CLINICAL CARDIOLOGICAL PARAMETERS IN WHIPPETS

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“On ne voit bien qu’avec le cœur. L’essentiel est invisible pour les yeux.”
Antoine de Saint-Exupéry (1900–1944)
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LIST OF ABBREVIATIONS

2D two-dimensional view
Ao aorta
AV aortic valve
bpm beats per minute
BSA body surface area
BW body weight
CO cardiac output
d diastole
ECG electrocardiogram
EPSS E-point to septal separation
ESVI end-systolic volume index
FS fractional shortening
Hb haemoglobin concentration
HCM hypertrophic cardiomyopathy
Hct haematocrit
HR heart rate
IVS interventricular septum
LA left atrium
(la) long axis
LV left ventricle
LVD left ventricular diameter
LVEF left ventricular ejection fraction
LVET left ventricular ejection time
LVW left ventricular wall
MEA mean electrical axis
MitrA mitral A-peak velocity
MitrE mitral E-peak velocity
MV mitral valve
PEP pre-ejection period
PMI point of maximal intensity of a murmur
PV pulmonic valve
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tr>
<td>RBC</td>
<td>red blood cell count</td>
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<tr>
<td>s</td>
<td>systole</td>
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<tr>
<td>(sa)</td>
<td>short axis</td>
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<tr>
<td>SD</td>
<td>standard deviation</td>
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<td>SV</td>
<td>stroke volume</td>
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<tr>
<td>T4</td>
<td>fourth thoracic vertebra</td>
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<tr>
<td>TricA</td>
<td>tricuspid A-peak velocity</td>
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<tr>
<td>TricE</td>
<td>tricuspid E-peak velocity</td>
</tr>
<tr>
<td>VAo</td>
<td>aortic peak velocity</td>
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<tr>
<td>VcF</td>
<td>velocity of circumferential fibre shortening</td>
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<td>VHS</td>
<td>vertebral heart size</td>
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<td>VPulm</td>
<td>pulmonic peak velocity</td>
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SECTION I

GENERAL INTRODUCTION
CLINICAL ADAPTATIONS OF THE HEART TO ATHLETIC TRAINING

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Introduction

A Whippet is a medium-sized sight hound, bred to hunt by sight, coursing game in open areas at high speeds. One of the theories on the origin of Whippets, is that they developed in Northern England during the late 19th century, when Greyhounds were crossed with small Terriers to produce a small, swift hound capable of hunting rabbits and other small game. During this era, the Whippet belonged mainly to the working class people of England. Because of this, the Whippet was called the “poor man’s Greyhound”, or the “poor man’s race horse”. During non-working days, owners raced their Whippets in fields and on town roads. Nowadays, Whippets are outstanding running dogs and are top competitors in lure coursing, straight racing and oval track racing, being the fastest domesticated animal of his weight. However, Whippet racing never gained the commercial appeal of Greyhound racing and so remains strictly an amateur sport. After the Whippet was officially recognized as a breed, it began to be appreciated for its aesthetic appeal, making beautiful exhibition dogs and devoted companions. Due to continuous selection for faster dogs during sight hound races on one hand, or for better performing dogs at exhibitions on the other hand, a slight difference in body conformation arose between race pedigree and show pedigree Whippets. Race pedigree dogs are a bit longer in loin and have a straight back; show pedigree dogs have a shorter body and a rounded, sloping down back. Shoulder heights for both types should be 44 to 47 cm for females and 47 to 51 cm for males.

Sight hound racing is a test of pure speed, combined with desire to chase an artificial lure without interfering with other hounds. In oval track racing, Whippets break out of starting boxes wearing muzzles and numbered blankets. The dogs run on a U-shaped or oval track with an inner rail and for a distance of 350 m (range 340-365 m), which usually takes 22-24 s. Whippets are also trained on 100 m sprints to improve their start during races and to provide anaerobic or resistance training for sprinting. They are also trained over long distances between races, often running for 60-90 min, to increase endurance through aerobic training. Due to the high speed during races, sudden changes in direction and possible collisions with other hounds and stationary objects, Whippets are prone to many musculoskeletal injuries. Tarsal, metatarsal, muscle and toe injuries are the most frequently encountered problems. Furthermore, acid-base imbalances, rhabdomyolysis and hyperthermia may occur after racing.
Two Whippets were presented at our clinic for a second opinion after they had been excluded from sight hound races by the referring veterinarian. The youngest was a six month old Whippet male bred out of race pedigree lines, with excellent performing parents. ‘Dicky Dik’ was referred because of a grade 1/6 midsystolic murmur with point of maximal intensity at the level of the aortic and pulmonic valve. On electrocardiography, a high R-wave amplitude (3.5mV) was noted in lead II, without other significant abnormalities. On echocardiography, a mild hypertrophy of the interventricular septum and left ventricular (LV) wall was noted, with a normal fractional shortening and no significant abnormalities on complete Doppler examination of both atrioventricular and semilunar valves. Another Whippet, a 3 years old, highly trained, intact male, ‘Oxy’, was referred because of abnormal electrocardiographic findings, from which the referring veterinarian concluded he had a cardiac problem (probably ventricular dilation) and he should never race again. No murmur was detected on auscultation. On electrocardiography, a mildly elevated P-wave amplitude (0.5mV), a high R-wave amplitude (3.8mV) and a slurring of the ST-segment were found. Echocardiography showed a mild to moderate hypertrophy of the interventricular septum and LV wall, and a rather low fractional shortening (19%), without any abnormalities on Doppler echocardiography of both atrioventricular and semilunar valves.

We assumed that these specific findings could be due to the breed (as it was previously reported that sight hounds have larger hearts), or to training, or both.

These two Whippets raise the question whether their enlarged heart, possibly with mild murmurs and/or electrocardiographic changes, are specific to Whippets compared to other dogs and animals (genetic influence), or an influence of training as seen in human medicine.

Looking for an explanation for these findings, brought us through a lot of evidence of cardiac adaptations to training, the so-called “athletic heart syndrome” in human medicine.
**Athletic heart syndrome in human medicine**

In 1899, Henschen described, for the first time, enlarged and thickened hearts in cross country skiers, detected by chest percussion (Urhausen and Kindermann, 1999). He interpreted his findings as structural and functional adaptations to regular physical exercise. Although the “athletic heart syndrome” has been extensively researched during the last 50 years, it still remains an area of debate. In 1968, Gott et al. defined the “athletic heart syndrome” as anatomical and physiological adjustments to strenuous exercise, possibly including biventricular cardiac enlargement; systolic ejection murmur; third heart sound; increased stroke volume, LV stroke work, and cardiac output; bradycardia and sinus arrhythmia; recurrent atrial and ventricular arrhythmias; cardiac conduction defects; ST-segment elevation, and T-wave alterations (Gott et al., 1968). The earliest observations on the cardiac structure of athletes had been gathered through electrocardiography and chest radiography (Morganroth et al., 1975). Since the mid-1970s, the definition of “athletic heart syndrome” has been fine-tuned with the help of echocardiography. Also, the different adaptation patterns to different kinds of training or sports – endurance training (also described as dynamic, isotonic or aerobic) versus resistance training (also described as static, isometric, anaerobic or power) – have been studied (Morganroth et al., 1975). LV cavity may dilate under an increased volume demand, such as during aerobic exercise. Based on LaPlace’s law, LV mass increases to normalize wall stress, as evidenced by increased LV septal and free wall thickness. This law, originally described in 1806 by Pierre Simon LaPlace, a French mathematician and astronomer, explains the equilibrium relationship in a spherical organ: \(2 \cdot \text{wall thickness} \cdot \text{wall stress} = \text{intraventricular pressure} \cdot \text{internal cardiac chamber radius}\) (Hamlin, 1999) (Fig. 1). Typically, the normal heart muscle grows to match the work load imposed on the ventricle, maintaining a constant relationship between systolic pressure and the ratio of wall thickness to ventricular radius, irrespective of ventricular size (Blomqvist and Saltin, 1983).
Figure 1: Law of LaPlace: \( P = 2rdT \): according to the law of LaPlace, as LV cavity pressure (\( P \)) increases (pressure overload), the wall thickness (\( d \)) increases (hypertrophy) to maintain wall stress (\( T \)). As the cavity dilates (volume overload), wall thickness increases to maintain cavity pressure.

(Adapted from Glantz and Kernoff, 1975)

Although both LV wall thickness and end-diastolic dimension increase, the mass-to-volume ratio remains constant. This increase in volume and wall thickness is considered a normal adaptation for athletes in which increased cardiac output occurs during exercise and is called eccentric hypertrophy (Huston et al., 1985). In resistance athletes, a significant pressure overload during isometric exercise occurs due to an extremely high systolic blood pressure, which may reach 300mmHg. These athletes demonstrate significant wall thickening that normalizes wall stress at high afterload, without an increase in LV volume (Huston et al., 1985).
Different diagnostic approaches

Auscultation

Resting sinus bradycardia (heart rate < 60 beats/min) is probably the most common finding among highly trained athletes (Gott et al., 1968; Morganroth et al., 1975; Ikaheimo et al., 1979; Cox et al., 1986; George et al., 1991). Murmurs and third and fourth heart sounds are common in highly trained athletes (Gott et al., 1968). Systolic and diastolic murmurs may be detected with high flow rates causing turbulent flow across normal semilunar or atrioventricular valves, respectively (George et al., 1991; O'Brien and Rogers, 1999). Morganroth et al. (1975) reported 12% innocent systolic ejection murmurs at the lower left sternal border, or apex, or both.

Chest radiography

From cardiac silhouettes, transverse and longitudinal diameters can be measured and cardiac volumes estimated. Several studies have reported globally enlarged hearts in athletes, with a cardiothoracic ratio approaching or exceeding the normal limit of 0.50 (Gott et al., 1968; George et al., 1991). Another study reported that 75% of endurance athletes and 20% of sprinters studied had a relative cardiac size above normal on chest x-ray (Ikaheimo et al., 1979). However, x-ray techniques cannot differentiate specific cardiac structures. It is therefore difficult to differentiate between pathological and physiological hypertrophy. X-ray has thus been replaced by techniques such as echocardiography (George et al., 1991).

Electrocardiography

Arrhythmias (such as sinus arrhythmia, sinus pauses, atrial or ventricular premature complexes or tachycardias) and conduction disturbances (such as atrioventricular and intraventricular conduction delays) are reported in highly trained athletes (Gott et al., 1968; Lichtman et al., 1973; Huston et al., 1985). Because these arrhythmias are usually abolished by exercise, they are believed to be due to enhanced vagal tone and suppression of the sinus or atrioventricular nodes (Morganroth and Maron, 1977). Morphologic changes in the P- and QRS-waves of the electrocardiogram (ECG), suggesting specific cardiac chamber enlargement, can also occur. Increased amplitude or duration of the P-wave are consistent with right or left atrial enlargement, respectively. Increased amplitude of the R- or S-waves in the standard or precordial leads, which frequently meet certain accepted ECG criteria for left or right ventricular hypertrophy, have been commonly described in athletes (17%-75% prevalence in the studies reviewed) (Morganroth and Maron, 1977; Huston et al., 1985; Cox.
et al., 1986). The duration of the QRS-complex tends towards the upper limit of normal (Lichtman et al., 1973). Most common ECG abnormalities observed at rest in endurance athletes are representations of the physiological adaptation to conditioning and should not be regarded automatically as a marker of pathologic heart disease (George et al., 1991).

**Echocardiography**
The introduction of echocardiography led to a big step forward in the research about “athletic heart syndrome”, making it possible to more accurately define the structural and functional characteristics of the heart in trained athletes. Echocardiographic studies of athletes have been reported since the mid-1970s, together with the description of sport-specific cardiac adaptations (Morganroth et al., 1975). Morganroth et al. (1975) were the first to compare LV dimensions in swimmers, runners, wrestlers and normal individuals. This study showed that the patterns of LV hypertrophy are different in athletes participating in sports requiring primarily isotonic (endurance) or isometric (resistance) efforts. The increase in calculated LV mass observed in athletes participating in endurance training (swimmers and runners) is associated with an increase in LV end-diastolic volume, but the ratio LV wall thickness/LV internal diameter remains normal. This adaptation may be due to an increase in cardiac output and a sustained hemodynamic load for many hours in endurance activities, which may be similar to the volume load imposed on a diseased heart (for example in aortic or mitral regurgitation), thus analogous to eccentric hypertrophy. In contrast, the increased LV mass observed in those athletes participating in resistance training (wrestlers) is associated with an increase in LV wall thickness, whereas LV end-diastolic volume remains normal. This may be due to an increase in systemic arterial pressure during the stress of strenuous Valsalva manoeuvres, which induces an increase in afterload upon the ventricle, similar to that induced by systemic hypertension or aortic stenosis, thus analogous to concentric hypertrophy (Morganroth et al., 1975; Morganroth and Maron, 1977) (Fig. 2). The results of these studies led to the so-called “Morganroth hypothesis” of cardiac response to training.
Figure 2: Hypothetical relationship between cardiac dimensions and type of physical conditioning: the so-called “Morganroth hypothesis”.

(Adapted from Morganroth and Maron, 1977; George et al., 1991)
A longitudinal study compared echocardiograms of the LV of 11 relatively inactive individuals before and after an intense endurance training program, providing an optimum training stimulus (Cox et al., 1986). They found an increased interventricular septal thickness during both systole and diastole, and an increased LV internal diameter in diastole, which fits eccentric hypertrophy expected in endurance training (Cox et al., 1986).

In 1991, a review article by George et al. (1991) compared the results of different studies, and concluded that male endurance athletes did display a modest eccentric cardiac enlargement, but the profile of a concentric enlargement in resistance athletes was lost when body size normalization was performed. The original sport-specific hypothesis of cardiac response to training may thus only be true for endurance trained athletes.

Later on, Spirito et al. (1994) studied 947 elite athletes engaged in 27 different sports, and assessed the relation of LV diastolic cavity dimension and wall thickness to type of sports, gender, age and body surface area (BSA). The calculated impact of the 27 sports on cardiac dimensions ranged from 0.0 to 5.91 mm on LV diastolic cavity dimension, and from 0.0 to 2.13 mm on LV wall thickness. Spirito et al. (1994) showed that most sports associated with a larger LV diastolic cavity dimension were also associated with a parallel increase in LV wall thickness. Especially endurance cycling, swimming, canoeing and rowing, all endurance type sports, had the largest impact on LV cavity dimension (5.91 mm, 4.90 mm, 4.23 mm and 3.87 mm, respectively) and LV wall thickness (2.02 mm, 1.71 mm, 1.70 mm and 2.13 mm, respectively) and were at the upper end of the spectrum of morphologic adaptations of the heart to athletic training (Fig. 3). Thirty-eight percent of athletes had a LV diastolic cavity dimension above normal (≥ 54 mm) (Spirito et al., 1994).
Figure 3: Calculated impact of different sports disciplines on LV diastolic cavity dimension (LVDd) and LV wall thickness (LVW) after adjustment for age, gender and body surface area.

(Adapted from Spirito et al., 1994; Naylor et al., 2008)

Most prominent exceptions to this pattern included weightlifting and wrestling, both resistance type sports, with an impact on LV cavity dimension of 1.32 mm and 1.25 mm, respectively, and an impact on LV wall thickness of 1.23 mm and 1.21 mm, respectively. Weightlifting and wrestling thus had a relatively higher impact on LV wall thickness compared to a relatively low impact on cavity dimension (Fig. 3). This suggests that resistance sports are associated with a disproportionate increase in wall thickness relative to cavity dimension. However, absolute values for wall thickness did not exceed the normal limit of 12 mm in human (Spirito et al., 1994).
Perrault and Turcotte (1994) critically re-evaluated several human and animal studies in the light of potential confounders. In contrast to the aforementioned adaptations of the heart to athletic training, they concluded that competitive athletes did not exhibit LV morphology outside the normal clinical range. Moreover, they stated that the reported increases in indices of LV dimensions, following endurance training, may be related to training-induced changes in resting heart rate or total blood volume in humans, rather than true eccentric hypertrophy.

Another large study evaluated LV cavity dimension in 1309 elite Italian athletes participating in 38 different sports (Pelliccia et al., 1999). In agreement with Spirito et al. (1994), LV cavity dimensions exceeded normal limits (≥ 54 mm) in 45% of athletes, 14% of the overall group even showed substantially enlarged dimensions (≥ 60 mm) (Pelliccia et al., 1999). Ventricular septal thickness exceeded the upper limits of normal (≥ 12 mm) only in 1.1% of athletes, whereas LV wall thickness was higher than normal only in 0.3% of athletes (Pelliccia et al., 1999).

More recent reports however all agree that, to some extent, cardiac adaptations to training occur, though adaptations to endurance type sports are generally more pronounced than the adaptations to resistance type sports (Spirito et al., 1994; Pluim et al., 2000; D’Andrea et al., 2002; Haykowsky et al., 2002; Fagard, 2003; Sharma, 2003).

A recent review of the “Morganroth hypothesis” re-evaluated several cross-sectional as well as longitudinal studies dedicated to the “athletic heart”, together with some methodological considerations. They concluded that the majority, but not all, of cross-sectional as well as longitudinal studies provide partial support to the eccentric form of cardiac hypertrophy in endurance trained athletes. The evidence in resistance trained athletes is inconsistent, and limited by poor scaling and measurement methodologies. Longitudinal studies using advanced imaging modalities such as MRI to determine the impact of exercise training on cardiac structural adaptations are needed to further evaluate the “Morganroth hypothesis” (Naylor et al., 2008).
Alternative explanations of cardiac adaptations

Training is probably not solely responsible for the differences found between athletes and non-athletes. Some other factors have to be taken into account.

Genetics

In the early years of echocardiography, it remained to be established whether the differences in cardiac dimensions observed in trained athletes were solely a result of intense prolonged physical conditioning, or were influenced substantially by genetic factors that predispose such individuals to become athletes initially (Morganroth et al., 1975; Morganroth and Maron, 1977).

Hereditary factors play a significant role in determining cardiac dimensions, either through a direct genetic role or through a genetic influence on cardiac trainability (George et al., 1991). Spirito et al. (1994) also stated that the association between type of sport and cardiac morphology may not entirely reflect a causal effect of athletic training on cardiac dimensions. The possibility that some athletes excelled in a certain sport because they had been pre-selected by some special genetic endowment that could have included the dimensions of the heart, cannot be excluded. Pellicia et al. (1999) mention the possibility that morphologic remodeling may be partially determined by a genetic predisposition that allows the LV cavity of certain athletes to become extremely enlarged.

In contrast, after a study of LV structure and exercise capacity in 7-year-old twins, Fagard’s research group concluded that the inheritance of cardiac structure at rest is limited, and that the structure of the heart of endurance athletes as observed at rest is probably not inherited but the result of other factors, particularly physical training (Bielen et al., 1990). From several other studies, the same research group also concluded that an inherited larger heart could contribute to the superior exercise capacity of endurance athletes (Fagard et al., 1987), but that the LV internal diameter was almost exclusively determined by environmental factors, which could include physical activity (Bielen et al., 1991). Therefore, they suggest that genes are not of major importance for the explanation of athlete’s heart, particularly not for the eccentric component (Fagard, 1996).
**Gender, age, body surface area**

In the earlier years, studies almost solely described the athletic heart features of male athletes. Later on, a few reports focused on the impact of gender on cardiac dimensions. Male gender was associated with larger cardiac dimensions than female gender, after adjustment for age, BSA and type of sport (Spirito et al., 1994). According to Spirito et al. (1994), Fagard (2003) also mentioned that female athletes have smaller LV cavity dimension and wall thickness than males of the same age and body size, who train in the same sport. These gender-specific differences may be partly related to several factors: 1/ lower body size and lean body mass of women, 2/ different gender-related hemodynamic responses to exercise, and 3/ higher circulating anabolic hormones in males, which promote increased skeletal muscle mass and permit training at greater intensities (Pelliccia and Maron, 1997; Sharma, 2003).

Older age was associated with larger LV diastolic cavity dimensions and wall thickness, probably due to the longer period of training of older athletes (Spirito et al., 1994; Sharma, 2003). Also, larger BSA was associated with larger LV diastolic cavity dimension and wall thickness (Spirito et al., 1994).

**Training regimens**

Most sports and training regimens are not exclusively isotonic or isometric, so the load on the heart is not purely of the volume or pressure type (respectively) (Fagard, 1996). In athletes engaged in predominantly isotonic sports, the LV hypertrophy is “predominantly” eccentric, and in athletes who perform predominantly isometric sports, the hypertrophy is “predominantly” concentric (Fagard, 1996, 1997).

Adaptation of the heart to endurance training with an increase in both diameter and wall thickness is considered to be a morphologic adaptation to changes in heart rate, cardiac output and blood pressure during intense exercise. Cardiac output of trained endurance athletes may increase six to eight times during maximal exercise. The heart adapts to this volume load with an increase in internal diameter. Blood pressure also increases during endurance exercise, although to a lesser extent than during strength training. Thus, pure volume load during endurance training does not exist (Pluim et al., 2000). Adaptation of the heart to strength training with a slight increase in LV internal diameter and a large increase in LV wall thickness can be explained on the basis of blood pressure response and cardiac output during static exercise. During heavy-resistance exercise, arterial blood pressure shows a large increase. However, heart rate and cardiac output also show a mild increase during strength training. Thus, pure pressure load during strength training does not exist (Pluim et al., 2000).
Rowing and cycling represent typical strength and endurance sports involving combined isotonic and isometric exercise of large groups of muscles. Top-level athletes can perform with a near-maximal heart rate for long periods of time, together with increased systolic and mean arterial blood pressures. The combination of both extreme volume load and extreme pressure load may explain why the largest increases in LV internal dimension and LV wall thickness are found in elite, highly trained athletes engaged in rowing, canoeing and cycling (Pelliccia and Maron, 1997; Pluim et al., 2000).

**Differentiation of physiologic versus pathologic hypertrophy and/or dilatation**

Differential diagnosis between structural heart disease such as hypertrophic cardiomyopathy (HCM) and physiologic LV hypertrophy associated with systematic training has become a dilemma with important clinical implications (Maron et al., 1995). For some athletes, LV wall thickness falls into a grey zone of overlap between mild HCM and athlete’s heart, with a wall thickness up to 16 mm (Maron et al., 1995). One study reported LV wall thickness exceeding the upper limit of 11 mm in 5% of 720 athletes, with 4% of the total group having a LV wall thickness ≥ 12 mm (Sharma et al., 2002). In these cases, careful analysis of other parameters should be performed, such as assessment of LV cavity dimension (often ≥ 55 mm in athlete’s heart), normal LV filling patterns, gender (female athletes rarely show absolute LV wall thickness ≥ 11 mm), and type of sport (rowing and cycling are most often associated with LV wall thickness ≥ 13 mm) (Lewis et al., 1992; Maron et al., 1995; Sharma et al., 2002). Based on these parameters, Maron et al. (1995) proposed an algorithm for differential diagnosis between HCM and athlete’s heart (Fig. 4).
Figure 4: Criteria used to distinguish hypertrophic cardiomyopathy (HCM) from athlete’s heart when the left ventricular (LV) wall thickness is within the shaded “grey zone” of overlap, consistent with both diagnoses.
(Adapted from Maron et al., 1995)

| + | Unusual patterns of LVH | - |
| + | LV cavity < 45 mm | - |
| - | LV cavity > 55 mm | + |
| + | Marked LA enlargement | - |
| + | Bizarre ECG patterns | - |
| + | Abnormal LV filling | - |
| + | Female sex | - |
| - | Decreased thickness with deconditioning | + |
| + | Family history of HCM | - |

LA: left atrial; LVH: LV hypertrophy.
Less frequently, athletes show markedly increased LV cavity dimensions (≥ 58 mm), falling into the same range of absolute values as those for patients with primary dilated cardiomyopathy (Pelliccia et al., 1999). Athletes with LV dimensions in this grey zone of overlap raise questions about the differential diagnosis between athlete’s heart and structural heart disease. However, none of these athletes had evidence of systolic dysfunction, segmental wall-motion abnormalities, or abnormal diastolic filling pattern (Maron et al., 1995; Pelliccia et al., 1999).

**Athletic heart syndrome in veterinary medicine**

The evidence of “athletic heart syndrome” in veterinary medicine is more sparse compared with human medicine. Dogs and horses are frequently reported as premium athletes, being used for different sports for hundreds of years.

One of the earliest observations on the heart weight/body weight ratio in dogs has been described in the beginning of the 20th century. Joseph (1908) reported heart weight/body weight ratio at necropsy (g/100g) to be 0.74 in male dogs and 0.76 in female dogs. At that time, he already commented on the pronounced effect of bodily exercise upon the size of the heart (Joseph, 1908). Later on, several ratios have been reported from different studies, using mongrel dogs, pedigree dogs and Greyhounds, comparing heart weight/body weight at necropsy. These ratios varied from 0.64 in mongrel dogs, over 0.90 in pedigree dogs to 1.35 in Greyhounds (Schneider et al., 1964). Three studies on a larger group of Greyhounds reported heart weight/body weight ratios varying from 1.16 to 1.24 in males, and from 1.21 to 1.27 in females (Schneider et al., 1964; Steel et al., 1976; Schoning et al., 1995).

Gunn (1989) reported heart weight/body weight ratios for trained Greyhounds compared with detrained Greyhounds and a group of other dogs, and for Thoroughbreds compared with a group of other horses. The ratio for trained Greyhounds was 1.48, being significantly larger than the ratio of 1.42 for detrained Greyhounds and of 0.96 for other dogs. The ratio for Thoroughbreds was 0.86, being larger than the ratio of 0.76 for other horses (Gunn, 1989). These findings are in contrast to the average ratio of 0.59 for the mammalian heart (Stahl, 1965).
Different diagnostic approaches

**Autopsy**
A cross-sectional study reported a significant difference in LV weight/body weight ratio in favour of treadmill trained mongrel dogs compared with sedentary control dogs (Riedhammer et al., 1976). Another study in mongrel dogs showed that treadmill running resulted in an increase in LV weight and LV posterior wall thickness measured at the base of the papillary muscle. Right ventricular weight was unchanged (Barnard et al., 1980).

**Auscultation**
Constable et al. (1994) reported that cardiac murmurs were detected with increasing frequency (up to 40%) as endurance training level in sled dogs increased. Most of these murmurs were grade 1 to 2/6 early- to midsystolic crescendo-decrescendo murmurs, with point of maximal intensity at the left heart base. A few dogs also had a soft murmur at right heart base or the left heart apex (Constable et al., 1994). Two other reports in Alaskan sled dogs also mentioned increasing prevalence of grade 1 to 3/6 left-sided systolic murmurs with endurance training, up to 45% (Stepien et al., 1998) or even 67.7% (Hinchcliff et al., 1997). In Thoroughbred horses, Young and Wood (2000) reported increasing prevalence of both tricuspid and mitral regurgitation when young horses are subjected to athletic training (from 12.7% to 25.5% for tricuspid regurgitation, and from 7.3% to 21.8% for mitral regurgitation). An earlier study reported no significant effect of age on prevalence of murmurs, supporting the hypothesis that training, not age, may be important in the development of valvular regurgitation in athletic horses (Patteson and Cripps, 1993). This hypothesis was confirmed by a large study by Kriz et al. (2000), who also reported an increase in tricuspid regurgitation murmurs from 16.1% to 28.4% during the period in which relatively untrained horses progressed to high intensity training.

**Chest radiography**
The influence of a 12 week training period of treadmill running on the heart of dogs was evaluated in a longitudinal study through the bead and clip technique (placed in the LV myocardium during open heart surgery). An increase in mean LV end-diastolic wall thickness was observed, without a change in LV end-diastolic volume, thus creating an increase in estimated LV mass (9%) (Wyatt and Mitchell, 1974). Through ventriculography, a significant increase in LV end-diastolic volume was reported after 10 weeks of treadmill training in a group of Beagles, which could not be ascribed to exercise-induced bradycardia, as heart rates
were almost identical before and after training (Ritzer et al., 1980). However, no differences were noted in LV weight/body weight ratio between the control group, the sedentary group and the exercised group of Beagles (Ritzer et al., 1980).

**Electrocardiography**
An early longitudinal study on the influence of physical training on the heart of dogs reported a marked decrease in resting and exercise heart rates already during the first 4 weeks of training (treadmill running) (Wyatt and Mitchell, 1974). In agreement, Constable et al. (1994) reported significantly lower heart rate and longer QT-interval in highly trained sled dogs compared with untrained sled dogs, both at rest. No premature (atrial nor ventricular) complexes were observed in any dog. They also reported that endurance training in sled dogs was associated with a significant increase in the amplitude of the Q- and R-waves in lead V_{10} and the R-wave in lead aVF, together with a significant right axis shift in the mean electrical axis in the frontal plane in the highly trained sled dogs (Constable et al., 1994). Another study on Alaskan sled dogs reported a low prevalence of atrial premature complexes (0.9%) or ventricular premature complexes (1.3%), and paroxysmal ventricular tachycardia in one dog out of 319 dogs (0.3%) while standing at rest (Hinchcliff et al., 1997).

**Echocardiography**
A group of 77 Alaskan sled dogs were studied before and after five months of endurance training. Training resulted in a significant increase in heart size evident as increases in LV internal diameter in diastole (4%), interventricular septal thickness in diastole (13%) and systole (15%), LV wall thickness in systole (9%) and left atrial diameter (5%) (Stepien et al., 1998). There was a disproportionately greater increase in LV wall thickness than in LV internal diameter (both in diastole). Heart size estimated by calculated LV mass increased significantly with training (24%) (Stepien et al., 1998). No changes were found in echocardiographically derived measures of LV function (fractional shortening, LV ejection fraction, stroke volume, cardiac output and cardiac index) (Stepien et al., 1998). The increase in estimated LV mass in Alaskan sled dogs is clearly larger than the 9% reported by Wyatt and Mitchell (1974) after treadmill running in mongrel dogs (Stepien et al., 1998). In Greyhounds, when indexed to BSA, training dogs showed a significantly thicker interventricular septum (systole) and LV free wall (systole) compared with non-training dogs (Lonsdale et al., 1998).
A study on Thoroughbreds, comparing horses in different types of races (from flat-racers to steeplechasers), reported the largest mean heart size parameters adjusted to weight in the long distance steeplechasers. This suggests that conditioned racehorses develop a cardiac morphology that is appropriate to the endurance component of their event, this component being smaller in the short distance flat-races compared with the long distance steeplechase (Young et al., 2005). A longitudinal study on Standardbred trotters reported a significantly larger LV internal diameter in diastole and LV mass in regularly racing horses at the time of the fourth examination (1.5 year follow-up) compared to non-racing horses (Buhl et al., 2005). No significant differences were observed for fractional shortening between racing and non-racing horses (Buhl et al., 2005). Overall, significant cardiac enlargement takes place in young Standardbred trotters between 2 and 3.5 years of age. Mean LV wall thickness, LV internal diameter in diastole and LV mass all increased during the study period, while in contrast, fractional shortening decreased significantly, but was independent of body weight and gender (Buhl et al., 2005).

Alternative explanations of cardiac adaptations

Genetics
There seems little doubt that selective breeding, training and racing of both racehorses and Greyhounds has led to unconscious selection for larger heart size (Steel et al., 1976). In adult Greyhounds, the larger heart compared to mongrel dogs could be due to greater exercise in the Greyhound group, to an intrinsically (genetically determined) greater heart size in Greyhounds, or a combination of these two factors (Cox et al., 1976). To answer this question, 15 Greyhound puppies and 17 black and tan Coonhound puppies were condemned at birth, and the heart weight/body weight ratios were compared. The Greyhound puppies’ ratios were significantly higher, which suggests that greater heart size in these Greyhounds is a genetically determined property of the breed (Cox et al., 1976). From a study on trained and non-trained Greyhounds and control dogs of the same body weight range, Carew and Covell (1978) concluded that although there may be a significant degree of hypertrophy in Greyhounds due to genetic factors alone, trained Greyhounds had even more extensive LV hypertrophy. In contrast, Rippe et al. (1982) found no significant differences in echocardiographic LV wall thickness or LV mass between racing and non-racing Greyhounds, but they did find a significant difference for both variables comparing Greyhounds with comparably sized mongrel dogs. Also, the heart weight/body weight ratios were nearly identical in racing and non-racing Greyhounds but significantly higher in both
groups compared to the mongrel dogs. Taking the smaller number of non-racing Greyhounds into account, this could however suggest that LV hypertrophy in the racing Greyhound reflects a genetic trait rather than a response to training (Rippe et al., 1982). The similar heart weight/body weight ratios between several groups of Greyhounds (trained versus detrained; trained versus non-trained and puppy) was confirmed in two other studies by the same study group (Pape et al., 1984; Pape et al., 1986).

**Gender, age, body surface area**

In a study on heart weight/body weight ratio in Greyhounds, a significant difference was reported between females and males, in favour of the females (12.07 ± 1.2 g/kg versus 11.58 ± 1.1 g/kg, respectively) (Steel et al., 1976). Similar findings were reported in two other studies on Greyhounds, however, the differences between females and males were not statistically significant (Pape et al., 1984; Schoning et al., 1995). It is known in Greyhound racing circles that females are often better stayers. This could partly be explained by the lower body weight of females, combined with almost 0.5 g/kg “more heart” than males (Steel et al., 1976).

An echocardiographic study on Greyhounds also reported a larger LV diameter (diastole) and a thicker LV free wall (diastole and systole) in females compared with males, after indexation of these parameters for BSA (Lonsdale et al., 1998). After indexation for body weight, even more parameters were significantly higher in females: interventricular septum (systole), LV internal diameter (diastole and systole) and LV free wall (diastole and systole) (Lonsdale et al., 1998). In contrast, one study reports a slightly lower heart weight/body weight ratio in females compared with males (Pape et al., 1986).

In a group of Thoroughbreds, male horses had significantly larger weight-adjusted heart size parameters for LV mass and LV internal diameter in diastole compared with females. However, there was little effect of gender on the comparison of weight-corrected parameters between racing types, indicating that gender did not explain the significant differences between the different racing types (Young et al., 2005). In contrast, Buhl et al. reported gender to be significantly correlated with LV internal diameter in diastole and LV mass in Standardbred trotters, with higher values in males than in females, but no significant differences between stallions and geldings (except for the interventricular septum thickness in diastole, being larger in stallions) (Buhl et al., 2005).
Schoning et al. (1995) studied the influence of age on the heart weight, body weight, and heart weight/body weight ratio in Greyhounds. Heart weight as well as body weight were significantly lower in young Greyhounds compared with adults, however, heart weight/body weight ratios were not significantly different in both age groups. No significant effect of age was found on body weight or cardiac size in Thoroughbreds. However, this could be due to the relatively short competitive career of commercial Thoroughbred racehorses, or be related to the absence of acquired cardiac, vascular or hypertensive disease in this group of mammalian athletes (Young, 2003; Young et al., 2005).

**Training regimens**

The disproportionate increase in LV wall thickness compared to the increase in LV internal diameter in Alaskan sled dogs suggests that LV wall thickening did not occur as an adaptation to LV dilatation alone (Stepien et al., 1998). Sled dogs are exposed to an isometric load (pulling the sled and musher) as well as an isotonic load (long distance running), and therefore show echocardiographic changes more typical of a “combined-load” human athlete rather than a runner (Stepien et al., 1998).

Also, the Alaskan sled dogs are submitted to a much larger work load (greater distances over a much longer time period) than dogs running on a treadmill, which could have contributed to a more marked increase in LV mass in these sled dogs (Stepien et al., 1998).

In Standardbred trotters, training intensity had a significant effect on LV internal diameter, with higher values in horses classified as having received high-grade training (Buhl et al., 2005).
Conclusions

A large number of studies have been conducted about the “athletic heart syndrome” in humans. Although the original “Morganroth hypothesis”, which states that different exercise training modalities (endurance versus resistance) produce divergent patterns of cardiac hypertrophy (eccentric versus concentric, respectively), may not completely be true, cardiac adaptations to endurance training have been supported in a multitude of studies. In some sports and athletes, this almost extreme eccentric hypertrophy, with larger LV diastolic cavity dimensions and larger LV wall thickness, may mimic structural heart disease. It is important to be aware of these physiological adaptations to training, in order to avoid overdiagnosis of cardiac disease in an athlete, which may lead to unnecessary withdrawal from training and competition.

Based on reports from Greyhounds, sled dogs and racehorses, it is suggested that the “athletic heart syndrome” also exists in these dogs and horses, influencing diverse cardiological parameters.

Therefore, the aim of our study was to determine the cardiological parameters in Whippets, and to evaluate whether these parameters would fit the description of “athletic heart syndrome”.
References


the left ventricle in the trained racing greyhound. *Basic Research in Cardiology* 77, 619-644.


SECTION II

SCIENTIFIC AIMS
SCIENTIFIC AIMS

In dogs, a large variation of height, weight and conformation exists. This implies a variation of cardiological parameters, particularly the weight-correlated ones. For sight hounds, years of selection towards speed and concurrent athletic training might also influence these cardiological parameters, resembling the athletic heart syndrome described in humans.

Therefore, the aim of our study was to determine the Whippet-specific cardiological parameters, and to compare these with reference values reported for the overall dog population:

1. Describe the presence and type of murmurs
2. Determine the vertebral heart size
3. Determine the electrocardiographic characteristics
4. Establish echocardiographic reference values

Furthermore, comparisons were made to determine the influence of pedigree lines and athletic training on these findings.
Chapter 1

AUSCULTATORY FINDINGS IN WHIPPETS
Chapter 1  Auscultatory findings in Whippets

AUSCULTATORY FINDINGS IN WHIPPETS:
Innocent murmurs and their relation to haematologic and echocardiographic findings

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Summary

Murmur prevalence was determined by auscultation of 105 apparently healthy Whippets without cardiac symptoms, and the influence of gender, pedigree line and training on these murmurs was evaluated. Several erythrocyte parameters and echocardiographic variables were compared between dogs with or without a murmur at the level of the aortic valve. Furthermore, a part of the dogs was auscultated by three independent observers to determine the agreement for murmur presence, point of maximal intensity and murmur grade.

Forty-four dogs (41.9%) had no murmur. A soft systolic murmur (grade 1 to 3/6) was present with point of maximal intensity at the level of the aortic valve in fifty dogs (47.6%), of the pulmonic valve in eight dogs (7.6%), and of the mitral valve in three dogs (2.9%). No significant differences were found comparing heart rate, rhythm, murmur presence, point of maximal intensity and murmur grade between male and female dogs, race and show pedigree dogs, or dogs in training and not in training. Dogs with a murmur at the level of the aortic valve had a significantly higher aortic (VAo) and pulmonic (VPulm) blood flow velocity than dogs without a murmur, VAo being 1.47 ± 0.24 m/s and VPulm being 1.19 ± 0.21 m/s in dogs with a murmur, compared to VAo being 1.29 ± 0.23 m/s and VPulm being 1.08 ± 0.24 m/s in dogs without a murmur. Cardiac output was also significantly higher in dogs with a murmur at the level of the aortic valve (5.06 ± 1.26 l/min) compared to dogs without a murmur (4.39 ± 1.34 l/min). A moderate to good agreement for murmur presence was found between the three observers.

Whippets have a high prevalence of soft systolic murmurs in the absence of any structural abnormalities, which fit the description of “innocent” murmurs.
**Introduction**

Auscultation has been one of the most important means to assess heart disease, but the widespread use of Doppler echocardiography in the last two decades has considerably diminished its use, causing parallel decreases in skill and confidence in its interpretation. Auscultation, however, remains the primary diagnostic tool for the interpretation of heart murmurs, and it is essential for making decisions about referring patients for echocardiography (Attenhofer Jost et al., 2000; Shub, 2003). Congenital or acquired heart disease can contribute to the development of systolic murmurs, but also physiologic factors (Sisson and Ettinger, 1999). Physiologic, functional or innocent murmurs are often caused by increased cardiac output or decreased blood viscosity, usually occur early in the systole, and are low in intensity (Sisson and Ettinger, 1999; Kvart and Häggström, 2002; Shub, 2003). They are the loudest at the aortic or pulmonic valve regions and do not radiate extensively (Sisson and Ettinger, 1999; Kvart and Häggström, 2002). In human as well as in veterinary medicine, several articles report the occurrence of systolic murmurs due to athletic training. Systolic murmurs of low intensity are noted in 30 to 50% of highly trained human athletes, and are probably related to the “athletic heart syndrome” (Huston et al., 1985; George et al., 1991; O'Brien and Rogers, 1999). In veterinary medicine, sled dogs and racehorses were reported to have higher prevalence of systolic murmurs due to athletic training (Constable et al., 1994; Young and Wood, 2000; Kriz et al., 2000; Young, 2003; Fabrizio et al., 2006; Lord et al., 2007). Retired racing Greyhounds were also reported to have a higher prevalence of systolic murmurs without any structural abnormalities (Fabrizio et al., 2006; Lord et al., 2007).

The purpose of this study was first to determine the prevalence of murmurs in Whippets and to characterise them, secondly to determine possible correlations with other Whippet-specific findings, and finally to determine the agreement between three observers with different degree of experience.
Materials and methods

**Dogs**

Privately owned, apparently healthy Whippets without cardiac symptoms \((n = 125)\) were recruited through contacts with breeders and owners who brought their dogs voluntarily. All dogs underwent complete physical and cardiologic examinations (auscultation, electrocardiography and echocardiography). Clinicopathological assessment was also undertaken. Erythrocyte parameters included haematocrit (Hct), haemoglobin concentration (Hb), and red blood cell count (RBC). Echocardiographic parameters were obtained as described previously (Bavegems et al., 2007): interventricular septal thickness in diastole and systole (IVSd/s), left ventricular internal diameter in diastole and systole (LVDd/s), left ventricular wall thickness in diastole and systole (LVWd/s), fractional shortening (FS), aortic root diameter (Ao), left atrial diameter (LA), aortic (VAo) and pulmonic blood flow velocity (VPulm), cardiac output (CO) and stroke volume (SV). Dogs less than 10 months of age \((n = 11)\) or with cardiac abnormalities (moderate to severe mitral regurgitation or a grade \(\geq 4/6\) murmur) \((n = 3)\) (being one dog with a systolic murmur grade 5/6 at the level of the mitral valve, and two dogs with moderate to severe mitral regurgitation on colour Doppler echocardiography) or with incomplete data \((n = 6)\) were excluded.

The study included 105 Whippets (51 males and 54 females), aged between 10 and 169 months \((59.7 \pm 39.3\) months; mean \pm standard deviation), weighing between 9.3 and 17.2 kg \((13.2 \pm 2.1\) kg). Dogs were recruited from race pedigree lines \((n = 89)\), from show pedigree lines \((n = 10)\) or were crosses between race and show pedigree lines \((n = 6)\). From the race pedigree dogs, six dogs were not yet in training, 62 dogs were in active training for sight hound races with a mean training period of 30.9 \pm 22.8 months (range 2 to 78 months), and 21 were retired and ceased training for 31.9 \pm 21.1 months (range 7 to 80 months).

**Auscultation**

All Whippets were auscultated quietly standing on an examination table by the first author (observer 1; VB), using a Littmann Classic II paediatric stethoscope (3M Health Care, USA). Heart rate (HR), rhythm, presence of cardiac murmurs and their timing in relationship to the cardiac cycle, point of maximal intensity and grade were recorded. Respiratory sinus arrhythmia is defined as an irregular sinus rhythm originating in the sino-atrial node, represented by alternating periods of slower and more rapid heart rates, related to respiration. Inspiration causes reflex inhibition of vagal tone, resulting in an increasing heart rate;
expiration results in a slowing heart rate. A grade 1/6 murmur is the faintest murmur that can be detected and is heard only with particular effort. A grade 2/6 murmur is a faint murmur clearly heard after a few seconds of auscultation by an experienced examiner. A grade 3/6 murmur is moderately loud and easily heard. A grade 4/6 murmur is a loud murmur that does not produce a palpable thrill. A grade 5/6 murmur is a very loud murmur that produces a thrill but is inaudible when the stethoscope is removed from the chest wall. A grade 6/6 murmur is a very loud murmur that produces a thrill and is still audible after the stethoscope is removed from the chest (Patteson and Cripps, 1993; Sisson and Ettinger, 1999). Depending on their presence the day the dogs came in, observer 2 (ADR) and observer 3 (DB) auscultated a smaller number of dogs (n = 94 and n = 80, respectively). Observer 2 used a Rappaport-Sprague acoustic stethoscope (Hewlett Packard Model 280), while observer 3 used the same Littmann Classic II paediatric stethoscope as observer 1. Observer 1 had four years of experience in small animal general practice followed by two years working in small animal cardiology at the time of this study. Observer 2 had 30 years of experience in small animal cardiology. Observer 3 had six years experience part-time in small animal general practice and part-time in small animal cardiology. The observers were blinded to the results of the other observers. However, observer 1 was not blinded to pedigree line or training status of the dogs.

**Statistical analysis**

Analysis of variance was used to compare gender, pedigree lines, and the effect of training within the race pedigree lines with respect to HR. The Fisher’s exact test was used to compare gender, pedigree lines and the effect of training within the race pedigree lines with respect to rhythm, murmur presence and point of maximal intensity. The Wilcoxon rank sum test was used to compare gender, pedigree lines and the effect of training within the race pedigree lines with respect to the murmur grade. Kappa statistics were determined to express agreement between the three observers with respect to murmur presence, point of maximal intensity and murmur grade. Finally, analysis of variance was used to compare dogs with or without murmurs at the level of the aortic valve with respect to erythrocyte and echocardiographic variables.
Results

Auscultatory findings and interobserver agreements

Eighty-three dogs (79.0% of all 105 Whippets) had a respiratory sinus arrhythmia with a mean HR of 89 ± 17 bpm, whereas 22 dogs (21.0%) had a regular rhythm with a mean HR of 116 ± 17 bpm. No cardiac arrhythmias were noticed during auscultation. Forty-four dogs (41.9%) had no murmur. Fifty dogs (47.6%) had a systolic murmur with point of maximal intensity at the level of the aortic valve, which was a grade 1/6 murmur in 29 dogs (27.6%), a grade 2/6 murmur in 17 dogs (16.2%) and a grade 3/6 murmur in four dogs (3.8%). Eight dogs (7.6%) had a systolic murmur with point of maximal intensity at the level of the pulmonic valve, which was a grade 1/6 murmur in four dogs (3.8%) and a grade 2/6 murmur in the other four dogs (3.8%). Three dogs (2.9%) had a systolic murmur with point of maximal intensity at the level of the mitral valve, which was a grade 1/6 murmur in one dog (0.9%) and a grade 2/6 murmur in the two other dogs (2.0%). No diastolic nor continuous murmurs were found.

Kappa values between the three observers are presented in Table 1. Kappa for murmur presence varied from 0.54 to 0.61. Kappa for point of maximal intensity varied from 0.47 to 0.55. And kappa for murmur grade varied from 0.45 to 0.54.

Table 1: Kappa statistics between the three observers with respect to murmur presence, point of maximal intensity and murmur grade

<table>
<thead>
<tr>
<th>Kappa</th>
<th>Murmur presence</th>
<th>PMI</th>
<th>Murmur grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obs 1 – Obs 2</td>
<td>0.61</td>
<td>0.54</td>
<td>0.45</td>
</tr>
<tr>
<td>Obs 1 – Obs 3</td>
<td>0.58</td>
<td>0.55</td>
<td>0.54</td>
</tr>
<tr>
<td>Obs 2 – Obs 3</td>
<td>0.54</td>
<td>0.47</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Obs 1: observer 1 (VB); Obs 2: observer 2 (ADR); Obs 3: observer 3 (DB); PMI: point of maximal intensity
Comparison between male and female dogs

Fifty-one males with mean age and weight of 53.6 ± 37.7 months and 14.5 ± 1.8 kg were compared with 54 females with mean age and weight of 65.4 ± 40.4 months and 11.9 ± 1.5 kg. Male dogs had a mean HR of 95.2 ± 22.1 bpm, of which 39 dogs (76.5%) had a respiratory sinus arrhythmia with a mean HR of 87.5 ± 16.9 bpm and 12 dogs (23.5%) had a regular rhythm with a mean HR of 120.3 ± 18.1 bpm. Female dogs had a mean HR of 93.9 ± 18.9 bpm, of which 44 dogs (81.5%) had a respiratory sinus arrhythmia with a mean HR of 89.8 ± 17.2 bpm and 10 dogs (18.5%) had a regular rhythm with a mean HR of 111.6 ± 16.2 bpm.

Murmur presence, point of maximal intensity and grades for male and female dogs are presented in Fig. 1. No significant differences were found between males and females with respect to HR (P = 0.73), rhythm (P = 0.63), murmur presence (P = 0.84), point of maximal intensity (P = 0.87) and murmur grade (P = 0.71).

Figure 1: Prevalence and frequencies of different systolic murmurs in male (n = 51) (a) and female (n = 54) (b) Whippets

AV: aortic valve; PV: pulmonic valve; MV: mitral valve; I: grade 1/6 murmur (yellow); II: grade 2/6 murmur (green); III: grade 3/6 murmur (blue).
Comparison between race pedigree dogs (in training and not in training) and show pedigree dogs

Eighty-nine dogs (43 males and 46 females) came out of race pedigree lines, and 10 dogs (4 males and 6 females) came out of show pedigree lines. Six dogs came out of crosses between these two pedigree lines and were excluded from this analysis. Six race pedigree dogs (4 males and 2 females) were not yet in training, weighing 12.6 ± 2.5 kg and aged 14.8 ± 6.8 months. Sixty-two race pedigree dogs (32 males and 30 females) were in active training, weighing 13.5 ± 2.0 kg and aged 46.6 ± 23.5 months. Twenty-one race pedigree dogs (7 males and 14 females) were retired and ceased training, weighing 12.3 ± 2.1 kg and aged 112.0 ± 31.3 months. The six dogs not yet in training were combined with the 21 retired dogs which ceased training to form the group of race pedigree dogs not in training. The mean age and weight of the show pedigree dogs was 58.8 ± 44.3 months and 13.5 ± 2.3 kg. Race pedigree dogs in training had a mean HR of 95.7 ± 20.4 bpm, of which 47 dogs (75.8%) had a respiratory sinus arrhythmia with a mean HR of 88.9 ± 15.6 bpm and 15 dogs (24.2%) had a regular rhythm with a mean HR of 117.1 ± 19.3 bpm. Race pedigree dogs not in training had a mean HR of 90.8 ± 15.6 bpm, of which 22 dogs (81.5%) had a respiratory sinus arrhythmia with a mean HR of 86.0 ± 12.5 bpm and five dogs (18.5%) had a regular rhythm with a mean HR of 112.0 ± 9.4 bpm. Show pedigree dogs had a mean HR of 101.6 ± 32.2 bpm, of which eight dogs (80.0%) had a respiratory sinus arrhythmia with a mean HR of 96.5 ± 33.0 bpm and two dogs (20.0%) had a regular rhythm with a mean HR of 122.0 ± 25.5 bpm.

Murmur presence, point of maximal intensity and grades for dogs in training and not in training within the race pedigree lines, and show pedigree dogs, are presented in Fig. 2. No significant differences were found between race and show pedigree dogs with regard to HR ($P = 0.29$), rhythm ($P = 1.00$), murmur presence ($P = 0.51$), point of maximal intensity ($P = 0.59$) and murmur grade ($P = 0.39$). Also, no significant differences were found between dogs in training and not in training within the race pedigree lines with regard to HR ($P = 0.27$), rhythm ($P = 0.78$), murmur presence ($P = 0.65$), point of maximal intensity ($P = 0.17$) and murmur grade ($P = 0.60$).
Figure 2: Prevalence and frequencies of different systolic murmurs in Whippets in training \((n = 62)\) (a), Whippets not in training \((n = 27)\) (both within the race pedigree lines) (b) and show pedigree Whippets \((n = 10)\) (c).

AV: aortic valve; PV: pulmonic valve; MV: mitral valve; I: grade 1/6 murmur (yellow); II: grade 2/6 murmur (green); III: grade 3/6 murmur (blue).
Comparison of erythrocyte and echocardiographic variables between dogs with or without a murmur at the level of the aortic valve

Eleven dogs had a murmur with point of maximal intensity at the level of the pulmonic (8 dogs) or mitral (3 dogs) valve. These dogs were excluded for this comparison. Forty-four dogs (46.8% of 94 Whippets) had no murmur at all. Fifty dogs (53.2%) had a systolic murmur with point of maximal intensity at the level of the aortic valve.

The values of Hct, Hb, RBC, IVSd/s, LVDd/s, LVWd/s, FS, Ao, LA, VAo, VPulm, CO and SV were compared between dogs with or without a murmur at the level of the aortic valve (Table 2). Dogs with a murmur at the level of the aortic valve had a significantly higher VAo, VPulm and CO ($P = 0.003$, $P = 0.013$ and $P = 0.023$, respectively), VAo being $1.47 \pm 0.24$ m/s (mean ± SD) for dogs with a murmur and $1.29 \pm 0.23$ m/s for dogs without a murmur, VPulm being $1.19 \pm 0.21$ m/s for dogs with a murmur and $1.08 \pm 0.24$ m/s for dogs without a murmur, and CO being $5.06 \pm 1.26$ l/min for dogs with a murmur and $4.39 \pm 1.34$ l/min for dogs without a murmur.
<table>
<thead>
<tr>
<th></th>
<th>Dogs with a murmur at the level of the aortic valve (n = 50)^a</th>
<th>Dogs without a murmur (n = 44)^b</th>
<th>(P) value</th>
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</thead>
<tbody>
<tr>
<td>Hct</td>
<td>46.4 ± 4.1</td>
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<tr>
<td>Hb</td>
<td>10.4 ± 1.0</td>
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<td>RBC</td>
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<td>6.7 ± 0.6</td>
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<td>36.9 ± 3.8</td>
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<td>LVWs</td>
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<tr>
<td>FS</td>
<td>27.5 ± 5.2</td>
<td>28.0 ± 5.3</td>
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<tr>
<td>Ao</td>
<td>18.9 ± 1.7</td>
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<tr>
<td>LA</td>
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</tbody>
</table>

Hct: haematocrit (%); Hb: haemoglobin concentration (mmol/L); RBC: red blood cell count \(10^{12}/\text{L}\); IVSd/s: interventricular septum thickness in diastole/systole (mm); LVDd/s: left ventricular internal diameter in diastole/systole (mm); LVWd/s: left ventricular wall thickness in diastole/systole (mm); FS: fractional shortening (%); Ao: aortic root diameter (2D) (mm); LA: left atrial diameter (2D) (mm); VAO: aortic blood flow velocity (m/s); VPulm: pulmonic blood flow velocity (m/s); CO: cardiac output (l/min); SV: stroke volume (ml/beat)

^a CO and SV missing for seven dogs

^b CO and SV missing for six dogs

* significant difference between groups
Discussion

In this study, a systolic murmur was found in 61 out of 105 Whippets (58.1%), which was aortic in origin in 50 Whippets (47.6%). No significant differences were found between male or female dogs, between dogs of race or show pedigree lines, nor between dogs in training or not in training within the race pedigree lines, with respect to HR, rhythm, murmur presence, point of maximal intensity and grade.

The prevalence of systolic murmurs in Whippets is lower than reported for retired race Greyhounds (67%) (Fabrizio et al., 2006), but higher than reported for highly trained sled dogs (39.6 to 45%) (Constable et al., 1994; Stepien et al., 1998). In human medicine, systolic murmurs are reported in 30 to 50% of highly trained athletes (Huston et al., 1985; George et al., 1991; O’Brien and Rogers, 1999). In racehorses, the prevalence of functional systolic murmurs was reported to be 53% to 57.7% (Patteson and Cripps, 1993; Marr and Reef, 1995; Kriz et al., 2000). In horses, the increase in the prevalence of murmurs associated with training is most often due to murmurs of atrioventricular valve regurgitations (Patteson and Cripps, 1993; Marr and Reef, 1995; Young and Wood, 2000; Kriz et al., 2000; Young, 2003; Young et al., 2008). In our study, only three dogs had a systolic murmur at the level of the mitral valve, which was a grade 1/6 in one dog aged 10 months, and a grade 2/6 in two dogs aged 107 and 169 months. No dog had a systolic murmur at the level of the tricuspid valve.

Several studies report a positive influence of training on the prevalence of murmurs in dogs as well as in horses (Constable et al., 1994; Young and Wood, 2000; Young, 2003). In our study, no significant difference in murmur presence was found between dogs in training or not in training. This could be due to the age difference between the groups. The group of dogs not in training consisted of the youngest dogs (14.8 ± 6.8 months) which did not start training yet, together with the oldest dogs (112.0 ± 31.3 months) which ceased training. The group of dogs in training consisted of dogs aged 46.6 ± 23.5 months. To be able to study the influence of training on the occurrence of murmurs in these Whippets, it would have been better to compare two groups of comparable age. This was not possible with the available population of dogs, because most of the dogs were from race pedigree lines, and actively trained.

In this study, the Whippets with a murmur at the level of the aortic valve had a significantly higher aortic and pulmonic blood flow velocity, and cardiac output. This is in agreement with the study on retired racing Greyhounds, where a mildly but significantly higher aortic velocity
in dogs with a left basilar systolic murmur was found (Fabrizio et al., 2006). Several articles in human medicine also describe higher stroke volume and aortic flow velocity across a normal aortic valve in children or adults with so-called “innocent” murmurs, compared with a control group (George et al., 1991; Smith, 1997; Spooner et al., 1998; O’Brien and Rogers, 1999; Celebi and Onat, 2006). Murmurs are generally produced by turbulence due to an increase in blood velocity, which may be caused either by a narrowing of the outflow tract or by an increase in stroke volume passing through this outflow tract, or both (Celebi and Onat, 2006). The occurrence of turbulence in a vessel with a uniform diameter can be explained by the Reynolds number, which can be defined as \( \text{Re} = \frac{D \times V \times \rho}{\eta} \), where \( D \) = diameter of the blood vessel, \( V \) = the mean flow velocity, \( \rho \) = blood density and \( \eta \) = blood viscosity (Sabbah and Stein, 1976; Stein and Sabbah, 1976; Murgo, 1998; Moïse and Fox, 1999; Celebi and Onat, 2006). The lower limit for the critical Reynolds number, above which murmurs can occur, is 2300 (Stein and Sabbah, 1976; Kittleson and Kienle, 1998; Moïse and Fox, 1999; Celebi and Onat, 2006). Blood viscosity correlates well with the haematocrit (Bodey and Rampling, 1998). However, no significant difference in aortic diameter nor haematocrit was found between the Whippets with or without a murmur at the level of the aortic valve, so this could not explain the occurrence of turbulence in these dogs. This also means that the increased flow velocity was not due to absolute stenosis at the level of the aortic valve. Turbulent flow patterns can occur in normal humans and animals under some circumstances such as during states of high cardiac output or with rapid blood flow in large vessels (Sabbah and Stein, 1976; Stein and Sabbah, 1976; Moïse and Fox, 1999). On echocardiographic examination, these dogs with innocent murmurs show normal cardiac structure and function, and Doppler echocardiographic studies reveal relatively normal flow dynamics, except for slightly increased flow velocities (Moïse and Fox, 1999).

“Innocent” or “physiological” murmurs are described as soft systolic murmurs (most often grade 1 – 3/6), never associated with a thrill. In human as well as in veterinary medicine, innocent murmurs are most often early to midsystolic and best heard over the left heart base (Smith, 1997; Spooner et al., 1998; Sisson and Ettinger, 1999; Moïse and Fox, 1999; Attenhofer Jost et al., 2000; Kvart and Häggström, 2002; Shub, 2003; Pelech, 2004; Biancamiello, 2005; Celebi and Onat, 2006). Most of the murmurs observed in this study had a point of maximal intensity over the left heart base with low intensities. This fits with the previously described innocent murmurs in dogs (Gompf, 1985; Constable et al., 1994; Kvart et al., 1998; Moïse and Fox, 1999; Sisson and Ettinger, 1999; Kvart and Häggström, 2002; Höglund et al., 2004; Fabrizio et al., 2006). To resume, we suggest that the increased aortic
and pulmonic blood flow velocities are a key determinant for the innocent murmurs in our Whippets.

Regarding the interobserver variability with respect to murmur presence, point of maximal intensity and murmur grade, the agreement was moderate to good for murmur presence, but only moderate for point of maximal intensity and murmur grade (Altman, 1991). One of the limitations of this study is that two different stethoscopes were used. However, the best agreement was obtained for murmur presence between observer 1 and 2, two observers using a different stethoscope. In contrast, the agreement for murmur grade was the lowest between observer 2 using the Rappaport-Sprague acoustic stethoscope and both other observers using the Littman Classic II Pediatric stethoscope. In veterinary medicine, several articles report poor to good interobserver agreements. In a study on dogs with mild mitral regurgitation, kappa values for presence of a left-sided heart murmur ranged from 0.27 to 0.74, which is a fair to good agreement. Levels of agreement between observers decreased with decreasing level of experience (Pedersen et al., 1999). Another study on low intensity heart murmurs in Boxer dogs reported kappa values from 0.14 to 0.75 (poor to good agreement for auscultation on dogs at rest) and from 0.02 to 0.35 (poor to fair agreement for auscultation on dogs after exercise) (Höglund et al., 2004). In human medicine, observational studies on the accuracy of heart auscultation are sparse. One report on the effect of teaching and type of stethoscope on cardiac auscultatory performance reveals a fair agreement ($\kappa = 0.38$ to 0.39) for the detection of whether there is a murmur or not versus a poor to moderate agreement ($\kappa = 0.01$ to 0.43) for the recognition of 5 categories of heart diseases (Iversen et al., 2006). In this study, there was no important improvement by type of stethoscope or by teaching of doctors. The moderate to good levels of agreement in this study should also be seen in the light of our study population, consisting of Whippets with low intensity murmurs. It has already been described that these murmurs are more difficult to discern (Pedersen et al., 1999; Höglund et al., 2004). Also, the lower the murmur intensity, the more variable its presence and grade (Heiene et al., 2000; Höglund et al., 2004).
Conclusions

The results of this study suggest that Whippets have a high prevalence of soft systolic murmurs in the absence of any structural abnormalities, most likely due to an increased aortic velocity. These murmurs fit the description of “innocent” murmurs.
References


Chapter 2

VERTEBRAL HEART SIZE RANGES SPECIFIC FOR WHIPPETS
VERTEBRAL HEART SIZE RANGES SPECIFIC FOR WHIPPETS

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Summary

To assess the influence of breed, breeding-lines and training on heart size, the vertebral heart size (VHS) was evaluated on left-to-right lateral, right-to-left lateral, dorsoventral and ventrodorsal thoracic radiographs from 44 Whippets free from cardiac and pulmonary disease. In lateral views, the VHS was 11.0 ± 0.5 vertebrae (mean ± SD) on right-to-left lateral and 11.3 ± 0.5 vertebrae on left-to-right lateral radiographs, being larger than the 9.7 ± 0.5 vertebrae proposed by Buchanan ($P < 0.0001$). The VHS on left-to-right lateral views was larger than on right-to-left lateral views ($P < 0.0001$). The VHS was 10.5 ± 0.6 vertebrae on dorsoventral radiographs and 11.1 ± 0.6 vertebrae on ventrodorsal radiographs. Both values were larger than the 10.2 ± 1.5 vertebrae (dorsoventral) ($P < 0.0082$) or 10.2 ± 0.8 vertebrae (ventrodorsal) ($P < 0.0001$) proposed by Buchanan. In addition, the VHS on ventrodorsal views was larger than on dorsoventral views ($P < 0.0001$). Dogs out of race pedigree lines had a significantly larger VHS than those out of show pedigree lines, and trained dogs had a significantly larger VHS than untrained dogs. Because most trained dogs came out of race pedigree lines, and all untrained dogs came out of show pedigree lines, however, it is difficult to determine whether the higher VHS for trained dogs is due to genetic influences or training, or both. In conclusion, it is important to take into account the breed and the radiographic view when evaluating heart size in thoracic radiographs of Whippets to avoid overinterpretation of cardiac enlargement in these dogs.
Introduction

Different methods have been developed to evaluate the canine cardiac silhouette on thoracic radiographs. Comparison of the cardiac silhouette with previous radiographs of the same dog or with radiographs of a dog of the same breed and size can be inaccurate when made by inexperienced observers (Suter and Lord, 1984). A frequently used tool to quantify cardiac size is the vertebral heart size (VHS), which is based on the strong correlation between heart weight and body length in cats. The mean VHS on lateral radiographs for 100 normal dogs of varying breeds was 9.7 ± 0.5 vertebrae (mean ± SD), and 10.2 ± 1.5 or 0.8 vertebrae on dorsoventral or ventrodorsal radiographs, respectively (Buchanan and Bücheler, 1995). However, differences in the appearance of the normal heart of varying canine breeds as well as variation due to projection, respiration phase and intrinsic movement of the heart are often greater than differences between normal and diseased hearts. Training, emaciation and obesity also influence the size, contour and opacity of the heart (Suter and Lord, 1984; Kittleson, 1998). Several breeds (Boxer, Labrador Retriever, Cavalier King Charles Spaniel and Dobermann) have been reported to have higher mean VHS values or a wider range than the reference values reported by Buchanan and Bücheler (Buchanan and Bücheler, 1995; Lamb et al., 2001). Therefore, it would be more accurate to use breed-specific normal ranges based on a larger number of dogs of each breed (Buchanan and Bücheler, 1995; Buchanan, 2000; Lamb et al., 2000; Lamb et al., 2001). The recognition of interbreed variations has already led to the development of breed-specific ranges for echocardiography (Morrison et al., 1992; Vollmar, 1999; della Torre et al., 2000). The aim of this study was to evaluate whether the normal VHS values proposed by Buchanan and Bücheler for lateral and dorsoventral or ventrodorsal radiographs are also applicable for Whippets, whether they are trained or untrained, out of race or show pedigree lines.
**Materials and methods**

**Dogs**
The radiographic examination included right-to-left and left-to-right lateral as well as dorsoventral and ventrodorsal thoracic radiographs from non-sedated, trained and untrained Whippets out of race and show pedigree lines. Forty-four dogs (27 males and 17 females) were recruited, aged between 11 and 142 months (mean 65 ± 34 months) and weighed between 9.3 and 17.2 kg (mean 13.7 ± 2.0 kg). Dogs were recruited from race pedigree lines \((n = 32)\), from show pedigree lines \((n = 8)\) or were crosses between race and show pedigree lines \((n = 4)\). Thirty-seven dogs were trained for sight hound races. The four dogs out of crossed race and show pedigree lines were not included for comparisons between pedigree lines and trained or untrained dogs (three trained and one untrained dogs). All dogs previously underwent a complete physical and cardiologic examination (auscultation, thoracic radiography, electrocardiography, and echocardiography) and were free from cardiac and pulmonary disease.

**Radiography**
For radiography, care was taken not to have any rotation of the body as this could influence the shape and size of the cardiac silhouette. VHS was measured by the first author in all four views for each dog as described previously (Buchanan and Bücheler, 1995). In right-to-left and left-to-right lateral radiographs, the long axis of the heart was measured from the ventral border of the left mainstem bronchus to the most distant ventral contour of the cardiac apex, using a measuring-rod. This was then repositioned over the thoracic vertebrae beginning from the cranial edge of the fourth thoracic vertebra (T4). The distance on the measuring-rod was then calculated to the nearest 0.1 vertebrae to obtain precise measurements for statistical analysis. The short axis of the heart was measured in the central third region, perpendicular to the long axis, and the number of vertebrae was calculated in the same manner as for the long axis, beginning from T4. Long and short axis dimensions were then summed to obtain a value that indicated heart size relative to vertebral length. In dorsoventral and ventrodorsal radiographs, the maximal long and short axes of the heart were determined in a similar fashion, and measured against thoracic vertebrae in the right-to-left lateral radiograph beginning from the cranial edge of T4.
Chapter 2 Vertebral heart size ranges specific for Whippets

**Statistical analysis**
A t-test was used to test whether the mean VHS in Whippets differed significantly from the mean reference value given by Buchanan and Bücheler (Buchanan and Bücheler, 1995). The effect of gender, pedigree lines (show and race) and training was evaluated in a fixed-effects model assuming normally distributed random error terms. First, the effect of each of these factors was evaluated separately in a univariate model, and then the three factors were evaluated jointly in a multivariable model including the three factors. Finally, comparison between right-to-left and left-to-right lateral VHS and between dorsoventral and ventrodorsal VHS was based on a linear mixed model, with dog as random effect and direction of view as fixed effects factor in order to take into account that the two measurements were performed on the same dog, and therefore correlated. All analyses were carried out at the 5% significance level.

**Results**

*Comparison of observed VHS measurements with previously reported reference values*
The mean VHS on 44 right-to-left lateral radiographs was 11.0 ± 0.5 vertebrae. The normal range encompassing 95% of the values is thus estimated to be 10.1-11.8. The mean VHS on 44 left-to-right lateral radiographs was 11.3 ± 0.5 vertebrae with a normal range encompassing 95% of the values equal to 10.3-12.3 (Fig. 1, Table 1). The mean VHS of the right-to-left lateral as well as the left-to-right lateral radiographs were significantly larger than the reference mean VHS of 9.7 vertebrae given by Buchanan and Bücheler (Buchanan and Bücheler, 1995) ($P < 0.0001$ for both views). The VHS on the left-to-right lateral radiographs was significantly larger than the VHS on the right-to-left lateral radiographs ($P < 0.0001$).
On the 44 dorsoventral radiographs, the mean VHS was 10.5 ± 0.6 vertebrae, with a normal range encompassing 95% of the values equal to 9.2-11.7. The mean VHS on the 44 ventrodorsal radiographs was 11.1 ± 0.6 vertebrae, with a normal range encompassing 95% of the values equal to 9.8-12.4 (Fig. 1, Table 1). The mean VHS on the dorsoventral as well as the ventrodorsal radiographs were significantly larger than the reference mean VHS of 10.2 vertebrae on ventrodorsal and dorsoventral views given by Buchanan and Bücheler (Buchanan and Bücheler, 1995) ($P < 0.0082$ for dorsoventral views, $P < 0.0001$ for ventrodorsal views). The VHS on ventrodorsal radiographs was significantly larger than the VHS on dorsoventral views ($P < 0.0001$).

On right-to-left lateral radiographs, 97.5% of the Whippets had a VHS ≤ 11.8 vertebrae, so this value could be used as a clinically useful upper limit for normal heart size in Whippets. On left-to-right lateral radiographs, this value would be 12.3 vertebrae. On dorsoventral and ventrodorsal radiographs, these values would be 11.7 and 12.4 vertebrae, respectively.

No significant differences could be found between the VHS of male and female dogs, in each of the four views (Table 1).
Table 1: Vertebral heart size in Whippets according to gender, breeding line and training level (mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>n †</th>
<th>Right-to-left lateral</th>
<th>Left-to-right lateral</th>
<th>Dorsoventral</th>
<th>Ventrodorsal</th>
</tr>
</thead>
<tbody>
<tr>
<td>All dogs</td>
<td>44</td>
<td>11.0 ± 0.5</td>
<td>11.3 ± 0.5</td>
<td>10.5 ± 0.6</td>
<td>11.1 ± 0.6</td>
</tr>
<tr>
<td>Male</td>
<td>27</td>
<td>11.0 ± 0.4</td>
<td>11.3 ± 0.5</td>
<td>10.5 ± 0.6</td>
<td>11.1 ± 0.7</td>
</tr>
<tr>
<td>Female</td>
<td>17</td>
<td>10.9 ± 0.6</td>
<td>11.2 ± 0.6</td>
<td>10.4 ± 0.7</td>
<td>11.1 ± 0.6</td>
</tr>
<tr>
<td>Race lines</td>
<td>32</td>
<td>11.1 ± 0.4</td>
<td>11.4 ± 0.4</td>
<td>10.6 ± 0.5</td>
<td>11.3 ± 0.6</td>
</tr>
<tr>
<td>Show lines</td>
<td>8</td>
<td>10.5 ± 0.6 *</td>
<td>10.8 ± 0.6 *</td>
<td>9.9 ± 0.8 *</td>
<td>10.4 ± 0.5 *</td>
</tr>
<tr>
<td>Trained</td>
<td>34</td>
<td>11.0 ± 0.4</td>
<td>11.4 ± 0.5</td>
<td>10.5 ± 0.5</td>
<td>11.2 ± 0.6</td>
</tr>
<tr>
<td>Untrained</td>
<td>6</td>
<td>10.6 ± 0.6 *</td>
<td>10.7 ± 0.5 *</td>
<td>9.9 ± 0.9 *</td>
<td>10.3 ± 0.4 *</td>
</tr>
</tbody>
</table>

* Significant difference at 5% significance level
† Four dogs out of crossed race and show pedigree lines were excluded for comparison between race/show lines and trained/untrained dogs

**Comparison between race and show pedigree dogs**

Differences were noted comparing the VHS between race and show pedigree lines, and between trained and untrained dogs (Table 1). On right-to-left lateral radiographs, the VHS of race pedigree dogs was significantly larger than the VHS of show pedigree dogs ($P = 0.0071$). On left-to-right lateral radiographs, the VHS of race pedigree dogs was also significantly larger than the VHS of show pedigree dogs ($P = 0.0026$). The VHS of race pedigree dogs on dorsoventral radiographs was significantly larger than the VHS of the show pedigree dogs with $P = 0.0049$. On ventrodorsal radiographs, the difference was also highly significant with $P = 0.0005$.

**Comparison between trained and untrained dogs**

On comparing trained and untrained dogs, a significantly larger VHS was found for trained dogs on right-to-left ($P = 0.045$) and left-to-right lateral radiographs ($P = 0.0045$). On dorsoventral radiographs, the VHS of trained dogs was significantly larger than the VHS of untrained dogs ($P = 0.029$). Also, on ventrodorsal radiographs the VHS of trained dogs was significantly larger than the VHS of untrained dogs with $P = 0.0003$. However, all but two of
the trained dogs in this study were from race pedigree lines, and all six untrained dogs were from show pedigree lines. When the three factors were evaluated jointly in a multivariable model including the three factors, no significant differences were found. On comparing VHS of Whippets trained for more than 18 months to VHS of Whippets in the beginning of their training (less than 6 months of training), no statistical differences could be found.

**Discussion**

This study was carried out to determine if the mean VHS of 9.7 ± 0.5 vertebrae on lateral radiographs and of 10.2 ± 1.5 or 0.8 vertebrae on dorsoventral or ventrodorsal radiographs (respectively), as determined by Buchanan and Bücheler (1995), was also applicable for Whippets. Interbreed variations of the VHS have been described, and it has been suggested that it would be more reliable to determine specific values for individual breeds by studying larger numbers of dogs of each breed (Buchanan and Bücheler, 1995; Buchanan, 2000; Lamb et al., 2000; Lamb et al., 2001). Sight hounds are also known to have a higher heart weight/body weight ratio, so a larger VHS could be expected for the Whippets also (Steel et al., 1976; Pape et al., 1984, 1986; Page et al., 1993; Snyder et al., 1995).

The mean VHS of these Whippets on lateral radiographs was significantly larger than the VHS reported by Buchanan and Bücheler. A significant difference was also found between right-to-left and left-to-right lateral radiographs, with a larger VHS on left-to-right lateral views. Due to the divergent X-ray beam and the left-sided position of the heart within the thorax, the degree of enlargement of the cardiac silhouette is always larger on left-to-right lateral than on right-to-left lateral radiographs. The degree of enlargement also depends on the relation between the distances from tube to object and object to film. Gravity and tilting of the heart within the thorax due to different recumbent positions also influence the cardiac silhouette (Suter and Lord, 1984). Slight but noticeable differences have been described between radiographs made in left versus right lateral recumbency, but no preference was adopted for one view (Suter and Lord, 1984). It is most important to standardise the position of the animal and to always use the same view in all animals (Suter and Lord, 1984). If left-to-right lateral radiographs are used in Whippets, the VHS will be larger than in right-to-left lateral radiographs, and different upper-limits should be used.

The mean VHS for Whippets in dorsoventral or ventrodorsal radiographs also was significantly larger than the 10.2 ± 1.5 or 0.8 vertebrae (respectively) stated by Buchanan and
Bücheler (1995). The mean VHS in ventrodorsal radiographs was significantly larger than the mean VHS in dorsoventral views. Positioning has been reported to play an important role in the appearance of the heart in ventrodorsal compared to dorsoventral views (Ruehl and Thrall, 1981). In ventrodorsal radiographs, the cardiac silhouette appeared longer and narrower than in dorsoventral radiographs, the cardiac apex was separated from the diaphragmatic cupula, and the heart was more nearly parallel to the spine. The cardiac silhouette had its longest craniocaudal axis in the ventrodorsal radiographs, most likely due to magnification associated with a greater cardiac-film distance. Displacement of the cardiac apex toward the left in dorsoventral radiographs is evidence that the heart is physically moved when the dog is in ventral recumbency (Ruehl and Thrall, 1981). Here again, standardisation is the most important, and if initial radiographs have been made in ventrodorsal or dorsoventral position, subsequent radiographs should be made in the same manner to allow comparison (Suter and Lord, 1984).

In contrast to Buchanan and Bücheler’s study, Whippets did not have a remarkably larger vertebral heart size in dorsoventral or ventrodorsal radiographs in comparison to the lateral radiographs. However, in accordance with Buchanan and Bücheler’s results, but in contrast to others, no significant differences were found between males and females in any of the four radiographic views (Buchanan and Bücheler, 1995; Lamb et al., 2001).

The Whippet population can mainly be divided in two pedigree lines: “race pedigree lines”, which consists of dogs specifically selected for their high speed during the sight hound races, and “show pedigree lines”, which consist of dogs selected for their show qualities. There is a slight difference in body conformation between these two pedigree lines, race pedigree dogs having a longer loin region and a straight back, whereas show pedigree dogs have a shorter body and a rounded, sloping down back. No differences were noted comparing the T4 length and the shoulder height between the two pedigree lines. Crosses between these two pedigree lines also occur, and these dogs are mainly used for races. Comparing race and show pedigree lines, the race pedigree dogs have a significantly higher VHS in all four views.

Another division can be made within this Whippet population: some of the dogs are trained on short- and long-distance runs several times a week to compete in sight hound races, whereas others live a sedentary life with only short walks. There is also a significant difference between these trained and untrained dogs, the trained dogs having a significantly higher VHS in all four views. Influence of training has previously been described as a
possible cause of physiologic enlargement of the heart on lateral radiographs (Schulze and Nölder, 1957; Suter and Lord, 1984). Studies with mongrel dogs reported a significant increase in left ventricular (LV) end-diastolic wall thickness, LV weight, and LV weight/body weight ratio due to training (Wyatt and Mitchell, 1974; Riedhammer et al., 1976). Others found no significant difference in LV mass in exercised Beagle dogs compared with control Beagles, but found a significant increase in LV volume after exercise training (Ritzer et al., 1980). Several studies concentrated on Greyhounds. One study suggested that a significant degree of hypertrophy in Greyhounds was due to genetic factors alone, but they found that trained Greyhounds had even more extensive LV hypertrophy and a higher LV weight/body weight ratio than untrained Greyhounds and normal dogs of the same body weight range (Carew and Covell, 1978). In contrast, another study reported a comparable heart weight/body weight ratio in the trained and control Greyhound adult and puppy groups, which supports the hypothesis that cardiac hypertrophy in the Greyhound is congenital and not acquired through exercise and training (Pape et al., 1986). Also, cardiac hypertrophy apparently did not regress in the Greyhounds after cessation of vigorous training and exercise, which suggests that the large heart in the Greyhound is congenital and not the result of exercise (Pape et al., 1984). The significantly higher VHS for trained dogs in this study would suggest an increase in LV mass due to training. However, if we take into account that there is a rather large difference in size of the various groups and that most of the trained dogs in this study were from race pedigree lines, and all untrained dogs were from show pedigree lines, no significant differences were found. Thus, no final conclusions can be made about the influence of training or pedigree line on the heart size. More detailed studies with larger number of animals will be needed to evaluate this influence.

Conclusions

In Whippets, the vertebral heart sizes are larger than those reported in the literature for a mixed population of dogs. It is therefore important to take the breed and the radiographic view into account, and to standardise the radiographic methods when evaluating heart size in thoracic radiographs to avoid overinterpretation of cardiac enlargement.
Chapter 2  Vertebral heart size ranges specific for Whippets

References


Chapter 2  Vertebral heart size ranges specific for Whippets
Chapter 3

ELECTROCARDIOGRAPHIC REFERENCE VALUES IN WHIPPETS
ELECTROCARDIGRAPHIC REFERENCE VALUES IN
WHIPPETS

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Summary

The aim of this study was to determine electrocardiographic characteristics of Whippets and to compare the results with published reference values for a general dog population. Electrocardiographic parameters from 105 healthy Whippets were used to establish reference values for the breed.

The most important differences compared to published reference values were the higher median R-wave amplitudes in leads II, CV₆LL and CV₆LU. For some parameters (P-wave amplitude, ST-segment deflection and T-wave amplitude in lead II; R-wave amplitude in CV₅RL), a marked percentage of Whippet values were above the published maximum reference data. The results confirmed that Whippets have electrocardiographic characteristics similar to those reported in athletic heart syndrome in humans. Some of these characteristics could be erroneously taken as evidence of cardiac disease and clinicians should be aware of these factors to prevent unnecessary investigations in healthy dogs.
Introduction

Electrocardiography is commonly performed on dogs in clinical practice and is a useful tool in diagnosing most cardiac arrhythmias and conduction disturbances, and in drawing inferences about cardiac chamber enlargement (Tilley, 1992; Coleman and Robson, 2005). An electrocardiogram (ECG) recorded in right lateral recumbency allows repeatable measurement of the deflections and identification of a mean electrical axis (MEA). Amplitude and duration of deflections are usually measured from lead II and then compared with established reference ranges (Tilley, 1992). Despite the low sensitivity and moderate specificity of this test, these indirect ECG deductions are commonly used to identify changes in cardiac size (Hamlin, 1968; George et al., 1991).

Reference values for ECG characteristics of dogs have usually been derived from the examination of findings from a relatively small number of dogs of various breeds, sizes and ages, or from examinations of a larger number of purpose-bred Beagles (Eckenfels and Trieb, 1979; Tilley, 1992; Hanton and Rabemampianina, 2006). Thus, such reference values are probably inappropriate for certain parameters of sight hounds such as those with a specific body conformation and/or racing dogs.

Racing is a test of speed, combined with desire to chase an artificial lure without interfering with other hounds. In oval track racing, dogs run on a U-shaped or oval track with an inner rail and for a distance of 350 m (range 340-365 m), which usually takes 22-24 s. Whippets are trained on 100 m sprints to improve their start during races and to provide anaerobic or resistance training for sprinting. They are also trained over long distances between races, often running for 60-90 min to increase endurance through aerobic training.

Selective breeding and training of racehorses, sight hounds or sled dogs has led to unconscious selection for large heart size (Steel et al., 1976). An ECG is frequently used as a screening method before Whippets are admitted to oval track races. Trained dogs, whether endurance or resistance trained, can show substantial changes in their ECG (Wyatt and Mitchell, 1974; Steel et al., 1976; Tilley, 1992; Hinchcliff et al., 1997; Constable et al., 1998, 2000) and some of these changes could be mistaken for evidence of pathological cardiac dilatation and/or hypertrophy. The present study was undertaken to determine the ECG characteristics of a large group of Whippets, and to compare the results with previously published reference values for dogs (Tilley, 1992).
**Materials and methods**

**Dogs**
Privately owned Whippets \((n = 125)\) were recruited voluntarily through contacts with breeders and owners. All dogs underwent a complete physical and cardiological examination (auscultation, electrocardiography and echocardiography), as well as a clinicopathological assessment that included conventional haematology and quantification of serum urea, creatinine, total protein, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and glucose. Dogs <10 months of age or with cardiac abnormalities (moderate to severe mitral regurgitation) were excluded.

The study included 105 Whippets (51 males, 54 females), between 10 and 169 months of age (median 50 months; interquartile range [IQR] 27-84 months) and weighing 9.3-17.2 kg (median 13.0 kg; IQR 11.7-14.6 kg). Dogs were recruited from race pedigree lines \((n = 89)\), show pedigree lines \((n = 10)\), or were crosses between race and show pedigree lines \((n = 6)\). Of the race pedigree dogs, six were not yet in training, 62 were in active training for sight hound races (median training period 24 months; IQR 12-47 months; range 2-78 months), and 21 were retired and had ceased training (median off-training period 27 months; IQR 12-44 months; range 7-80 months).

**Electrocardiographic measurements**
The unsedated dogs were positioned and manually restrained in right lateral recumbency, with the front legs placed parallel to each other and perpendicular to the long axis of the body, and the hind limbs in a neutral semiflexed position. The animals were allowed some time to acclimatise so that the ECG could be taken from dogs that were relaxed. All ECGs were recorded by the first author using a Cardiofax V Ecaps 12 Nihon Kohden electrocardiograph. The ECG leads were attached to the skin by alligator clips at the palmar aspect of the left and right foreleg over or just distal to the olecranon; at the cranial aspect of the left and right hind limb over the patellar ligament; at the right fifth intercostal space at the edge of the sternum (CV₅RL); at the left sixth intercostal space at the edge of the sternum (CV₆LL); at the left sixth intercostal space at the costochondral junction (CV₆LU); and at the dorsal spinous process of the seventh thoracic vertebra (V₁₀). The points of electrode attachment were moistened with 70% denatured alcohol and the ECG recorded at a frequency range of 0.05-75 Hz. To avoid lowering wave amplitudes we did not use a filter to minimise baseline interference.
When stable, leads I, II, III, aVR, aVL, aVF, CV₃RL, CV₆LL, CV₆LU and V₁₀ were printed at 25 mm/s and 10 mm/mV. If amplitudes were too large, the recording amplitude was reduced to 5 mm/mV. A 30 s strip of leads I, II and III was also recorded at 50 mm/s and 10 mm/mV. The cardiac rhythm was observed for about 5 min to detect arrhythmias. After the ECG recording, a complete echocardiography was performed with simultaneous ECG recordings, during which the cardiac rhythm was further observed to detect arrhythmias. Five representative consecutive beats in leads II, CV₃RL, CV₆LL, CV₆LU and V₁₀ at 50 mm/s and 10 mm/mV (unless reduced to 5 mm/mV) were used to measure various ECG variables manually. Variables measured in lead II recordings were heart rate (HR) in beats per minute (bpm) based on the RR-interval of the five representative consecutive beats used, rhythm (regular rhythm, respiratory sinus arrhythmia, pathological arrhythmias), P-wave amplitude and duration, PQ-interval, Q-wave amplitude, R-wave amplitude, S-wave amplitude, QRS-complex duration, ST-segment deflection, T-wave amplitude and QT-interval, with amplitudes in mV and durations in seconds. The MEA was calculated automatically by the electrocardiograph and manually checked. R-wave amplitude was also measured from leads CV₃RL, CV₆LL, CV₆LU and V₁₀ in mV. All measurements were performed by the first author using callipers.

**Statistical analysis**

The median and IQR values were used as summary statistics. The percentages of observed values in lead II and of R-wave amplitudes in leads CV₃RL, CV₆LL, CV₆LU and V₁₀ that fell outside the reference values given by Tilley (1992) also were determined. Different ECG parameters were compared between males and females, race and show pedigree dogs, and dogs in training and not in training within the race pedigree lines using the Wilcoxon rank sum test. This non-parametric test was used because the assumption of normality was rejected for most of the variables according to the Shapiro-Wilk test. The normal distribution assumption, however, was not rejected for R-wave amplitudes in leads II, CV₃RL, CV₆LL, CV₆LU and V₁₀. For these variables, we also fitted analysis of variance models with normally distributed error terms, to study whether a significant result for the covariate of interest (male versus female dogs, race versus show pedigree lines, dogs in training versus not in training) remains when adjusted for the possibly confounding factors of weight and age. Finally, Pearson correlation coefficients \( r \) were calculated between the R-wave amplitude in lead II and the vertebral heart size (VHS) measured from thoracic radiographs of 34 dogs taken in both left and right lateral recumbency (Bavegems et al., 2005), and between the R-wave...
amplitude in lead II and the echocardiographic left ventricular (LV) internal diameter in diastole and systole of 105 dogs (Bavegems et al., 2007). All analyses were carried out at the 5% significance level.

**Results**

Comparison of observed ECG measurements with previously reported reference values

Median HR and different variables in lead II and R-wave amplitude in CV$_{RL}$, CV$_{LL}$, CV$_{LU}$ and V$_{10}$ of all dogs are presented in Table 1. Of 105 dogs, 32 (30.5%) had a regular rhythm at a median HR of 154 bpm (IQR 132-164 bpm) and 73 (69.5%) had a respiratory sinus arrhythmia at a median HR of 111 bpm (IQR 99-126 bpm). No atrial or ventricular premature beats, nor ventricular conduction disturbances, were observed in any of the dogs in the study.

The ECG of Whippets differed markedly from the reference ECG values previously reported by Tilley (1992) (Fig. 1). The most important differences were higher median R-wave amplitudes in leads II, CV$_{LL}$ and CV$_{LU}$ compared with the reference values. For some parameters (P-wave amplitude, R-wave amplitude, ST-segment deflection and T-wave amplitude in lead II, R-wave amplitude in CV$_{RL}$, CV$_{LL}$ and CV$_{LU}$), a marked percentage of the Whippet values fell above the maximum reference values reported by Tilley (1992) (Table 1).
Table 1: Median and interquartile range (IQR) range of electrocardiographic values in 105 Whippets measured from lead II unless specified otherwise, with the percentage of values outside the maximum reference data reported by Tilley (1992)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Median</th>
<th>IQR</th>
<th>Reference value</th>
<th>% Out</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (bpm)</td>
<td>121</td>
<td>106 to 144</td>
<td>≤ 0.40</td>
<td>28.6</td>
</tr>
<tr>
<td>P-amplitude (mV)</td>
<td>0.36</td>
<td>0.30 to 0.42</td>
<td>≤ 0.04</td>
<td>0.0</td>
</tr>
<tr>
<td>P-duration (s)</td>
<td>0.03</td>
<td>0.03 to 0.03</td>
<td>≤ 0.04</td>
<td>0.0</td>
</tr>
<tr>
<td>PQ-interval (s)</td>
<td>0.09</td>
<td>0.08 to 0.10</td>
<td>0.06 to 0.13</td>
<td>0.0</td>
</tr>
<tr>
<td>QRS-duration (s)</td>
<td>0.04</td>
<td>0.04 to 0.04</td>
<td>≤ 0.05</td>
<td>1.0</td>
</tr>
<tr>
<td>Q-amplitude (mV)</td>
<td>−1.04</td>
<td>−0.78 to −1.40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R-amplitude (mV)</td>
<td>3.54</td>
<td>3.02 to 4.32</td>
<td>≤ 3.0</td>
<td>75.2</td>
</tr>
<tr>
<td>S-amplitude (mV) (^a)</td>
<td>0.00</td>
<td>0.00 to 0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electrical axis (degree)(^b)</td>
<td>81</td>
<td>72 to 86</td>
<td>40 to 100</td>
<td>0.0</td>
</tr>
<tr>
<td>ST-segment (mV) (^c)</td>
<td>−0.14</td>
<td>−0.06 to −0.20</td>
<td>−0.20 ≤ ST ≤ 0.15</td>
<td>21.0</td>
</tr>
<tr>
<td>T-amplitude (mV) (^d)</td>
<td>−0.60</td>
<td>−0.42 to −0.84</td>
<td>T-wave ≤ 25% R-wave</td>
<td>21.0</td>
</tr>
<tr>
<td>R-amplitude CV(_3)RL (mV) (^e)</td>
<td>2.55</td>
<td>2.15 to 3.14</td>
<td>≤ 3.0</td>
<td>26.9</td>
</tr>
<tr>
<td>R-amplitude CV(_6)LL (mV)</td>
<td>3.94</td>
<td>3.32 to 4.58</td>
<td>≤ 3.0</td>
<td>81.0</td>
</tr>
<tr>
<td>R-amplitude CV(_6)LU (mV)</td>
<td>4.26</td>
<td>3.50 to 5.12</td>
<td>≤ 3.0</td>
<td>81.0</td>
</tr>
<tr>
<td>R-amplitude V(_{10}) (mV)</td>
<td>1.00</td>
<td>0.70 to 1.20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>QT-interval (s)</td>
<td>0.18</td>
<td>0.16 to 0.19</td>
<td>0.15 ≤ QT ≤ 0.25</td>
<td>1.9</td>
</tr>
</tbody>
</table>

\(a\) S-amplitude: 79.0% of dogs had no S-wave in lead II

\(b\) Three dogs had an electrical axis perpendicular to the frontal plane

\(c\) ST-segment: 14.3% of dogs had an isoelectric ST-segment

\(d\) T-amplitude: 97 dogs (92.4%) had a negative T-wave, 8 dogs (7.6%) had a positive T-wave

\(e\) Lead CV\(_3\)RL missing for one dog
Figure 1: Representative ECG of a female Whippet recorded at 10 mm/mV and 50 mm/s using leads I, II and III. Note the tall R-waves in leads II and III and the ST-segment slurring.

For 34 dogs, VHS from radiographs in left lateral and right lateral recumbency, as well as R-wave amplitudes from lead II were available. There was a moderate but statistically significant correlation between the R-wave amplitude in lead II and the VHS from radiographs in left lateral recumbency ($r = 0.49$ with $P = 0.003$), as well as between the R-wave amplitude in lead II and the VHS from radiographs in right lateral recumbency ($r = 0.44$ with $P = 0.009$) (Bavegems et al., 2005). For 105 dogs, there was a weak but statistically significant correlation between the R-wave amplitude in lead II and the echocardiographic LV internal diameter in diastole and systole ($r = 0.35$ with $P = 0.0002$ and $r = 0.38$ with $P = 0.0001$, respectively) (Bavegems et al., 2007).

Three dogs (2.9%) had isoelectric QRS-complexes in all frontal plane leads, suggesting the MEA was perpendicular to the frontal plane. In lead II, 22 dogs (21.0%) had an S-wave, whereas 83 dogs (79.0%) did not. The ST-segment was isoelectric in 15 dogs (14.3%), but showed a positive deflection in one dog (0.9%), with a value of 0.08 mV, and a negative deflection in 89 dogs (84.8%), with a median value of $-0.16$ mV (IQR $-0.08$ to $-0.20$ mV). More specifically, 59/89 dogs (66.3%) had ST-segment slurring (median $-0.18$ mV; IQR
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-0.14 to -0.24 mV), rather than a true ST-segment depression. Thirty dogs (33.7%) had no slurring of the ST-segment, but just a slight negative deflection with values within the reference range (median -0.08 mV; IQR -0.06 to -0.14 mV). The T-wave was positive in eight dogs (7.6%), with a median value of 0.39 mV (IQR 0.22-0.47 mV), and was negative in 97 dogs (92.4%), with a median value of -0.64 mV (IQR -0.48 to -0.90 mV).

Comparison between male and female dogs
Fifty-one males (median age 44 months, IQR 26-74 months; median weight 14.6 kg, IQR 13.2-16.3 kg) were compared with 54 females (median age 61 months, IQR 28-91 months, median weight 11.9 kg, IQR 10.8-12.9 kg). Sixty-six (62.9%) of the dogs were in training, of which 36 were males (54.5%) and 30 females (45.5%). There was no significant difference in age between both groups (P = 0.11), however there was a significant difference in weight, with males weighing more than females (P < 0.0001).
Males had a significantly larger R-wave amplitude in CV<sub>6</sub>LU (P = 0.049) with R-CV<sub>6</sub>LU being 4.58 mV (IQR 3.68-5.24 mV) and 4.13 mV (IQR 3.04-4.80 mV) for males and females, respectively. This difference, however, was no longer significant when the model was adjusted for weight and age (P = 0.28).

Comparison between race and show pedigree dogs
Eighty-nine dogs (43 males, 46 females) were from race pedigree lines and 10 (four males, six females) were from show pedigree lines. Six dogs were crosses between these two pedigree lines and were excluded from the analysis. The median age and weight of the race pedigree dogs was 50 months (IQR 27-84 months) and 12.9 kg (IQR 11.6-14.7 kg), respectively. The median age and weight of the show pedigree dogs was 50 months (IQR 37-77 months) and 13.1 kg (IQR 12.2-14.3 kg), respectively. There were no significant differences in age and weight between the race and show pedigree dogs (P = 0.93 and P = 0.62, respectively)
Dogs from race pedigree lines had significantly higher R-wave amplitudes in CV<sub>3</sub>RL and CV<sub>6</sub>LU (P < 0.0001 and P = 0.028, respectively). For race pedigree dogs, median R-wave amplitude was 2.65 mV (IQR 2.20-3.30 mV) in CV<sub>3</sub>RL and 4.28 mV (IQR 3.56-5.14 mV) in CV<sub>6</sub>LU. For show pedigree dogs, median R-wave amplitude was 1.66 mV (IQR 1.20-2.08 mV) in CV<sub>3</sub>RL and 3.23 mV (IQR 2.32-4.70 mV) in CV<sub>6</sub>LU. These differences remained significant when the model was adjusted for weight and age (CV<sub>3</sub>RL: P < 0.0001, CV<sub>6</sub>LU, P = 0.016).
The median MEA was 83° (IQR 75-86°) for race pedigree dogs and 67° (IQR 58-72°) for show pedigree dogs, and the difference was significantly different ($P<0.0001$). Race pedigree dogs had a significantly lower HR than show pedigree dogs ($P = 0.011$), the median HR for race pedigree dogs being 118 bpm (IQR 105-136 bpm) and for show pedigree dogs being 153 bpm (IQR 134-164 bpm).

In line with the negative correlation between HR and QT-interval (the slower the HR, the longer the QT-interval), race pedigree dogs had a significantly longer QT-interval ($P = 0.0004$), the median QT-interval being 0.18 s (IQR 0.17-0.19 s) in race pedigree dogs compared to 0.16 s (IQR 0.15-0.16 s) in show pedigree dogs. Despite similar median QRS-duration of 0.040 s (IQR 0.040-0.040 s) for race and show pedigree dogs, the QRS-duration was also significantly longer in the race pedigree dogs compared with the show pedigree dogs ($P = 0.011$).

**Comparison between dogs in training and not in training within the race pedigree lines**

Six dogs (four males, two females) not yet in training had a median age of 12 months (IQR 11-16 months) and a median weight of 13.2 kg (IQR 10.0-14.4 kg). Sixty-two dogs (32 males, 30 females) were in training for a median period of 24 months (IQR 12-47 months; range 2-78 months). The median age of these dogs was 39.5 months (IQR 27-62 months) and they had a median weight of 13.4 kg (IQR 12.1-14.8 kg). Twenty-one dogs (7 males, 14 females) were retired and had ceased training, with a median off-training period of 27 months (IQR 12-44 months; range 7-80 months). These dogs had a median age of 99 months (IQR 86-138 months) and a median weight of 12.6 kg (IQR 10.6-13.6 kg). No significant differences were found between the lead II parameters of dogs not yet in training and retired dogs ($P > 0.23$ for all parameters). These data were thus grouped as dogs not in training, and compared with the dogs in training.

Dogs in training had a significantly higher R-wave amplitude in lead II ($P = 0.011$), the R-wave amplitude for dogs in training being 3.75 mV (IQR 3.18-4.40 mV) in lead II compared with 3.28 mV (IQR 2.56-3.74 mV) in lead II for dogs not in training. This difference was no longer significant when the model was adjusted for weight and age, although the trend towards higher R-wave amplitudes in lead II for dogs in training remained ($P = 0.068$).
Discussion

There are diverse opinions in the literature on the correct positioning of the dog for optimal and reproducible ECGs. Many authors favour the right lateral recumbent position (Hamlin, 1968; Wyatt and Mitchell, 1974; Steel et al., 1976; Tilley, 1992; Constable et al., 1998; Rishniw et al., 2002), while others use sternal recumbency, or the sitting or standing position (Eckenfels and Trieb, 1979; Eckenfels, 1980, 1986; Constable et al., 1994, 1996, 1998; Hanton and Rabemampianina, 2006).

Changes in body position alter the shape of numerous diagnostically relevant components of QRS-complexes recorded in normal dogs. ECGs recorded from dogs in the sitting or standing position show significantly different amplitudes (larger as well as smaller) in the P-, Q-, R- and S-waves of the different ECG leads, as well as a change in the MEA (Rishniw et al., 2002; Coleman and Robson, 2005). Wave durations and intervals are unchanged in the sitting position and in sternal recumbency, compared to right lateral recumbency (Rishniw et al., 2002; Coleman and Robson, 2005). For this reason, sternal recumbency or the standing position should only be used to analyse the cardiac rhythm and electrocardiographic intervals, or in animals with severe respiratory distress (Tilley, 1992).

In the present study, the ECG of the Whippets was found to differ markedly from the reference ECG values previously reported by Tilley (1992) (Table 1). HR was significantly lower in race pedigree dogs compared to show pedigree dogs, which is consistent with several articles in veterinary and human medicine reporting a decrease in HR with training (Wyatt and Mitchell, 1974; Bjornstad et al., 1991; Constable et al., 1994, 1998; O’Brien and Rogers, 1999) attributed to an increased ratio of parasympathetic to sympathetic tone (O’Brien and Rogers, 1999).

P-wave amplitude can be elevated for several reasons. P-pulmonale is not always specific for right atrial enlargement or pulmonary disease. For example, a rapid HR alone can cause an increase in amplitude of the P-wave and simulate P-pulmonale, as there is a statistically significant positive correlation between HR and P-wave amplitude (Tilley, 1992; Hanton and Rabemampianina, 2006). However, as the observed median HR was 121 bpm (IQR 106-144 bpm), this does not explain the increased P-wave amplitude. Another study reported that the P-wave amplitude in lead II was > 0.40 mV in 45% of endurance-trained sled dogs (Hinchcliff et al., 1997) but the ECGs were recorded while dogs were standing, so the results may not be comparable to those obtained from dogs in lateral recumbency. In humans, increased P-wave amplitude and notching are occasionally noted with athletic heart syndrome.
(Huston et al., 1985; George et al., 1991). We assume that P-wave amplitude can also be increased because of a reduced distance between the electrodes and the heart in thin, narrow-chested dogs, as has been reported for the R-wave amplitude (Steel et al., 1976; George et al., 1991; Tilley, 1992).

The QRS-complex represents depolarisation of the ventricles and its duration can be prolonged with LV dilation and/or hypertrophy, or may be due to conduction disturbances (Tilley, 1992). The QRS-duration was significantly longer in the race pedigree dogs. In Greyhounds, a good correlation has been reported between QRS-duration and heart weight (Steel et al., 1976). QRS-duration also increases with endurance training and performance levels in Alaskan sled dogs (Constable et al., 1994, 1996). Free-ranging grey wolves had an increase in QRS-duration compared with captive sedentary wolves (Constable et al., 1998).

The R-wave amplitude can be influenced by several factors. An enlarged ventricle with an increased surface area and thickened walls produces greater potentials than does a normal ventricle (Tilley, 1992). Voltages recorded, particularly in the precordial leads, are influenced by the distance between the electrodes and the heart. With LV enlargement, the heart is closer to the chest wall, so the voltage recorded (especially in the precordial leads) is greater. In young, emaciated, or narrow-chested dogs, the criteria for increased voltage are not as valid (Tilley, 1992). In agreement with this, Steel et al. (1976) report that very high voltage deflections often occur in Greyhounds, so 5 mm/mV recordings were used whenever the amplitude of the waveforms was greater than the width of the recording paper. This finding is also true for humans, as increased precordial voltage is common in young thin people, whether trained or not (Lichtman et al., 1973; George et al., 1991), and thin chest walls may partially explain higher precordial voltage in endurance runners compared with sprinters (Ikaheimo et al., 1979).

In our study we also found significantly higher R-wave amplitudes in several leads in race pedigree lines compared with show pedigree lines. In two previous reports on Whippets, larger VHS and larger LV internal diameter were observed on echocardiography in race pedigree dogs (Bavegems et al., 2005, 2007). A significant correlation between the R-wave amplitude in lead II and the VHS from radiographs in left lateral and right lateral recumbency, as well as between the R-wave amplitude in lead II and the LV internal diameter in systole and diastole was found. This seems to indicate that ventricular enlargement is, at least in part, an explanation for the increased R-wave amplitude. Moreover, several articles have reported higher R-wave amplitude due to athletic training. In grey wolves, the ECG of free-ranging wolves, the archetypal endurance athlete, differed markedly from that of captive sedentary
wolves, with a generalised increase in ECG voltages consistent with cardiac chamber enlargement (Constable et al., 1998). Similar generalised increases in R-wave amplitude have been observed in humans with exercise-induced cardiac chamber enlargement (Zehender et al., 1990; Bjornstad et al., 1991; Sharma et al., 1999; Pelliccia and Maron, 2001).

Race pedigree dogs had a median MEA of 83 degrees (IQR 75-86 degrees), which was significantly different from the median MEA of 67 degrees (IQR 58-72 degrees) for show pedigree dogs, but remained within the reference values. This finding is in agreement with previous reports of right axis shift in the MEA in highly trained sled dogs and human endurance athletes (Huston et al., 1985; Zehender et al., 1990; Constable et al., 1994; Sharma et al., 1999).

The QT-interval represents the duration of the ventricular electrical activity. The normal range of QT-intervals in the dog reported in the literature is 0.15-0.25 s at normal HR (Tilley, 1992; Miller et al., 1999; Martin, 2000; Tilley and Goodwin, 2001; Gauvin et al., 2006). There is a negative correlation between the QT-interval and the HR: the faster the HR, the shorter the QT-interval (Eckenfels and Trieb, 1979; Tilley, 1992; Constable et al., 1994; Hanton and Rabemampianina, 2006). This could explain the significantly longer QT-interval in race pedigree dogs in our study, as they also had a significantly lower HR than show pedigree dogs. Correction of the QT-interval to QTc using the formulas of Bazett (1920) or Fridericia (1920) blunted the differences in QT-intervals between race and show pedigree dogs, even though both formulae seem to undercorrect for the influence of HR on QT-duration (Matsunaga et al., 1997; Raunig et al., 2001; Hamlin et al., 2003; Tattersall et al., 2006). Thus, the prolonged QT-interval in our race pedigree Whippets can be explained by decreased heart rate.

In contrast, an influence of training on the QT-interval has been reported with a significantly longer QT-interval in highly trained sled dogs compared to untrained sled and mongrel dogs as a result of LV hypertrophy and/or altered autonomic tone (Constable et al., 1994). Free-ranging wolves had an increase in QT-interval and a decrease in HR compared with captive sedentary wolves (Constable et al., 1998). The 20% prolongation in QT-interval in these free-ranging wolves was consistent with exercise-induced cardiac chamber enlargement; the QT-interval is prolonged by 10-15% in canine and human athletes, the degree of prolongation being training dependent (Zehender et al., 1990; Constable et al., 1994).
The two major limitations to the present study may be, first, the difficulty in separating race and show pedigree dogs from dogs in training and those not in training, and, second, the lack of blood pressure recordings. Of the race pedigree dogs, 69.7% were in training, whereas only 20% of the show pedigree dogs were in training, which could have influenced the results of the comparison between types of dog. Normal blood pressure values are said to be breed-specific and those for Greyhounds and racing hounds in general tend to be higher (Egner et al., 2003). Elevated blood pressure could induce LV hypertrophy, which in turn could result in higher R-wave amplitudes and longer QRS-complex durations. This could explain the general influence (larger R-wave amplitude than reference value) for our whole Whippet population, but would not explain the differences between race pedigree and show pedigree dogs.

In humans, there is good evidence that aerobic endurance training, as well as resistance training, reduces resting blood pressure (Kelley and Kelley, 2000; Fagard, 2001; Cornelissen and Fagard, 2005). In veterinary medicine, a recent article describes the influence of resistance training in rats in which four weeks of resistance training induced cardiac hypertrophy, accompanied by a significant reduction in resting blood pressure (Barauna et al., 2005). Therefore, we do not believe that blood pressure changes could cause the trend to larger R-wave amplitudes in trained versus untrained dogs.

Several other articles have also reported various influences of training on the canine heart, although there has been a lot of debate whether the higher heart weight/body weight ratio in sight hounds or other working dogs is an outcome of training, or due to a genetic influence, or both (Carew and Covell, 1978; Barnard et al., 1980; Rippe et al., 1982; Pape et al., 1984; Huston et al., 1985; Pape et al., 1986; Constable et al., 1994; Schoning et al., 1995; Hinchcliff et al., 1997; Lonsdale et al., 1998).

**Conclusions**

The results of this study confirm that Whippets have ECG characteristics in line with those reported for sled dogs and humans with athletic heart syndrome, probably due to the fact that they are not only sprinters, but also receive considerable endurance training between races. Some of these characteristics could be mistakenly taken as evidence of cardiac disease. The clinician should be aware of these specific ECG characteristics for Whippets to prevent unnecessary investigations in healthy dogs.
References


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Chapter 4

ECHOCARDIOGRAPHIC REFERENCE VALUES IN WHIPPETS
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ECHOCARDIOGRAPHIC REFERENCE VALUES IN
WHIPPETS

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Chapter 4   Echocardiographic reference values in Whippets

Summary

The aim of the study was to establish reference echocardiographic values for Whippets, to compare these values with previously published reference values for the general dog population, and to determine whether there is an influence of gender, breeding lines and training on echocardiographic measurements. Echocardiographic parameters from 105 apparently healthy Whippets without cardiac symptoms were used to establish reference values for the breed and to compare these values with two previously reported reference ranges. The coefficients of the allometric equation $Y = aM^b$, useful to reconstruct normal M-mode and two-dimensional average values for Whippets of varying weights, were calculated, as well as the lower and upper limits of the 95% prediction interval. First, we found that Whippets have a significantly larger left ventricular diameter, increased left ventricular wall and interventricular septal thickness than expected, in diastole as well as in systole. Fractional shortening was significantly lower than the reference value. Second, comparing males and females, taking body weight differences into account, females had a significantly larger left ventricular diameter in diastole and systole. Minor differences were found between race and show pedigree dogs, and between trained and untrained dogs. In conclusion, the results of this study confirm that breed specific reference values are needed in echocardiography. In Whippets, the values found in this study can be used as references in order to avoid overinterpretation of cardiac dilation, hypertrophy, and/or decreased contractility in these dogs.
**Introduction**

Reference echocardiographic values for healthy dogs have been published (Boon et al., 1983; Lombard, 1984; O'Grady et al., 1986; Jacobs and Mahjoob, 1988b; Rishniw and Erb, 2000; Goncalves et al., 2002; Brown et al., 2003; Cornell et al., 2004). However, due to the large variation in canine size and somatotypic conformation, reference ranges are very broad, limiting their clinical usefulness. Therefore, some breed-specific reference values have been defined (Gooding et al., 1986; Morrison et al., 1992; Page et al., 1993; Snyder et al., 1995; Vollmar, 1999; della Torre et al., 2000; O'Leary et al., 2003). For example, sight hounds have a higher heart weight/body weight ratio compared with other breeds due to left ventricular dilation and myocardial thickening (Steel et al., 1976; Rippe et al., 1982; Pape et al., 1984, 1986; Schoning et al., 1995). Whippets have also been reported to have a larger vertebral heart size on thoracic radiographs (Buchanan and Bucheler, 1995; Bavegems et al., 2005). Although Whippets comprise a small fraction of canine patients, they may be examined for inadequate race performance. The aim of this study was to establish reference echocardiographic values for Whippets, to compare these values with published reference values for the general dog population, and to determine whether there is an influence of gender, breeding lines, and training on echocardiographic measurements.

**Materials and methods**

**Dogs**

Privately owned Whippets, $n = 125$, were recruited through contacts with breeders and owners. All dogs underwent physical and cardiologic examinations. Clinicopathologic assessment was also carried out and included conventional haematology and quantification of serum urea, creatinine, total protein, aspartic aminotrasferase, alanine aminotransferase, alkaline phosphatase and glucose. Dogs < 10 months of age or with cardiac abnormalities (moderate to severe mitral regurgitation) or dogs with incomplete data for M-mode or two-dimensional (2D) echocardiography were excluded. Lower age limit was set at 10 months as this is the age at which Whippets are fully grown, according to the breeders and owners who regularly measure shoulder height to subscribe in the appropriate racing class. One-hundred-and-five Whippets (51 males and 54 females), aged between 10 and 169 months ($59.7 \pm 39.3$ months; mean ± standard deviation), weighing between 9.3 and 17.2 kg ($13.2 \pm 2.1$ kg) were
studied. Dogs were recruited from race pedigree lines \((n = 89)\), from show pedigree lines \((n = 10)\) or were crosses between race and show pedigree lines \((n = 6)\). From the race pedigree dogs, six dogs were not yet in training, 62 dogs were trained for sight hound races during \(30.9 \pm 22.8\) months (range 2-78 months) and 21 were retired and had ceased training for \(31.9 \pm 21.1\) months (range 7-80 months).

**Echocardiographic measurements**

The unsedated Whippets were consecutively positioned in right and left recumbency (the former for right parasternal M-mode and 2D measurements and the Doppler study of the pulmonic valve; the latter for the Doppler study of the aortic, mitral and tricuspid valve). All echocardiographic studies were performed by the first author using a Vingmed CFM 800 unit (GE Medical Systems, Horten, Norway) with a 5 MHz mechanical sector transducer with colour and spectral Doppler capabilities. All echocardiographic measurements were made in accordance to the guidelines of the American Society of Echocardiography using the leading-edge to leading-edge method of measurement. For all M-mode and 2D measurements, a lead II electrocardiogram was recorded simultaneously, and three representative cycles were measured and averaged, together with the respective heart rate.

The following parameters were obtained from 2D views: aortic root diameter \((Ao)\) and left atrial diameter \((LA)\) from right parasternal short-axis view and LA from right parasternal long-axis four-chamber view. From right parasternal short axis M-mode view at the chordae level, interventricular septal thickness \((IVS)\), left ventricular internal diameter \((LVD)\) and left ventricular wall thickness \((LVW)\) in diastole \((d)\) and systole \((s)\) as well as E-point to septal separation \((EPSS)\) were obtained. Aortic pre-ejection period \((PEP)\) and left ventricular ejection time \((LVET)\) were obtained from right parasternal long-axis five-chamber view. Peak velocities for pulmonary and aortic flow \((VPulm\) and \(VAo\), respectively) were measured from spectral Doppler echocardiography, as well as from mitral and tricuspid E- and A-peak velocities \((MitrE, MitrA, TricE\) and \(TricA\), respectively). \(VPulm\) was obtained from the right parasternal short-axis view of the right ventricular outflow tract at the aortic valve level with the sample gate positioned in the pulmonary artery just distal to the pulmonic valve; \(VAo\) was obtained from left parasternal apical five-chamber view with the sample gate positioned in the ascending aorta just distal to the aortic valve and sinus of Valsalva. Mitral inflow velocities were obtained from the left parasternal apical four-chamber view with the sample gate positioned at the tips of the mitral valve leaflets when they are wide open; tricuspid inflow velocities were obtained from left parasternal view between apical four-chamber and
transverse view to optimize the view on tricuspid valve opening, with the sample gate positioned at the tips of the tricuspid valve leaflets when they are wide open. No angle corrections were needed as parallel alignment of the Doppler gate was possible in all dogs. Regurgitations through each of these four valves were subjectively quantified from colour Doppler profiles. Aortic and pulmonic valve regurgitations were evaluated from the above described views for spectral Doppler measurements. Mitral and tricuspid valve regurgitations were evaluated from the above described views for spectral Doppler measurements as well as from the right parasternal long-axis four-chamber view. The largest regurgitant jet was withheld. Mitral valve regurgitations for example were quantified as trivial regurgitations (jets not extending more than 1 cm past the mitral valve annulus), mild regurgitations (jets occupying < 20% of the atrium), moderate regurgitations (jets occupying 20-50% of the atrium) and severe regurgitations (jets occupying > 50% of the atrium) (Boon, 1998). Cardiac output (CO) was measured from the aortic flow profiles with Doppler envelope tracing, with CO (l/min) = \(6\pi(Ao/2)^2 V_{\text{mean}}\) with Ao in cm from right parasternal short-axis view and \(V_{\text{mean}}\) in m/s.

The following parameters were calculated: LA/Ao, PEP/LVET, fractional shortening FS % = \[(LVDd–LVDs)/LVDd\]100, left ventricular ejection fraction LVEF % = \[(LVDd^3–LVDs^3)/LVDd^3\]100. End systolic volume index (ESVI) was calculated according to the corrected Teichholz formula: ESVI (ml/m²) = \((7LVDs^3)/(2.4+LVDs)\text{BSA}\), with LVDs in cm and BSA in m² (Teichholz et al., 1976). Velocity of circumferential fibre shortening (VcF) was calculated as VcF (cm/s)= \((LVDd–LVDs)/(LVDd \times LVET)\) with LVDd and LVDs in cm and LVET in s. Stroke volume (SV) was calculated as SV (ml/beat) = \((CO/HR)1000\). Body surface area (BSA) was calculated as BSA (m²) = \((10.1BW^{2/3})/10^4\), with body weight (BW) expressed in grams (Owen, 1983).

The Whippet echocardiographic measurements were compared with the expected values for general population previously reported (Boon et al., 1983; Cornell et al., 2004).


**Statistical analysis**

First, a paired Student’s t-test was used to evaluate whether the observed M-mode measurements (IVS, LVD, LVW and EPSS), parameters of function (FS, PEP, LVET, PEP/LVET, VcF) and HR differed significantly from the reference values (Boon et al., 1983; Cornell et al., 2004).

Linear regression analyses were performed after logarithmic transformation of the data. The coefficients of the allometric equation \( Y = aM^b \) as well as the lower and upper limits of the 95% prediction interval were calculated for each of the BW-dependent M-mode and 2D measurements as described previously (Cornell et al., 2004). In this equation, “\( Y \)” represents a measure of heart size, “\( M \)” is BW, and “\( a \)” and “\( b \)” are parameters. Finally, Bland-Altman plots were made for the observed and expected LVWd.

Second, the percentage of dogs that fell out the reference ranges was determined (Cornell et al., 2004). This percentage was further subdivided in dogs that fell below and above the reference range.

Finally, males were compared with females, race pedigree dogs were compared with show pedigree dogs, and within the race pedigree lines, trained dogs were compared with untrained dogs, using analysis of variance, both in a univariate model and in a multivariate model with weight, age and regurgitation as covariates. The difference in the occurrence of mitral valve regurgitations between race and show pedigree lines was compared by the \( \chi^2 \)-test. All analyses were carried out at the 5% significance level.

**Results**

**Comparison of observed echocardiographic measurements to previously reported reference values**

Mean BW, HR, M-mode and 2D measurements of all dogs are presented in Table 1. Functional parameters are presented in Table 2, and Doppler derived parameters are presented in Table 3.
Table 1: Body weight, body surface area, heart rate, M-mode and two-dimensional (2D) measurements in 105 Whippets

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>Mean ± 2 SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Weight (kg)</td>
<td>13.2</td>
<td>2.1</td>
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<td>9.3 - 17.2</td>
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<tr>
<td>Body Surface Area (m²)</td>
<td>0.56</td>
<td>0.06</td>
<td>0.44 - 0.68</td>
<td>0.45 - 0.68</td>
</tr>
<tr>
<td>Heart Rate (bpm)</td>
<td>93.9</td>
<td>22.7</td>
<td>48.5 - 139.3</td>
<td>54.0 - 158.0</td>
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<td>M-Mode (mm)</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>IVSd</td>
<td>9.4</td>
<td>1.2</td>
<td>7.0 - 11.8</td>
<td>7.1 - 12.9</td>
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<tr>
<td>LVDd</td>
<td>37.3</td>
<td>3.8</td>
<td>29.7 - 44.8</td>
<td>25.7 - 47.5</td>
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<tr>
<td>LVWd</td>
<td>8.8</td>
<td>1.1</td>
<td>6.6 - 10.9</td>
<td>6.4 - 11.5</td>
</tr>
<tr>
<td>IVSs</td>
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<td>1.5</td>
<td>9.0 - 15.1</td>
<td>9.0 - 15.5</td>
</tr>
<tr>
<td>LVDs</td>
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<td>3.6</td>
<td>19.8 - 34.1</td>
<td>17.0 - 36.1</td>
</tr>
<tr>
<td>LVWs</td>
<td>12.4</td>
<td>1.5</td>
<td>9.3 - 15.4</td>
<td>8.6 - 17.2</td>
</tr>
<tr>
<td>EPSS</td>
<td>4.2</td>
<td>1.4</td>
<td>1.4 - 7.1</td>
<td>0.4 - 9.2</td>
</tr>
<tr>
<td>2D</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ao(sa) (mm)</td>
<td>19.0</td>
<td>1.7</td>
<td>15.7 - 22.3</td>
<td>14.8 - 24.0</td>
</tr>
<tr>
<td>LA(sa) (mm)</td>
<td>26.5</td>
<td>3.2</td>
<td>20.2 - 32.8</td>
<td>18.4 - 33.7</td>
</tr>
<tr>
<td>LA/Ao</td>
<td>1.4</td>
<td>0.1</td>
<td>1.1 - 1.7</td>
<td>1.1 - 1.7</td>
</tr>
<tr>
<td>LA(la) (mm)</td>
<td>32.0</td>
<td>2.8</td>
<td>26.5 - 37.6</td>
<td>23.5 - 38.7</td>
</tr>
</tbody>
</table>

M-mode measurements: IVSd: interventricular septal thickness in diastole; LVDd: left ventricular internal diameter in diastole; LVWd: left ventricular wall thickness in diastole; IVSs: interventricular septal thickness in systole; LVDs: left ventricular internal diameter in systole; LVWs: left ventricular wall thickness in systole; EPSS: E-point to septal separation.

Table 2: Functional Parameters in 105 Whippets

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>SD</th>
<th>Mean ± 2SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>FS (%)</td>
<td>27.7</td>
<td>5.2</td>
<td>17.4 - 38.1</td>
<td>18.1 - 39.2</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>61.3</td>
<td>8.1</td>
<td>45.1 - 77.5</td>
<td>44.7 - 77.3</td>
</tr>
<tr>
<td>ESVI (ml/m²)</td>
<td>48.9</td>
<td>13.9</td>
<td>21.1 - 76.6</td>
<td>18.5 - 83.6</td>
</tr>
<tr>
<td>PEP (ms)</td>
<td>51.9</td>
<td>9.7</td>
<td>32.5 - 71.3</td>
<td>35.0 - 85.0</td>
</tr>
<tr>
<td>LVET (ms)</td>
<td>167.2</td>
<td>22.1</td>
<td>123.0 - 211.4</td>
<td>125.0 - 255.0</td>
</tr>
<tr>
<td>PEP/LVET</td>
<td>0.314</td>
<td>0.059</td>
<td>0.196 - 0.432</td>
<td>0.159 - 0.457</td>
</tr>
<tr>
<td>VcF (circ/s)</td>
<td>1.69</td>
<td>0.39</td>
<td>0.91 - 2.47</td>
<td>0.98 - 3.05</td>
</tr>
</tbody>
</table>

FS: fractional shortening; LVEF: left ventricular ejection fraction; ESVI: end systolic volume index; PEP: aortic pre-ejection period; LVET: left ventricular ejection time; VcF: velocity of circumferential fibre shortening.

Table 3: Doppler derived parameters in Whippets

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>Mean ± 2*SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic velocity (m/s)</td>
<td>105</td>
<td>1.39</td>
<td>0.25</td>
<td>0.90 - 1.89</td>
<td>0.78 - 2.13</td>
</tr>
<tr>
<td>Pulmonic velocity (m/s)</td>
<td>105</td>
<td>1.14</td>
<td>0.22</td>
<td>0.69 - 1.59</td>
<td>0.61 - 1.81</td>
</tr>
<tr>
<td>Mitral E (m/s)</td>
<td>105</td>
<td>0.77</td>
<td>0.13</td>
<td>0.51 - 1.02</td>
<td>0.48 - 1.08</td>
</tr>
<tr>
<td>Mitral A (m/s)</td>
<td>105</td>
<td>0.50</td>
<td>0.09</td>
<td>0.33 - 0.68</td>
<td>0.30 - 0.80</td>
</tr>
<tr>
<td>Tricuspid E (m/s)</td>
<td>105</td>
<td>0.75</td>
<td>0.15</td>
<td>0.45 - 1.05</td>
<td>0.45 - 1.52</td>
</tr>
<tr>
<td>Tricuspid A (m/s)</td>
<td>105</td>
<td>0.49</td>
<td>0.11</td>
<td>0.26 - 0.71</td>
<td>0.25 - 1.01</td>
</tr>
<tr>
<td>Cardiac output (l/min)</td>
<td>90</td>
<td>4.8</td>
<td>1.3</td>
<td>2.2 - 7.3</td>
<td>1.9 - 7.7</td>
</tr>
<tr>
<td>Stroke volume (ml/beat)</td>
<td>90</td>
<td>49.2</td>
<td>11.0</td>
<td>27.2 - 71.3</td>
<td>24.2 - 74.7</td>
</tr>
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</table>

The coefficients of the allometric equation \( Y = aM^b \) were calculated for each of the BW-dependent M-mode and 2D measurements (see Table 4). These coefficients can be used to reconstruct normal M-mode and 2D average values for Whippets of varying weights. For example, the LVDd for a 10 kg Whippet can be calculated as LVDd = 16.212 x 10^{0.323} = 34.1 mm. These M-mode and 2D average values together with their 95% prediction interval are shown in Table 5. The slope of the regression line “b” is similar to what was previously
reported (Cornell et al., 2004), although the dogs in our study only represent a narrow range in body weight.

Table 4: Coefficients of the allometric equation $Y = aM^b$ for each of the body weight-dependent M-mode or two-dimensional (2D) measurements

<table>
<thead>
<tr>
<th>M-mode</th>
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<tbody>
<tr>
<td>IVSd</td>
<td>3.770</td>
<td>0.352</td>
</tr>
<tr>
<td>LVDd</td>
<td>16.212</td>
<td>0.323</td>
</tr>
<tr>
<td>LVWd</td>
<td>3.490</td>
<td>0.355</td>
</tr>
<tr>
<td>IVSs</td>
<td>5.383</td>
<td>0.311</td>
</tr>
<tr>
<td>LVDs</td>
<td>9.819</td>
<td>0.390</td>
</tr>
<tr>
<td>LVWs</td>
<td>5.239</td>
<td>0.332</td>
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<table>
<thead>
<tr>
<th>2D</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Ao(sa)</td>
<td>9.278</td>
<td>0.277</td>
</tr>
<tr>
<td>LA(sa)</td>
<td>11.017</td>
<td>0.339</td>
</tr>
<tr>
<td>LA(la)</td>
<td>14.241</td>
<td>0.314</td>
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</table>

M-mode measurements: IVSd: interventricular septal thickness in diastole; LVDd: left ventricular internal diameter in diastole; LVWd: left ventricular wall thickness in diastole; IVSs: interventricular septal thickness in systole; LVDs: left ventricular internal diameter in systole; LVWs: left ventricular wall thickness in systole; EPSS: E-point to septal separation.

Table 5: Reconstruction of normal M-mode and two-dimensional average values and 95% prediction intervals for Whippets of varying weights

<table>
<thead>
<tr>
<th>BW</th>
<th>IVSd</th>
<th>LVDd</th>
<th>LVWd</th>
<th>IVSs</th>
<th>LVDs</th>
<th>LVWs</th>
<th>AO</th>
<th>LA (sa)</th>
<th>LA (la)</th>
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<tr>
<td>7.0</td>
<td>7.5</td>
<td>30.4</td>
<td>7.0</td>
<td>9.8</td>
<td>21.0</td>
<td>10.0</td>
<td>15.9</td>
<td>21.3</td>
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<tr>
<td></td>
<td>5.9-9.5</td>
<td>25.2-36.5</td>
<td>5.6-8.7</td>
<td>7.7-12.5</td>
<td>16.3-27.0</td>
<td>7.9-12.6</td>
<td>13.6-18.6</td>
<td>17.0-26.7</td>
<td>22.6-30.5</td>
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<td>5.8-9.1</td>
<td>8.1-13.0</td>
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</table>

BW: body weight in kg.

M-mode measurements (in mm): IVSd: interventricular septal thickness in diastole; LVDd: left ventricular internal diameter in diastole; LVWd: left ventricular wall thickness in diastole; IVSs: interventricular septal thickness in systole; LVDs: left ventricular internal diameter in systole; LVWs: left ventricular wall thickness in systole.

2D measurements (in mm): Ao(sa): aortic root diameter from short-axis view; LA(sa): left atrial diameter from short-axis view; LA(la): left atrial diameter from long-axis view.
Out of 105 dogs, no dog had aortic regurgitation and 36 (34.3%) had pulmonic regurgitation, which was mild in one and trivial in 35. Forty-five dogs (42.9%) had mitral regurgitation, which was mild in 12 and trivial in 33. Finally, 29 dogs (27.6%) had tricuspid regurgitation, which was mild in 4 and trivial in 25. Thirteen of 105 dogs had slight mitral valve thickening (only the central part of the septal leaflet) without any degree of prolapse. Seven of these 13 dogs (53.8%) had trivial regurgitation, whereas six (46.2%) had mild regurgitation. This means that six dogs with mild mitral regurgitation had no remarkable changes to their mitral valve. Only three of the 12 dogs with mild mitral regurgitation had a systolic murmur with point of maximal intensity at the level of the mitral valve, one with a grade 2/6 murmur and two with a grade 3/6 murmur. The 12 dogs with mild mitral regurgitation were all previously trained and/or racing dogs from race pedigree lines, except one dog out of crossed race and show pedigree lines, between 5 and 14 years old (64, 78, 86, 87, 88, 99, 107, 123, 124, 140 and 169 months old). The mitral valve thickening in these dogs occurred in the dogs of 64, 86, 107, 123, 140 and 169 months of age.

Compared with published regression equations, adjustment based on BSA (Boon et al., 1983), the Whippet values for IVS in diastole and LVD and LVW in diastole and systole were significantly higher ($P < 0.0001$), as was EPSS ($P = 0.0003$). On the other hand, IVSs, FS, PEP, LVET and VcF were significantly lower than the reference values ($P < 0.0001$). No significant difference was noted for PEP/LVET and HR compared to published values (Boon et al., 1983), although there is a tendency for Whippets to have a lower heart rate than expected. For most parameters, a marked percentage of Whippet values fell out of the reference range (see Table 6) (Boon et al., 1983).
Table 6: Percentage of Whippet values below and above published reference ranges (Boon et al., 1983; Cornell et al., 2004)

<table>
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<tr>
<th></th>
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<th>Boon %Above</th>
<th>Cornell %Below</th>
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M-mode measurements: IVSd: interventricular septal thickness in diastole; LVDd: left ventricular internal diameter in diastole; LVWd: left ventricular wall thickness in diastole; IVSs: interventricular septal thickness in systole; LVDs: left ventricular internal diameter in systole; LVWs: left ventricular wall thickness in systole; EPSS: E-point to septal separation; HR: heart rate; FS: fractional shortening; PEP: aortic pre-ejection period; LVET: left ventricular ejection time; VcF: velocity of circumferential fibre shortening.

Compared with the allometric equations (Cornell et al., 2004), the Whippet values for IVS, LVD, and LVW in diastole and systole were significantly higher than those expected ($P < 0.0001$), and none of these values fell below the reference range (Cornell et al., 2004). The percentage of values which fell above the reference range predicted by the allometric equations however, is for most parameters smaller than the percentage obtained from the regression equations based on BSA (Table 6 and Fig. 1) (Boon et al., 1983; Cornell et al., 2004).
The Bland-Altman plots clearly show that the discrepancy between the observed and expected LVWd increases with increasing body surface area (Boon et al., 1983) or with increasing weight (Cornell et al., 2004) (Fig 2).

Finally, comparing the Whippet ESVI to the maximum value of 30 ml/m² (Knight, 1995), 96 dogs (91.4%) had a higher value, and only 9 dogs (8.6%) had a value below this maximum value.

Figure 1: Comparison of Whippet left ventricular wall thickness in diastole (LVWd) observed values to previously published reference ranges. Data in the left panel are from Boon et al. (1983) and in the right panel from Cornell et al. (2004).

Individual values for the LVWd of the 105 Whippets in this study (dots) are compared with the regression line and 95% confidence interval of LVWd according to Boon et al. (1983) (left panel) and to the regression line and 95% prediction interval of LVWd according to Cornell et al. (2004) (right panel).
Figure 2: Bland-Altman plots of Whippet left ventricular wall thickness in diastole (LVWd) observed values compared with expected values from Boon et al. (1983) (left panel) and Cornell et al. (2004) (right panel)

Dotted lines represent the mean difference between the observed LVWd and the LVWd given by Boon et al. (1983) (left panel) / Cornell et al. (2004) (right panel).
Dashed lines in the left panel represent the 95% confidence interval of the difference between the observed LVWd and the LVWd given by Boon et al. (1983) (left panel).
Dashed lines in the right panel represent the 95% prediction interval of the difference between the observed LVWd and the LVWd given by Cornell et al. (2004) (right panel).

Comparison between male and female dogs
In the univariate model, in the female dogs, a significantly lower value was observed for IVS and LVW in diastole and systole, Ao, LA(sa), LA(la), PEP/LVET, VPulm, TricE, CO and SV ($P < 0.05$). However, there was also a statistically significant difference in BW, males weighing on average $14.5 \pm 1.8$ kg (range 9.6 to 17.2 kg) and females $11.9 \pm 1.5$ kg (range 9.3 to 14.7 kg). In the multivariate model with weight, age and regurgitation as covariates, females had a significantly larger LVD in diastole and systole ($P = 0.0054$ and $P = 0.0188$, respectively).
respectively), a significantly higher EPSS ($P = 0.0204$), LVET ($P = 0.0367$), ESVI ($P = 0.0227$) and a significantly lower VPulm ($0.0258$) and VcF ($P = 0.0469$), with no significant difference any longer for CO and SV.

Comparison between race and show pedigree dogs

Eighty-nine dogs (43 males and 46 females) came out of race pedigree lines, and 10 dogs (four males and six females) came out of show pedigree lines. Six dogs came out of crosses between these two pedigree lines and were excluded from this analysis. The mean age and weight of the race pedigree dogs was $59.9 \pm 39.0$ months and $13.2 \pm 2.1$ kg. The mean age and weight of the show pedigree dogs was $58.8 \pm 44.3$ months and $13.5 \pm 2.3$ kg. In race pedigree dogs, 43 dogs (48.3%) had mitral regurgitation, which was mild in 11 and trivial in 32. In show pedigree dogs, in contrast, only one previously trained dog (10%) had mitral regurgitation, which was trivial. The occurrence of mitral regurgitations was significantly higher in race pedigree dogs compared with show pedigree dogs ($p = 0.033$).

In the univariate model, only LA(sa) and MitrE were significantly different, LA(sa) being significantly larger in race pedigree dogs ($P = 0.022$) and MitrE being significantly lower in race pedigree dogs ($P = 0.0041$). There was also a tendency for Ao and LVET to be higher in race pedigree dogs ($P = 0.068$ and $P = 0.081$, respectively). In the multivariate model with weight, age and regurgitation as covariates, LVDd ($P = 0.0159$), Ao ($P = 0.0063$), LA(sa) ($P = 0.0067$) and LVET ($P = 0.0263$) were significantly higher in race pedigree dogs, and MitrE was significantly lower in race pedigree dogs ($P = 0.0036$). There was a tendency for LA(la), LA/Ao and EPSS to be higher in race pedigree dogs ($0.0989$, $P = 0.0575$ and $P = 0.0895$, respectively).

Comparison between trained and untrained dogs within the race pedigree line

Sixty-two dogs (32 males and 30 females) were in active training for $30.6 \pm 22.8$ months (range 2-78 months), weighing $13.5 \pm 2.0$ kg and aged $46.6 \pm 23.5$ months. Six dogs (4 males and 2 females) were not yet in training, weighing $12.6 \pm 2.5$ kg and aged $14.8 \pm 6.8$ months. Age differed significantly between trained and untrained dogs ($P = 0.0002$). In the univariate model, LVDs, LA(sa) and ESVI were significantly larger in the trained dogs, with $P = 0.013$, $P = 0.042$, and $P = 0.031$, respectively. Furthermore, trained dogs had a significantly lower VcF compared with untrained dogs ($P = 0.0089$). In the multivariate model with weight, age and regurgitation as covariates, LVDs and LA(sa) remained significantly larger in the trained
dogs compared with the untrained dogs ($P = 0.045$ and $P = 0.044$, respectively), and VcF remained significantly lower in the trained dogs ($P = 0.025$).

**Discussion**

Several reference ranges for echocardiographic measurements in dogs are adjusted for BW, BSA or other size measurements (Boon et al., 1983; Lombard, 1984; O'Grady et al., 1986; Goncalves et al., 2002; Brown et al., 2003; Cornell et al., 2004). Often, these reference ranges are based on various breeds of dogs as well as on mongrels, over a large weight range. However, breed, in addition to weight, is an important factor in the determination of normal M-mode variables, but only few articles describe reference ranges for a specific breed of dog (Gooding et al., 1986; Morrison et al., 1992; Page et al., 1993; Vollmar, 1999; della Torre et al., 2000; O'Leary et al., 2003). Two reference ranges were used for comparison with the Whippet values obtained in this study, being the regression equations based on BSA (Boon et al., 1983) and allometric equations (Cornell et al., 2004).

*Comparison of observed echocardiographic measurements to previously reported reference values*

Reference regression equations are based on 20 dogs (eight males and 12 females), weighing between 9.8 and 28.6 kg (mean 19.3 kg); the breeds included were one terrier cross, one English setter, one English springer, three Doberman crosses, three dingo crosses, one Beagle, four German shepherd crosses, three Golden retrievers, one Dalmatian and two unknown mixes (Boon et al., 1983). Reference allometric equations are based on retrospectively collected data from 494 dogs, weighing between 2.2 and 95.0 kg, comprising 33 Dachshunds, 57 Cavalier King Charles spaniels, 20 Italian greyhounds, 12 English cocker spaniels, 20 Whippets, 20 Greyhounds, 75 Boxers, 144 Irish wolfhounds and 113 dogs of mixed or unknown breeds. These dogs were examined by nine investigators (Cornell et al., 2004). Compared with reference values for dogs of the same weight range, the Whippets in our study had a larger LVD, a thicker LVW and IVS, and a higher EPSS (Boon et al., 1983; Cornell et al., 2004). These findings are in agreement with previous studies describing a larger heart weight/body weight ratio in other sight hounds such as Greyhounds. However, some authors only found a consistently thicker LVW in systole and diastole (Page et al., 1993), while others also found increased LVD and IVS (Snyder et al., 1995; della Torre et al., 2000). Heart rate did not differ significantly from the published reference value (Boon et al., 1983), so this
cannot explain the larger LVD (Jacobs and Mahjoob, 1988a, 1988b). The values obtained for the Whippets in this study correlate very well with other values in Whippets, although dogs in the other study were sedated (della Torre et al., 2000).

The fractional shortening, PEP, LVET and VcF were significantly lower in our Whippets compared with reference values (Boon et al., 1983). In our study, mean FS was 27.7% (range 18.1-39.2%), with 39 out of 105 dogs (37%) having a FS < 25%. In another study, 95% of all dogs had a FS > 25%; in the dogs with FS < 25%, Greyhounds were disproportionately represented, and almost half of the Greyhounds had a FS < 25% (Cornell et al., 2004). The finding that the Whippet FS was lower than expected for dogs of comparable size (Boon et al., 1983; Cornell et al., 2004) is therefore not surprising. In addition, the echocardiographic measurement of FS is subject to a number of possible error sources (Page et al., 1993).

Moreover, although FS is often used as an estimation of left ventricular global systolic function, it does not allow to detect changes in contractility when preload and/or afterload (or wall stress) are not controlled for (Blomqvist and Saltin, 1983; Fagard, 2003). In another echocardiographic study in Whippets, a mean FS value of 32% was found (della Torre et al., 2000). However these dogs were sedated using acepromazine and morphine. This intervention might have influenced preload, afterload and also contractility, making comparison difficult. In Greyhounds, FS values ranged from 25 to 36% depending on the study (Page et al., 1993; Snyder et al., 1995; Lonsdale et al., 1998; della Torre et al., 2000) also reflecting the dependence of FS on many variables. Nevertheless, the clinician should be aware of the occurrence of low FS values in Whippets at rest in order to avoid misdiagnosis of myocardial failure.

ESVI is also higher than expected in our Whippets. ESVI was calculated according to the corrected Teichholz formula: ESVI (ml/m²) = (7LVDs³)/(2.4+LVDs)BSA), with LVDs in cm and BSA in m² (Teichholz et al., 1976). As Whippets have a significantly higher LVDs than expected for their body weight (which is in part due to a lower FS than expected), and this parameter is used in a second degree relation, it is clear that the result of the equation is greater than expected.

There was a remarkable difference in the percentage of Whippet values that fell out (below or above) of the reference ranges (see Table 6, Figures 1 and 2) (Boon et al., 1983; Cornell et al., 2004). The reference range predicted by the allometric equations (Cornell et al., 2004) is much broader and the expected value for a given BW is higher due to several factors. First, that paper describes the 95% prediction interval for individual observations, which is broader than the 95% confidence interval for the mean value of an M-mode variable for all dogs of a
particular weight. Secondly, an obvious source of variability in the prior study is the diverse source of data, which were collected by many different observers using different equipments in different environments. Finally, the sample group in the prior study contained 204 sight hounds (20 Greyhounds, 20 Whippets, 20 Italian greyhounds and 144 Irish wolfhounds) out of 494 dogs (41%), in contrast to the regression equation study where no sight hounds were included (Boon et al., 1983). This could have influenced the values towards higher means. Nevertheless, it seems that the Whippet values in our study are even higher, which can be due to the fact that our population is a 100% sight hound population. It was however not determined how well the allometric equations would predict M-mode dimensions in animals that differ substantially from the sample group, and as observed for our data, it cannot be extrapolated to all breeds of dogs (Cornell et al., 2004).

**Comparison between male and female dogs**

Male dogs had significantly higher IVS, LVW, Ao, LA(sa), LA(la), CO and SV than female dogs. However, these are BW-related parameters, and after multivariate analysis with weight, age and regurgitation as covariates, females had a significantly larger LVD in diastole and systole, and a significantly higher EPSS and ESVI. These findings are in accordance with an earlier study in training Greyhounds, where female training Greyhounds had a significantly greater IVSs, LVD and LVW in diastole and systole, Ao, FS and EPSS following normalization to BW (Lonsdale et al., 1998). A possible explanation for this is the larger mean heart weight/body weight ratio for females compared with males (Steel et al., 1976; Pape et al., 1984). In contrast, in horses, males had a significantly larger weight-adjusted LV mass and LVDd compared with females (Buhl et al., 2005; Young et al., 2005). Furthermore, no gender difference was found after allometric scaling in humans (George et al., 1999).

**Comparison between race and show pedigree lines**

Dogs of race pedigree lines had a significantly larger LA(sa) than dogs of show pedigree lines, and there was also a tendency for Ao to be higher in race pedigree dogs. Race pedigree dogs also had a significantly higher prevalence of mitral valve regurgitations. However, LA(sa) remained significantly higher in race pedigree dogs after multivariate analysis with weight, age and regurgitation as covariates.

Several articles in humans report the influence of training and ageing on mitral and tricuspid valve regurgitation. Grossly, valves become thicker and more opaque with advancing age. These changes are both genetically determined and age related. Longstanding mechanical
stress also may play a role in producing regurgitation. The left-sided valves, aortic and mitral, are exposed to high pressures and may therefore undergo degenerative changes earlier than right-side valves (Akasaka et al., 1987; Yoshida et al., 1988; Klein et al., 1990). Moreover, one article reports that the prevalence of both mitral and tricuspid regurgitation in Thoroughbred horses are subjected to athletic training. Prior to training, the prevalence of mitral regurgitation murmurs was 7.3% and the prevalence of tricuspid regurgitation murmurs was 12.7%. After 9 months of training, the prevalence proportions increased to 21.8% and 25.5% respectively (Young and Wood, 2000). Studies by pulsed Doppler echocardiography in man have also shown that atrioventricular valvular regurgitation is detected more commonly in endurance-trained athletes compared with sedentary controls, and that it did not imply structural valvular abnormalities (Pollak et al., 1988; Douglas et al., 1989; Oakley, 2001). These reports are in agreement with our findings that mitral regurgitations are more common in trained dogs from race pedigree lines.

**Comparison between trained and untrained dogs within the race pedigree lines**

There has been debate whether the higher heart weight/body weight ratio in sight hounds or other working dogs is an influence of training, a genetic influence, or both. In humans, a distinction is made between the effects on the heart of isometric (resistance) versus isotonic (endurance) training, the former inducing a concentric hypertrophy with a thicker LVW and IVS without LV dilation, and the latter inducing an eccentric hypertrophy with LV dilation and proportional increase in LVW and IVS thickness (Blomqvist and Saltin, 1983; Huston et al., 1985; Fagard, 1996; Oakley, 2001; Fagard, 2003; Sharma, 2003; Maron, 2005). Many athletic endeavours, as well as the Whippet training, are a combination of isometric and isotonic work, and thus may produce a combination of both morphologic patterns (Blomqvist and Saltin, 1983; Huston et al., 1985; Fagard, 1996; Oakley, 2001; Fagard, 2003; Sharma, 2003; Maron, 2005). Several articles describe various influences of training on the canine heart. The most consistent finding throughout different studies is a higher heart weight/body weight ratio in trained dogs as compared with untrained control dogs of the same breed or BW range. This could in part be due to a 50% thicker LVW in these trained Greyhounds (Carew and Covell, 1978; Barnard et al., 1980). Others reported a 30% higher LV weight to BW ratio in trained compared with control mongrel dogs (Riedhammer et al., 1976), which is similar to another study reporting that the exercise program resulted in an elevation in LV weight and LVW thickness, and a significantly lower HR at rest and at submaximal work loads in trained mongrel dogs (Barnard et al., 1980).
In contrast to the previous references, several articles report no significant difference in LVW thickness, LV mass or heart weight/body weight ratio between trained, detrained and control Greyhounds, although all variables were significantly higher in all groups compared to mongrel dogs of comparable BW (Rippe et al., 1982; Pape et al., 1984, 1986; Schoning et al., 1995). This suggests that LV hypertrophy in racing Greyhounds reflects a genetic trait rather than a response to training. Moreover, the exercise component may be too small and the individual variability too great to show difference by comparing small groups of different animals (Rippe et al., 1982; Pape et al., 1984, 1986; Schoning et al., 1995). In addition, no significant difference in LV mass was found between the exercise and sedentary group of Beagles (Ritzer et al., 1980).

It should be emphasized that two articles reviewing previous results of research on exercise-induced cardiac hypertrophy reveal that a number of problems associated with the measurement techniques and methodology cast some doubt on the validity of the conclusions that both animal and human research has provided a strong argument in favour of a physiological cardiac hypertrophy as an outcome of chronic exercise (George et al., 1991; Perrault and Turcotte, 1994).

Another possible influence of training on the heart is LV dilation. One study on Greyhounds reported significantly larger echocardiographic parameters for trained compared with untrained Greyhounds (Lonsdale et al., 1998), while another reported a LV dilation of approximately 30% in hearts of trained Greyhounds compared with normal dogs of similar BW (Carew and Covell, 1978; Barnard et al., 1980). Another study supports this finding, reporting a significant increase in ventricular volume between the exercise and sedentary group of Beagles (Ritzer et al., 1980). In these Beagles, no significant difference in resting HR between the exercised and the sedentary Beagles was found (Ritzer et al., 1980). This is in accordance with the findings in our study, where the trained Whippets had a significantly larger LVD and LA compared with the untrained dogs, without a significant difference in HR. In contrast, lowering of the HR at rest and during standard work load was reported by several authors (Wyatt and Mitchell, 1974; Stone, 1977; Barnard et al., 1980). This lowering of the heart rate might explain the larger LVD for trained dogs in several studies, as it has previously been described that cycle length had a significant influence on LVD in clinically normal dogs, in a way that, as cycle length increases (and thus HR decreases), LVD increases (Jacobs and Mahjoob, 1988a, 1988b).
Conclusions

We confirm that Whippets have a larger LVD, a thicker IVS and LVW and a lower FS than expected for dogs of comparable body weight. The clinician should be aware of these specific differences in Whippets to avoid misdiagnosis of cardiac dilation, hypertrophy, and/or myocardial failure in these dogs. The values reported in this study can be used as reference values specific for Whippets.
References


SECTION IV

GENERAL DISCUSSION
**General discussion**

This thesis studied the clinical cardiological parameters in Whippets, and compared these to reference values for the overall dog population. Furthermore, the influence of pedigree lines and athletic training on these parameters was studied to determine whether the enlarged heart in Whippets is an influence of training, or a genetic trait, or both.

**Determining the parameters specific for whippets, and compare these with reference values reported for the overall dog population**

In our study on auscultation of Whippets, 58% of dogs had a soft systolic murmur, which was aortic in origin in 48% of all dogs. Only 3% of all dogs had a soft systolic murmur at the level of the mitral valve. No dog had a murmur at the level of the tricuspid valve. No significant differences were found between male and female dogs with respect to heart rate, rhythm, murmur presence, point of maximal intensity and grade.

The prevalence of systolic murmurs in Whippets in our study is lower than reported for retired racing Greyhounds (67%) (Fabrizio et al., 2006), but higher than reported for highly trained sled dogs (40 to 45%) (Constable et al., 1994; Stepien et al., 1998), although one study reported systolic murmurs in sled dogs up to 68% (Hinchcliff et al., 1997). In racehorses, the prevalence of functional systolic murmurs was reported to be up to 58%; yet, these training associated murmurs were most often due to tricuspid regurgitation (Patteson and Cripps, 1993; Marr and Reef, 1995; Kriz et al., 2000a, 2000b; Young and Wood, 2000; Young, 2003; Young et al., 2008). In human medicine, systolic murmurs are reported in 30 to 50% of highly trained athletes (Huston et al., 1985; George et al., 1991; O'Brien and Rogers, 1999).

In agreement with a study on retired racing Greyhounds, the Whippets with a murmur at the level of the aortic valve had a significantly higher aortic and pulmonic blood flow velocity and a higher cardiac output compared with dogs without a murmur, although both blood flow velocities remained within the reference values (Fabrizio et al., 2006). Murmurs are generally produced by turbulence due to an increase in blood flow velocity, which may be caused either by a narrowing of the outflow tract or by an increase in stroke volume passing through this outflow tract, or both (Celebi and Onat, 2006). However, no significant difference in aortic diameter was found between Whippets with or without a murmur at the level of the aortic valve, which means the increased velocity was rather due to a relative stenosis and not to an absolute stenosis at the level of the aortic valve. Several reports in human medicine also describe higher stroke volume and aortic flow velocity across a normal aortic valve in
children or adults with innocent murmurs (George et al., 1991; Smith, 1997; Spooner et al., 1998; O'Brien and Rogers, 1999; Celebi and Onat, 2006).

The type and origin of murmurs in the Whippet population fit the description of innocent or physiological murmurs as described in human as well as veterinary medicine: soft, early to midsystolic murmurs best heard over the left heart base (Smith, 1997; Spooner et al., 1998; Sisson and Ettinger, 1999; Moïse and Fox, 1999; Attenhofer Jost et al., 2000; Kvart and Häggström, 2002; Shub, 2003; Pelech, 2004; Biancaniello, 2005; Celebi and Onat, 2006).

Interbreed variations in **vertebral heart size** (VHS) have been described previously, and it has been suggested that it would be more reliable to determine specific values for individual breeds by studying larger numbers of dogs of each breed (Buchanan and Bucheler, 1995; Buchanan, 2000; Lamb et al., 2000, 2001). Sight hounds are known to have a higher heart weight/body weight ratio (Schneider et al., 1964; Steel et al., 1976; Pape et al., 1984, 1986; Page et al., 1993; Snyder et al., 1995), as well as larger echocardiographic parameters (interventricular septum thickness, left ventricular diameter and/or left ventricular wall thickness) (Rippe et al., 1982; Page et al., 1993; Snyder et al., 1995; della Torre et al., 2000) compared with mongrel dogs, so a larger VHS could be expected in Whippets also. Accordingly, in our study on VHS in Whippets, the mean VHS on right-to-left lateral and left-to-right lateral, as well as dorsoventral and ventrodorsal radiographs, was significantly larger than the reference values given by Buchanan and Bücheler (Buchanan, 2000). No significant differences were found between males and females, in each of the four views. A significant difference was found between right-to-left and left-to-right lateral radiographs, as well as between dorsoventral and ventrodorsal radiographs. Gravity and tilting of the heart within the thorax due to different recumbent positions influence the cardiac silhouette, but no preference was adopted for one view (Ruehl and Thrall, 1981; Suter and Lord, 1984). It is important to standardize the position of the animal, to always use the same view in all animals, and especially to make subsequent radiographs in the same manner to allow comparison (Suter and Lord, 1984).

In conclusion, in Whippets, it should be taken into account that the VHS from a left-to-right lateral view is larger than the VHS from a right-to-left lateral view, and the VHS from a ventrodorsal view is larger than the VHS from a dorsoventral view, and Whippet-specific upper limits should be used.
The third study on **electrocardiographic parameters** in Whippets revealed significant differences compared with previously reported reference values for the general dog population (Tilley, 1992). The most important differences were higher median R-wave amplitudes in leads II, CV₆LL and CV₆LU, compared with the reference values. For some parameters (P-wave amplitude, R-wave amplitude, ST-segment deflection and T-wave amplitude in lead II, R-wave amplitude in CV₆RL, CV₆LL and CV₆LU), a marked percentage of the Whippet values fell above the maximum reference values reported by Tilley (1992). No significant differences were found between males and females when adjusted for age and weight.

Voltages recorded are influenced by the distance between the electrodes and the heart, especially in the precordial leads. With left ventricular enlargement, the heart is closer to the chest wall, and due to an increased surface area and thickened walls, greater potentials are produced, which leads to greater voltages recorded. In young, emaciated, or narrow-chested dogs such as sight hounds, the criteria used for increased voltage are thus not as valid (Tilley, 1992). According to this, two studies on Greyhounds reported very high voltages, so that recording amplitudes had to be reduced to 5 mm/mV to avoid the amplitude of the waveforms to be greater than the width of the recording paper (Schneider et al., 1964; Steel et al., 1976). This is also true for humans, where increased precordial voltages are common in young, thin people, whether trained or not (Lichtman et al., 1973; George et al., 1991), and thin chest walls may partially explain higher precordial voltages in endurance runners compared with sprinters (Ikaheimo et al., 1979).

Breed, in addition to weight, is an important factor in the determination of normal M-mode variables on **echocardiography**, but only a few articles describe reference ranges for a specific breed of dog (Gooding et al., 1986; Morrison et al., 1992; Page et al., 1993; Vollmar, 1999; della Torre et al., 2000; O'Leary et al., 2003; Lobo et al., 2008). Echocardiographic parameters of Whippets from the present study, compared with two previously reported reference ranges for a mixed population of dogs (Boon et al., 1983; Cornell et al., 2004), showed a significantly larger left ventricular (LV) diameter, a thicker LV wall and interventricular septum, and a higher E-point to septal separation than expected for dogs of the same body weight range. These findings are in agreement with previous studies, reporting larger echocardiographic parameters (LV diameter, interventricular septum and/or LV wall) in other sight hounds such as Greyhounds, compared with mongrel dogs (Rippe et al., 1982; Page et al., 1993; Snyder et al., 1995; della Torre et al., 2000), as well as a higher heart
weight/body weight ratio (Schneider et al., 1964; Steel et al., 1976; Pape et al., 1984, 1986; Page et al., 1993; Snyder et al., 1995). Moreover, the values for the Whippets in our study corresponded very well with previously reported values in Whippets (della Torre et al., 2000). The fractional shortening (FS) was significantly lower in the Whippets compared with reference values (Boon et al., 1983), with 37% of dogs having a FS < 25%. This is in accordance with another study reporting 45% of the Greyhounds having a FS < 25% (Cornell et al., 2004). The lower FS in Whippets at rest, together with the larger LV diameter, could erroneously be interpreted as myocardial failure.

Confirming an earlier study on training Greyhounds (Lonsdale et al., 1998), the female Whippets in our study had a larger LV diameter and a higher E-point to septum separation and end-systolic volume index compared with males, taking weight, age and regurgitation into account. A possible explanation for this, is the larger heart weight/body weight ratio for female Greyhounds compared with males (Steel et al., 1976; Pape et al., 1984). This is in contrast to horses, where larger LV diameter and LV mass were found in males (Young et al., 2005; Buhl et al., 2005a). Furthermore, no gender difference was found in humans after allometric scaling (George et al., 1999).

In the Whippets in the present study, there was a discrepancy between the frequency of audible murmurs and the detection of valvular regurgitations on echocardiography. Mitral regurgitation was found in 45 dogs, of which only three had a systolic murmur at the level of the mitral valve; no dog had a systolic murmur at the level of the tricuspid valve, although tricuspid valve regurgitation was found in 29 dogs. This is in accordance with a study on Beagle dogs without murmurs, where the prevalence of pulmonary, mitral, aortic and tricuspid valve regurgitation was 75%, 15%, 10% and 0%, respectively (Nakayama et al., 1994). Similar findings are reported in horses, with higher valvular regurgitation frequencies compared with murmurs frequencies (Marr and Reef, 1995; Buhl et al., 2005b; Young et al., 2008). However, the prevalence of mitral and tricuspid valve regurgitation in our Whippets (42.9% and 27.6%, respectively), was higher than reported for normal Beagle dogs (Nakayama et al., 1994).
Evaluating the influence of pedigree lines and athletic training on these findings

A possible confounding effect in comparing race and show pedigree dogs, is the presence of training. Almost 70% of race pedigree dogs were in training, while 80% of the show pedigree dogs were not in training. This could have influenced the comparison between both types of dogs, and thus is a major limitation of the present study. Additionally, there was an important difference in group size, with 89 race pedigree dogs compared to 10 show pedigree dogs. Both types of dogs are slightly different in body conformation; no differences, however, were observed comparing shoulder height and weight of race and show pedigree dogs.

In the first two studies on auscultatory findings and VHS, there were no significant differences comparing race and show pedigree dogs. In the subsequent studies, on electrocardiographic and echocardiographic parameters, several differences between race and show pedigree dogs remained significant after multivariate analysis with several covariates (weight and age in the electrocardiographic study; weight, age and regurgitation in the echocardiographic study). Electrocardiographically, race pedigree dogs had a significantly higher R-wave amplitude in two precordial leads compared with the show pedigree dogs, and also a significantly lower heart rate, a longer QRS-duration and longer QT-interval. Echocardiographically, race pedigree dogs had a higher prevalence of mitral valve regurgitation, as well as a larger LV diameter, aorta and left atrium, and a longer LV ejection time. They also had a lower mitral E-peak velocity.

Comparing trained and untrained Whippets within the race pedigree lines is another limitation of this study, since gathering an equivalent number of dogs in the three groups (not yet in training, in training and ceased training) was not evident. First, there was a significant age difference between these three groups, which could have influenced certain parameters. Second, the number of dogs in training ($n = 62$) was rather large compared with the number of dogs not yet in training ($n = 6$) and the retired dogs which ceased training ($n = 21$). As there was no significant difference in auscultatory or electrocardiographic findings between dogs not yet in training and retired dogs which ceased training, we were able to combine these two groups in both studies to obtain a group of dogs not in training with a somewhat larger number of 27 dogs. However, this was not possible in the echocardiographic study, since we found significant differences between the dogs not yet in training and the retired dogs.
Comparing dogs in training and not in training, no significant differences were noted in the studies on auscultation, VHS and electrocardiography, after multivariate analysis (where appropriate). The last echocardiographic study showed significantly larger LV and left atrium diameters in the dogs in training, after multivariate analysis with weight, age and regurgitation as covariates and despite important group size difference.

Several studies report an influence of training in dogs and horses (Riedhammer et al., 1976; Carew and Covell, 1978; Barnard et al., 1980; Ritzer et al., 1980; Lonsdale et al., 1998; Stepien et al., 1998; Young, 1999; Young and Wood, 2000; Kriz et al., 2000b; Young et al., 2005; Buhl et al., 2005a, 2005b; Young et al., 2008). We clearly found different cardiac parameters compatible with the “athletic heart syndrome” in humans, as well as similar findings compared with sled dogs and race horses. This could mean that the selection towards faster dogs for about a century, has led to an unconscious selection towards larger hearts. From this study, we would suggest that the eccentric hypertrophy in Whippets is a genetic trait, more than an effect of training.

This hypothesis is strengthened by a number of studies, reporting a genetic effect on cardiac parameters. Heart weight/body weight ratio, heart score and echocardiographic LV dimensions have been reported to be higher in Greyhounds compared with mongrel dogs (Schneider et al., 1964; Steel et al., 1976; Carew and Covell, 1978; Page et al., 1993; Snyder et al., 1995).

Cox et al. (1976) stated that the large hearts in adult Greyhounds compared with mongrels, could be due to greater exercise in the Greyhound group (secondary hypertrophy), to an intrinsically (genetically determined) greater heart size in Greyhounds, or some combination of these two factors. To clarify this, they compared the heart weight/body weight ratio of newborn Greyhound puppies to newborn black and tan Coon hound puppies, and found a significantly higher ratio for the Greyhound puppies. This indicates that earlier physical training may not be a significant factor in the hemodynamic differences found between Greyhounds and mongrels, and that the greater heart size in Greyhounds is a genetically determined property of the breed.

In two other studies, heart weight/body weight ratios were nearly identical in trained and detrained greyhounds, and significantly higher in both groups compared to mongrels (Rippe et al., 1982; Pape et al., 1984). This also suggests that the LV hypertrophy in the racing Greyhound reflects a genetic trait rather than a response to training. Pape et al. (1984)
provided three possible explanations for the lack of difference between trained and detrained Greyhounds. First, the exercise component may be too small and the individual variability too great to show difference by comparing small groups \((n = 12)\) of different animals. Second, if exercise hypertrophy is a small component of overall cardiac hypertrophy in these animals, early regression might have occurred during the two to four weeks of inactivity before the control Greyhounds were euthanized. A third possible explanation is that there is no difference because regression of cardiac hypertrophy does not occur with cessation of exercise training in the Greyhound.

A third study from the same research group compared adult trained racing Greyhounds to Greyhounds completely untrained from birth. According to their previous studies, the presence of comparable heart weight/body weight ratios in the trained and untrained Greyhound adult groups in this study, again supports the hypothesis that cardiac hypertrophy in the Greyhound is congenital and not acquired through exercise and training (Pape et al., 1986). Later on, a large study on Greyhounds by Schoning et al. (1995) confirmed the similarity in heart weight/body weight ratio between racing and nonracing groups.

As Whippets and Greyhounds share a common ancestral gene pool (Parker et al., 2004), we assume that the findings in Greyhounds towards a genetically larger heart, may also be true for Whippets.

We assume that the differences between race and show pedigree dogs are in part due to an influence of training, as 70% of race pedigree dogs were in training, while 80% of the show pedigree dogs were not in training. These two parameters (race versus show pedigree lines, and trained versus untrained) are inextricably bound up with each other, which hampers the clear differentiation between pedigree lines and influence of training. As such, the difference between race and show pedigree dogs adds further weight to the hypothesis that the larger heart in Whippets in the present study is a genetic influence due to a century of selection toward faster dogs, rather than an effect of training.

Furthermore, a recent study found a mutation in the myostatin gene in Whippets, which increases muscle mass and enhances racing performance (Mosher et al., 2007). Interestingly, there was a significant positive correlation between racing grade and the frequency of dogs carrying the mutation (more dogs carrying the mutation were found in the fastest racing classes) (Mosher et al., 2007). In addition, there was also a significant difference in the
mutation genotype frequency in Whippets that participated in races versus exhibitions where dogs are judged based on their conformation. Of the racing Whippets, 16.8% were heterozygous for the mutation, while only 4.7% of Whippets competing in conformation events were heterozygous, and those dogs were reported to show poorly (Mosher et al., 2007). This is the first example of breeders unknowingly selecting for individuals with a single polymorphism that increases athletic performance.

**Limitations and weaknesses**

The most important limitations of the present study are the difficulties separating race and show dogs from trained and untrained dogs, the influence of age and the rather important difference in group sizes, as reported earlier.

Another limitation is the absence of blood pressure measurements in the Whippets. These were not done because of the difficulties to obtain reliable results in a group of dogs. Measurements are mainly influenced by stress in the individual animal and by cuff size. Ideally, the dogs should be conditioned for blood pressure measurement to be able to obtain reliable results to make comparisons between dogs. Normal blood pressure values for Greyhounds and racing hounds tend to be higher, which could induce LV hypertrophy (Egner et al., 2003). This could explain the general influence of larger R-wave amplitudes and thicker IVS and LVW for the whole Whippet population in this study, however, it would not explain the differences between race and show pedigree dogs. There is good evidence in humans as well as in veterinary medicine that training reduces resting blood pressure (Kelley and Kelley, 2000; Fagard, 2001; Cornelissen and Fagard, 2005; Barauna et al., 2005). Therefore, we do not believe that blood pressure changes could be responsible for the changes between race and show pedigree dogs.
**Recommendations for further research**

To study the influence of training on the heart of Whippets more extensively, two larger groups of dogs (one group of untrained dogs and one group of trained dogs, within the race pedigree line) would be needed, consisting of an equal proportion of males and females, and with comparable ages. However, as most of the dogs out of race pedigree lines are meant to train and race, it may not be feasible to obtain a sufficiently large group of adult, untrained, race pedigree dogs. Another possibility would be a longitudinal study, in which each dog serves as his/her own control, and could be followed from the untrained to the fully trained stage. An inconvenience of this kind of study, is the influence of age on different parameters.

**Clinical relevance**

To make the distinction between physiologic or pathologic patterns of hypertrophy in trained dogs, we suggest a few guidelines. First, it is important to register the breed, age and gender of the dog, and to determine previous athletic training and/or exercise intolerance. Physiologic cardiac adaptation is suggested when a combination of two or more of the following findings occur: a soft (mid)systolic murmur at the left heart base on auscultation, a higher VHS without signs of congestion nor obvious left or right atrial dilatation on thoracic radiography, a resting bradycardia, eventually combined with larger R-wave amplitude in one or more leads on electrocardiography, and finally, a thicker interventricular septum and LV wall, larger LV diameter, normal left atrium/aorta ratio, (low) normal FS with bradycardia on echocardiography. It would be most interesting to compare these echocardiographic findings to breed specific reference values to avoid misinterpretation of results.

**Conclusions**

In conclusion, this thesis provides reference values specific for Whippets. It is important to know that these dogs have cardiological features resembling the “athletic heart syndrome”, in order to avoid misinterpretation of their specific cardiological parameters. In addition, we identified important differences between race and show pedigree dogs. Therefore, we would suggest that the eccentric hypertrophy in Whippets in the present study is a genetic influence due to selection towards faster dogs, more than an effect of training.
References


SUMMARY
Summary

“Athletic heart syndrome” is a well-known feature in human medicine, but has been far less studied in veterinary medicine. The original “Morganroth hypothesis” in humans described different patterns of left ventricular hypertrophy in athletes participating in sports requiring primarily isotonic (endurance) or isometric (resistance) efforts. Endurance type sports result in an eccentric hypertrophy, while resistance type sports result in a more concentric hypertrophy. However, most sports are not exclusively isotonic or isometric, so the load on the heart is not purely a volume or pressure load (respectively), and intermediate cardiac adaptation results.

Whippets are sprinters during sight hound races (resistance effort), running about 350 meters in 22-24 seconds, but are trained on long distances in between races (endurance effort) to increase their aerobic capacity. If cardiac adaptation to training would occur, we would expect a larger left ventricular diameter as well as a thicker interventricular septum and left ventricular wall in these dogs. Two Whippets, presented at our clinic, were different from the overall dog population by a number of specific findings: a soft midsystolic murmur at the left heart base, high R-wave amplitude, mild to moderate hypertrophy of the interventricular septum and left ventricular wall, low fractional shortening. A differentiation between physiologic of pathologic cardiac adaptation was imperative. Knowing that sight hounds such as Greyhounds were previously reported to have larger hearts compared to other breeds of comparable weight, brought us to the potential of a physiological adaptation.

The question arose whether the findings in these two Whippets were an influence of training, a genetic influence, or a combination of both.

This led to the present study, where the aim was to determine the Whippet-specific cardiological parameters on the basis of four diagnostic methods (auscultation, thoracic radiography with measurement of the vertebral heart size, electrocardiography and echocardiography with Doppler), and to compare these with reference values reported for the overall dog population. Furthermore, comparisons were made to determine the influence of pedigree lines and athletic training on these findings.
In the **first chapter**, the auscultatory findings in 105 Whippets were described, and the influence of gender, pedigree line and training on these murmurs was evaluated.

No murmur was detected in 41.9% of dogs, whereas soft systolic murmurs were detected in 47.6% of dogs at the level of the aortic valve, in 7.6% of dogs at the level of the pulmonic valve, and in 2.9% of dogs at the level of the mitral valve. No significant differences were found between the different groups of dogs (male versus female, race versus show pedigree, in training versus not in training).

Furthermore, several blood parameters as well as echocardiographic variables were compared between dogs with a murmur at the level of the aortic valve, or dogs without a murmur. Dogs with murmur at the level of the aortic valve had a significantly higher aortic and pulmonic flow velocity, and a higher cardiac output.

We concluded that Whippets have a high prevalence of soft systolic murmurs which fit the description of “innocent murmurs”.

In the **second chapter**, the vertebral heart size of 44 Whippets was reported in four different views (left-to-right lateral, right-to-left lateral, dorsoventral and ventrodorsal), and the influence of gender, pedigree line and training on the vertebral heart size was evaluated.

The vertebral heart size from Whippets was significantly larger than the reference values, in all four views. Also, a significant difference was found between the two lateral views, as well as between the dorsoventral and ventrodorsal view. This implicates that standardisation of thoracic radiographs is important, to compare different radiographs. No significant effect of gender was found in all four views.

Furthermore, race pedigree dogs had a larger vertebral heart size than show pedigree dogs, and trained dogs had a larger vertebral heart size than untrained dogs. However, all untrained dogs were from show pedigree lines, and all but two trained dogs were from race pedigree lines, which makes it difficult to separate the effect of pedigree line from the effect of training.
We concluded that it is important to take the breed and radiographic position into account when evaluating the vertebral heart size of Whippets, to avoid overinterpretation of cardiac enlargement in these dogs.

In the third chapter, electrocardiographic parameters of 105 Whippets were reported, and the influence of gender, pedigree line and training on these parameters was evaluated.

Whippets showed some important differences compared with reference values for the overall dog population. First, R-wave amplitude in lead II and two precordial leads, was significantly higher than the reference values. Second, for P-wave amplitude, R-wave amplitude, ST-segment deflection, and T-wave amplitude in lead II; and for R-wave amplitude in CV3RL, a marked percentage of Whippet values fell above the previously published reference values.

Taking weight and age into account as confounding effect, no significant differences were found between males and females, nor between dogs in training and not in training. However, race pedigree dogs had a significantly higher R-wave amplitude in two precordial leads compared to show pedigree dogs, as well as a lower HR and longer QRS-duration and QT-interval.

These findings are similar to electrocardiographic characteristics reported in “athletic heart syndrome” in humans, as well as to findings reported in highly trained sled dogs and free ranging grey wolves.

In the fourth chapter, echocardiographic parameters of 105 Whippets were described, and the influence of gender, pedigree line and training was evaluated. Second, these parameters were used to determine the coefficients of the allometric equation \( Y = aM^b \), useful to reconstruct normal M-mode and two-dimensional average values for Whippets of varying weights.

The most important findings for the Whippets in the present study, were a significantly larger left ventricular diameter and a thicker left ventricular wall and interventricular septum than expected for dogs of the same body weight range. The fractional shortening was significantly lower than the previously published reference value, with 37% of dogs having a fractional shortening less than 25%.
Taking weight, age and regurgitation into account as confounding effects, several differences remained significant. Comparing both genders, the female Whippets in our study had a larger left ventricular diameter and a higher end-systolic volume index compared with males. Race pedigree dogs had a higher prevalence of mitral valve regurgitations, as well as a larger left ventricular diameter, aorta and left atrium, compared with show pedigree dogs. And finally, trained dogs had a larger left ventricular diameter and left atrium compared with untrained dogs.

The results of this study confirm that breed specific echocardiographic reference values are needed. The lower fractional shortening in Whippets at rest, together with the larger left ventricular diameter, could erroneously be interpreted as myocardial failure. Therefore, we propose that the normal M-mode and two-dimensional average values obtained through the coefficients of the allometric equation $Y = aM^b$ from the present study, could be used as reference values in Whippets.

**General conclusion**

In conclusion, the present study brought new insights in the Whippet-specific cardiological parameters, through different diagnostic methods. The presence of a soft systolic murmur, an enlarged vertebral heart size, heightened R-wave amplitude, or left ventricular dilatation with or without lowered fractional shortening, could erroneously lead to the diagnosis of cardiac pathology, and unnecessary withdrawal of a Whippet from training and racing. It is therefore important to be aware of these Whippet-specific findings.
SAMENVATTING
Samenvatting

In de humane geneeskunde is het “sporthart” oftewel “athletic heart syndrome” goed gekend, maar in de diergeneeskunde zijn hieromtrent slechts weinig gegevens beschikbaar. De oorspronkelijke “Morganroth-hypothese” uit de humane geneeskunde beschrijft twee verschillende patronen van linker ventrikel hypertrofie, naargelang atleten deelnemen aan sporten die hoofdzakelijk een isotone inspanning (duurtraining) of een isometrische inspanning (krachttraining) vragen. Duursporten resulteren in een excentrische hypertrofie, terwijl krachtsporten eerder resulteren in een concentrische hypertrofie. De meeste sporten bestaan echter niet uit een “zuiver” isotone of isometrische inspanning, waardoor de belasting op het hart ook niet resulteert in een (respectievelijk) zuivere volume- of drukoverbelasting, maar eerder in een gecombineerde adaptatie.

Tijdens de rennen, waarbij ongeveer 350 meter in 22-24 seconden wordt afgelegd, zijn Whippets eerder sprinters (krachttraining). Zij worden eveneens getraind op langere afstanden (duurtraining) tussen de rennen door, om hun aerobe capaciteit te verbeteren. Indien een adaptatie aan training zou optreden, wordt aldus een grotere linker ventrikel diameter in combinatie met een dikker interventriculair septum en een dikkere linker ventrikel wand verwacht. In onze kliniek werden twee Whippets aangeboden met een aantal specifieke cardiologische bevindingen, verschillend van de normale hondenpopulatie: namelijk een zacht systolisch bijgeruis met punt van maximale intensiteit ter hoogte van de linker hartbasis, een verhoogde R-golf amplitude, een milde tot matige hypertrofie van het interventriculair septum en de linker ventrikel wand, en een lage verkortingsfractie. Een onderscheid tussen fysiologische en pathologische adaptatie drong zich op. Aangezien voor windhonden, zoals Greyhounds, beschreven wordt dat zij een ruimer hart hebben vergeleken met andere rassen van eenzelfde gewicht, bracht dit ons tot een mogelijk fysiologische adaptatie.

De vraag rees of de bevindingen bij deze twee Whippets een invloed was van training, een genetische invloed, of een combinatie van beide.

Dit gaf aanleiding tot de huidige studie. Het doel was de Whippet-specifieke cardiale parameters te beschrijven aan de hand van vier verschillende diagnostische methodes (auscultatie, thoraxradiografie met bepalen van de “vertebral heart size”, elektrocardiografie en echocardiografie met Doppler), en deze te vergelijken met voordien gepubliceerde
Samenvatting

referentiewaarden, opgesteld voor de algemene hondenpopulatie. Verder werden vergelijkingen gemaakt om de invloed van afkomst (stamboomlijnen) en training op deze cardiale parameters te bepalen.

Het eerste hoofdstuk beschrijft de bevindingen bij auscultatie van 105 Whippets, en de invloed van geslacht, stamboomlijn en training op het voorkomen van bijgeruisen.

Bij 41.9% van de honden werd geen bijgeruis gedetecteerd, terwijl bij 47.6% van de honden een zacht systolisch bijgeruis ter hoogte van de aortaklep werd gedetecteerd, bij 7.6% ter hoogte van de pulmonalisklep, en bij 2.9% ter hoogte van de mitralisklep. Er werden geen significante verschillen gevonden tussen de verschillende groepen onderling (reu versus teef, renlijn versus showlijn, in training versus niet in training).

Bovendien werden ook verschillende bloedparameters en echocardiografische waarden vergeleken tussen honden met een bijgeruis ter hoogte van de aortaklep, en honden zonder bijgeruis. Honden met een bijgeruis ter hoogte van de aortaklep hadden een significant hogere bloedsnelheid ter hoogte van de aorta- en de pulmonalisklep, en een hogere cardiac output.

Tot besluit kunnen we stellen dat zachte systolische bijgeruisen vaak voorkomen bij de Whippet, en dat deze bijgeruisen vallen onder de noemer “onschuldige bijgeruisen”.

Het tweede hoofdstuk beschrijft de “vertebral heart size” van 44 Whippets, bepaald in vier verschillende opnamerichtingen (rechts laterale decubitus, links laterale decubitus, dorsoventraal en ventrodorsaal). Hier werd eveneens de invloed van geslacht, stamboomlijn en training bepaald.

De “vertebral heart size” bij Whippets was significant groter dan de referentiewaarden, in de vier opnamerichtingen. Ook werd een significant verschil gevonden tussen de twee laterale opnamerichtingen, alsook tussen de dorsoventrale en ventrodorsale opnamerichting. Standaardisatie is dus erg belangrijk bij het nemen van thorax radiografieën, teneinde opnamen onderling te kunnen vergelijken. Er werd geen invloed van geslacht gevonden in de verschillende opnamerichtingen.
Honden uit renlijnen hebben een hogere “vertebral heart size” dan deze uit showlijnen, en getrainde honden hebben een hogere waarde dan niet-getrainde honden. Echter, alle niet-getrainde honden waren honden uit showlijnen, terwijl alle getrainde honden (met uitzondering van twee) honden waren uit renlijnen. Hierdoor is de invloed van stamboomlijn en training moeilijk te ontrafelen.

Uit deze studie kunnen we besluiten dat het belangrijk is zowel het ras als de opnamerichting in acht te nemen bij het beoordelen van de “vertebral heart size” bij Whippets, om overinterpretatie van hartvergroting te voorkomen bij deze honden.

Het derde hoofdstuk beschrijft de elektrocardiografische parameters bij 105 Whippets, en bestudeert de invloed van geslacht, stamboomlijn en training op deze parameters.

In vergelijking met referentiewaarden voor de algemene hondenpopulatie, vertoonden Whippets een aantal belangrijke verschillen. Ten eerste was de R-golf amplitude in afleiding II en twee precordiale afleidingen significant groter dan de referentiewaarde. Ten tweede viel een bepaald percentage van de Whippet waarden boven de voordien gepubliceerde maximum waarden, en dit voor de P-golf amplitude, R-golf amplitude, ST-segment deflectie en T-golf amplitude in afleiding II, en voor de R-golf amplitude in CV3RL.

Er werden geen significante verschillen gevonden tussen reuen en teven, noch tussen honden in training of niet in training, rekening houdend met gewicht en leeftijd als covariaten. Er werden echter wel significante verschillen gevonden tussen honden uit renlijnen en showlijnen, waarbij honden uit renlijnen een grotere R-golf amplitude hadden in twee precordiale afleidingen, evenals een lagere hartfrequentie en een langere QRS-duur en QT-interval.

Deze bevindingen stemmen overeen met de elektrocardiografische parameters beschreven bij het sporthart bij de mens, evenals de bevindingen bij sterk getrainde sledehonden en in het wild levende grijze wolven.

Het vierde hoofdstuk beschrijft de echocardiografische parameters van 105 Whippets, en evaluateert de invloed van geslacht, stamboomlijnen en training. Deze parameters worden dan verder gebruikt om de coëfficiënten van de allometrische vergelijking \( Y = aM^b \) te bepalen,
waarmee basis M-mode en tweedimensionale waarden voor Whippets van variërend gewicht kunnen berekend worden.

De belangrijkste bevindingen bij de Whippets uit deze studie, waren een significant ruimere linker ventrikel diameter en een hypertrofie van het interventriculair septum en de linker ventrikel wand ten opzichte van de verwachte waarde voor honden van eenzelfde gewichtsklasse. De verkortingsfractie was significant lager dan verwacht, waarbij 37% van de honden een verkortingsfractie hadden kleiner dan 25%.

Bij het vergelijken van de groepen onderling, werd rekening gehouden met de invloed van gewicht, leeftijd en het voorkomen van regurgitaties. Toch werden nog een aantal significante verschillen gevonden. Whippet teven hadden een ruimere linker ventrikel diameter en een hogere eind-systolische volume index ten opzichte van reuen. Honden uit renlijnen vertoonden meer regurgitaties ter hoogte van de mitralisklep, en hadden een grotere linker ventrikel diameter, aorta en linker atrium in vergelijking met honden uit showlijnen. Tenslotte hadden getrainde honden ook een grotere linker ventrikel en linker atrium diameter in vergelijking met niet getrainde honden.

Deze resultaten bevestigen dat rasspecifieke referentiewaarden voor echocardiografie waardevol zijn. De combinatie van een lagere verkortingsfractie in rust, samen met een grotere linker ventrikel diameter, zou bij Whippets verkeerdelijk kunnen leiden tot de diagnose van myocardfalen. De basis M-mode en tweedimensionale waarden uit deze studie, bekomen door het bepalen van de coëfficiënten van de allometrische vergelijking $Y = aM^b$, kunnen gebruikt worden als referentiewaarden voor Whippets.

**Algemeen besluit**

Deze studie brengt nieuwe inzichten in de Whippet-specifieke cardioligische parameters, op basis van verschillende diagnostische methodes. Het voorkomen van een zacht systolisch bijgeruis, een verhoogde “vertebral heart size”, een verhoogde R-amplitude, of linker ventrikel dilatatie al dan niet in combinatie met een verlaagde verkortingsfractie, zou verkeerdelijk kunnen leiden tot de diagnose van myocardfalen, en dus tot het onnodig uitsluiten van een Whippet voor het trainen en rennen. Daarom is het van belang op de hoogte te zijn van deze Whippet-specifieke bevindingen.
Curriculum Vitae


Valérie Bavegems is auteur of mede-auteur van 13 wetenschappelijke publicaties. Tevens heeft ze verschillende posters en abstracts gepresenteerd op internationale en nationale wetenschappelijke congressen, en heeft ze vele postuniversitaire opleidingen gegeven voor practici.
BIBLIOGRAPHY
Publications


Oral presentations, abstracts and posters


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