproximal to the carpus (radial artery) or to the hind limb above the hock (saphenous artery) to obtain systolic, diastolic and mean blood pressure.

Standard 10-lead ECGs were recorded using the leads I, II, III, aVR, aVL, aVF, $CV_5RL$, $CV_6LL$, $CV_6LU$, and $V_{10}$ (EKG Praktik Veterinary®, Seiva, Czech Republic). The recording limb electrodes were made of flattened alligator clips and were attached to the skin using a non-saline ultrasound gel at (or just distal to) the elbows and at the level of (or slightly proximal to) the stifle. Left chest leads were placed at the 6$^{th}$ intercostal space at the edge of the sternum ($CV_6LL$ [$r_2$]), and at the costochondral junction ($CV_6LU$ [$v_4$]). The right chest lead was placed at the 5$^{th}$ intercostal space at the edge of the sternum ($CV_5RL$ [$rv_2$]). Lead $V_{10}$ was place at the dorsal spinous process of the 6$^{th}$ to 7$^{th}$ thoracic vertebra. The speed and voltage were set at 50 mm/s and 10 mm/mV, respectively, with a 60 Hz AC external filter (Dvir et al. 2002) and the sampling rate was determined every 10 s. ECG traces were analysed in at least ten (10) P-QRS-T complexes thus: HR, P wave (length, width, morphology), PR interval, QRS complex, R wave voltage, ST segment, interval QT, and T wave. ECG waves and intervals were calculated using the software provided by the ECG manufacturer and checked manually.

### Walking test

The 6-MWT was elected for this study. Dogs were walked with the owners in a corridor measuring 17.9 m free from obstacles and distractions and located at the facilities of the CDCD-VFU. A technician was instructed to conduct and encourage the owner and patient through the desired trace over the course of exactly 6 min. Time was digitally controlled. BP and ECG were once more sampled immediately after the test.

Table 1. Average of blood pressures obtained by oscilometry before and after the 6-MWT

| | At rest | | | 6-MWT | | |
|---|---|---|---|---|---|---|
| | SBP | DBP | MBP | SBP | DBP | MBP |
| ME-1 | 150.6 | 94.6 | 115 | 155.5 | 96.1 | 111.9 |
| ME-2 | 154.9 | 97.7 | 112.8 | 153.2 | 96.4 | 108 |
| Control | 149 | 89.2 | 116.6 | 154 | 92.3 | 114.3 |

SBP = systolic blood pressure; DBP = diastolic blood pressure; MBP = mean blood pressure

### Statistical analysis

The Kruskall-Wallis test was used to compare age, weight, HR, BP, and the distance walked in 6 min between the groups. Dunn's multiple comparison test was used to detect differences between groups. The Wilcoxon test was used to compare HR and ECG parameters at rest and after the test. Tests were two-sided. The correlation between 6-MWT with echocardiography (once before testing), and ECG values was calculated using Spearman correlation. A *P*-value of less than 0.05 denoted a statistically significant difference.

## RESULTS

### Systolic blood pressure

There were no changes in the blood pressure (systolic, diastolic and mean) between the studied groups (Table 1).

### Six-minute walking test

There was a significant difference (*P*: 0.002) in the distance walked during 6 min between the groups (Figure 1). *Post hoc* analysis showed that control subjects walked longer distances in comparison with both ME groups. There were no complications for patients during the protocol.

### Heart rate

The HR of ME-1 and ME-2 dogs was significantly higher at rest (*P*: 0.04) and at the end of the 6-MWT (*P*: 0.003) than control subjects. Post hoc analysis demonstrated that control subjects had lower HR in comparison with the ME groups.

Table 2. ECG parameters with significant differences at rest and after the 6-MWT

| ECG parameter | Rest | | | | 6–MWT | | |
|---|---|---|---|---|---|---|---|
| | Lead | Control dogs | ME-1 dogs | ME-2 dogs | Control dogs | ME-1 dogs | ME-2 dogs |
| P wave (ms) | III | 35.2*+ | 39.4* | 40.6* | 35.3*+ | 40.1* | 42.7* |
| | aVL | 37.7+ | – | – | 40.1+ | – | – |
| Q wave (mV) | aVL | –0.06* | –0.08 | –0.27* | –0.07* | 0,1 | –0.2* |
| R wave (mV) | – | | – | – | 0.06 ($V_{10}$)* | | 0.11 ($V_{10}$)* |
| ST segment (mV) | I | 0.05* | –0.03* | –0.05* | – | – | – |
| | III | 0.03* | –0.01* | –0.01* | – | – | – |

*differences between groups
+difference between rest and the 6-MWT in a defined group

Also, control dogs were found to have significantly increased HR from rest to the end of the 6-MWT (*P*: 0.002) (Figure 2).

## ECG parameters

There were differences between groups in the P wave (width), Q wave, R wave and ST segment. The P wave (width) increased significantly in duration from rest to 6-MWT in control patients (Table 2). In addition, the QT interval had a strong negative association with the 6-MWT (lead I: –0.86, lead aVL: –0.95).

## DISCUSSION

This study confirmed the hypothesis that dogs with heart disease have reduced FC expressed as exercise intolerance and worse performance of normal daily activities, which has been reported to be among the first clinical signs in humans with heart disease (O'Keeffe et al. 1998; Singh 2007). Reference values have been published for the 6-MWT in human beings with an age from 40 to 80 years old: the median distance walked was 576 m for healthy men and 494 m for healthy women (Weisman and Zeballos 2002). Comparable values have been determined in normal dogs. Healthy young dogs in a weight range

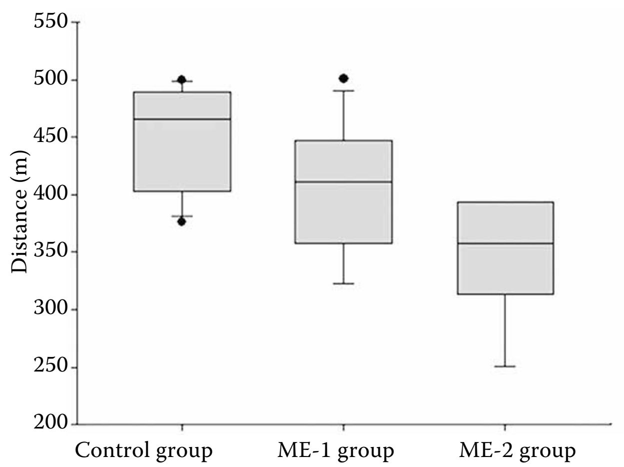


Figure 1. Box-plot showing the distance walked in 6 min for all groups. Control patients had a better performance compared with any of the groups of patients with heart disease (averages: control 448.92 m; ME-1: 406.89 m; ME-2: 350.04 m)

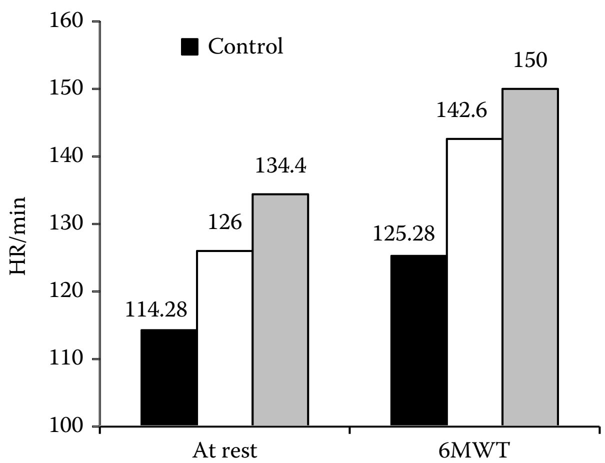


Figure 2. HR values in normal and heart-diseased dogs. Both groups of ME dogs showed higher HR both at rest and after the 6-MWT than control subjects whereas ME-2 dogs showed the highest HR. A gradual increase in HR for all groups from the resting status to the end of the 6-MWT was also noted

of 25 to 37 kg covered an average distance of 573 ± 85.5 m walking in a 22.73 m long corridor (Boddy et al. 2004). Another study performed in a mixed healthy population of dogs (approx. weight 22.9 ± 11.2 kg) also showed similar characteristics (526 ± 52.4 m) in a 15.24 m long corridor (Swimmer and Rozanski 2011). We established from the results of this work that the average distance walked in 6 min in a healthy small-breed geriatric dog (~9-year, ~10 kg dog) is approximately 450 m. Human beings with chronic heart disease and chronic respiratory disease usually walk shorter distances than healthy human beings in the same age group (Weisman and Zeballos 2002; Rostagno et al. 2003). In veterinary medicine a similar behaviour has been noted. One study (Boddy et al. 2004), showed that dogs with artificially-induced heart failure covered a mean distance of 526 ± 99.4 m. More recently, another study (Swimmer and Rozanski 2011) evaluated dogs with chronic bronchopulmonary disease and confirmed this finding (384.8 ± 41 m). The lower values of the 6-MWT obtained in our patients compared to the above described veterinary studies are probably due to differences in the size of the dogs and the length of the corridor. Larger dogs with longer extremities have a more effective step range than the expected from two-to-three fold smaller individuals. Moreover, it has been claimed based on human studies that in a shorter corridor, the distance walked could be lesser because more turns are involved (Weisman and Zeballos 2002). It is possible that many other factors could be associated with these differences such as breed shape and size (our study used a high number of short-legged dogs), unnoticed concomitant disease (i.e., orthopaedic or neurological conditions), degree of motivation of the dog and owner and others.

Most human reports state that regurgitation of the mitral valve (orifice, volume, velocity) is modestly linked to FC, whereas left ventricular diastolic dysfunction and atrial fibrillation independently determined FC (Drory et al. 1989). Dogs with DMVD are typically older, and left ventricular relaxation can be impaired as a function of age or associated conditions such as systemic hypertension (Bonagura and Schober 2009). Although both groups of dogs with DMVD in our study had reduced FC in comparison with normal dogs, ME-2 dogs had the worst performance and this can be the result of an even more advanced left ventricular dysfunction than might be present in ME-1 dogs. Both systolic and diastolic dysfunction have been reported in symptomatic dogs with DMVD due to several factors such as altered left ventricular geometry, increased ventricular stiffness, high atrial and venous pressures or pulmonary hypertension (Bonagura and Schober 2009). Based on the results of the present and previous studies we presume that patients with DMVD have a certain degree of ventricular dysfunction; however, other determinants of left ventricle function were not determined during or after the test.

HR is controlled by the sympathetic and parasympathetic components of the autonomic nervous system. There is a normal physiological increase of the HR during the first few seconds of exercise as a consequence of the progressive parasympathetic tone inhibition, regardless of exercise intensity (Chung 1983; O'Leary 2006). The higher HR observed in ME dogs at rest indicates the chronic hormonal activation that accompanies heart disease. The plasma concentration of noradrenalin in patients with congestive heart disease is elevated at rest (Uechi et al. 2002). The same effect may also explain the differences after completion of the 6-MWT.

All the three studied groups had exponential increases in the HR from resting values to the end of the 6-MWT (Figure 2); but interestingly, only control subjects showed relevant differences that can also explain the negative association with the QT interval. When the HR was experimentally increased at rest either by atrial or ventricular pacing, QT interval shortening did occur but to a lesser degree when exercise-induced. This suggests that the HR is only one of the determinants of the QT interval duration. We believe that the degree of exertion is not the only explanation for these findings, but that there could also be other influencing factors such as the effect of circulating catecholamines, ventricular fitness, decreases in end systolic volume, changes in hematocrit and serum electrolytes, and others (Fananapazir et al. 1983). In human beings, there is evidence of increased sympathetic activity with age due to increased plasma catecholamine concentration. This has been explained by the noted decreases in excretion of catecholamines from the circulation due to a fall in uptake into sympathetic nerves or other sympathetic effector organs (Appenzeller and Oribe 1997); furthermore there is an age-related decrease in acetylcholine synthesis and binding (Kelly and Roth 1997) leading to a global positive sympathetic effect that can be associated with increments in the HR in healthy patients of this study.

The ECG differences (longer P waves, taller R waves, and negative ST segments) found between groups could be the reflection of some of the typical ECG changes seen in dogs with DMVD as a result of the enlargement of the left atrium and left ventricle. Unfortunately, an explanation for the Q-wave changes was not found. One study reports that P wave duration is more closely related to increases in pressure than the diameter of the left atrium (Foggiano et al. 1997). Increases in the P wave duration in control dogs from rest and after the 6-MWT may reflect a physiological response to an increase in the workload and increasing distention of the LA during an exertion.

## CONCLUSIONS

This study demonstrated that the 6-MWT is safe, inexpensive and easy to perform in owned dogs with heart disease. The results of this test demonstrated that dogs with heart disease have decreased physical performance and ECG changes that can be worse in advanced stages of the disease. This is the first time the 6-MWT was performed in dogs with naturally acquired heart disease. The results are consistent with previous human and veterinary studies and may constitute an alternative to other tests in that it can evaluate FC in relation with heart disease in a more compassionate and more objective approach. The 6-MWT might have an important future application for evaluating exercise performance and heart disease because it had great acceptance from owners and dogs and spontaneous responses were obtained. However, further studies should be held to determine the importance of the test in the treatment and prognosis of cardiac disease.

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