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Prevalence and diagnostic characteristics of non-clinical mitral regurgitation murmurs in North American Whippets

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KEYWORDS
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Abstract *Objectives:* To assess the prevalence of functional ejection murmurs and murmurs of mitral regurgitation (MR) due to myxomatous mitral valve disease in healthy whippets; to assess the diagnostic value of auscultation to detect MR; and investigate the relationship between age and presence of echocardiographically documented MR (MR_{echo}).
Animals: A total of 200 healthy client-owned Whippets, recruited at national shows between 2005 and 2009 were involved in this study.
Methods: Cross-sectional study. Dogs were examined by auscultation by one examiner and Doppler echocardiography by another, and results were compared. Prevalence of types of murmurs and MR_{echo} were calculated and correlated to age. Accuracy of auscultation to predict MR_{echo} was calculated.
Results: Left-sided systolic heart murmurs were detected in 185/200 (93%) of dogs. Left apical systolic murmurs (L_{apex}) were detected in 57/200 (29%) and left basilar systolic murmurs (L_{base}) in 128/200 of the dogs (64%). MR_{echo} was present in 76/200 (38%) dogs. Prevalence MR_{echo} was correlated with age ($r = 0.96$, p=0.0028). Mitral regurgitation detected by echocardiography was present in 12/78 (15%) of the dogs $\leq$ 2 years of age and in 59% of the dogs at 7–8 years old. Detection of L_{apex} predicted MR_{echo} with sensitivity 65%, specificity 94%, positive predictive value 86%, and negative predictive value 81%; and accuracy improved when only dogs with more intense L_{apex} (grade $\geq$ 3/6) were considered.

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Conclusions: Systolic murmurs are common in North American Whippets and this breed exhibits a high prevalence of MR_{echo}, which may be documented at a relatively early age. Whippets with non-clinical MR_{echo} may not be identifiable by auscultation alone; echocardiographic examination may be required to exclude a diagnosis of MR. Louder heart murmurs allow more accurate localization in this population.

Abbreviations

L_{apex}	left apical systolic murmur
L_{base}	left basilar systolic murmur
LA	left atrium
LR	likelihood ratio
MMVD	myxomatous mitral valve disease
MR	mitral valve regurgitation
MR_{echo}	mitral valve regurgitation detected by echocardiography
MV	mitral valve
NPV	negative predictive value
PPV	positive predictive value
SE	sensitivity
SP	specificity

Introduction

Adult onset myxomatous mitral valvular heart disease (MMVD) resulting in valvular regurgitation is the most common form of heart disease in dogs and may account for up to 75—80% of canine heart disease cases [1]. This type of heart disease is more prevalent in some breeds, suggesting a heritable component. Genetic tests are currently lacking in these breeds, and 'screening' for this adult onset disease in breeding animals at risk is currently focused on detection of left apical systolic heart murmurs by auscultation, sometimes with additional testing by Doppler echocardiography [1—4].

'Athletic' or 'functional' heart murmurs (also called 'flow', 'physiologic', 'non-pathological' or 'innocent' murmurs) are associated with ejection of blood through normal valves and vessels. These murmurs are noted to be more common in healthy Sighthounds, athletic breeds and other breeds in some circumstances[c] [5—7]. Functional murmurs are typically loudest over the left heart base, and these systolic murmurs may be confused with the left apical systolic murmurs of mitral regurgitation (MR) [8]. Whippets are noted to be both at increased risk of MMVD [9] and to commonly have functional heart murmurs [10].

The aims of this prospective cross-sectional study were to assess the prevalence of functional ejection murmurs and of MR due to MMVD in a population of healthy North American Whippets, to assess the diagnostic value of auscultation to detect MR in this population and to investigate the relationship between age and presence of MR.

Animals, materials and methods

Dogs were prospectively recruited from a healthy population attending the American Whippet Club National Specialty between 2005 and 2009. Dogs were submitted for examination by their owners and enrolled without regard to age, breeding status, or athletic condition. Although no systematic overall health evaluation was performed, dogs with known systemic disease conditions were excluded and all dogs were without clinical signs of heart disease at the time of examination, based on owner history. Each dog contributed data from a single examination. This study was approved by the University of Wisconsin School of Veterinary Medicine Animal Care and Use Committee.

Physical examination

Cardiac auscultation was performed by one observer (RLS) blinded to any previous cardiac information known by the owner. Dogs stood at rest with their owners/handlers for auscultation, during which heart rate and presence of any heart murmurs were recorded. The most intense (i.e. highest grade) heart murmur detected per dog was used for analysis, and murmurs were characterized by timing (systolic vs. diastolic), intensity (grade 1—6 with grade 1 as the lowest detectable intensity murmur and grade 6 as a murmur audible with a stethoscope lifted slightly off the chest) and

[c] Olsen LH, Hjarback R, Pedersen HD. Physiological flow murmurs in Cavalier King Charles Spaniels (abstract). J Vet Intern Med. 2006;20(3):748.

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point of maximal intensity (right or left heart base, right or left apex). Auscultatory findings were withheld from the echocardiographer until after the echocardiographic examination.

Echocardiographic examination

All dogs had echocardiograms recorded[d] by a single operator (VLF). Complete two-dimensional, M-mode, color and spectral Doppler images and cine loops were stored on optical discs for later off-line analysis. Echocardiograms were recorded with the dogs gently restrained in right and left lateral recumbency with particular attention to color-flow Doppler images of the mitral valve (MV) and left atrium (LA) from the right parasternal long axis view and two- or four-chamber left apical views to identify any MR jets. Color settings were adjusted to provide maximal color traces without evidence of overgaining. Images were recorded from the dependent side of the dog, using typical recommended views [11]. All dogs had continuous electrocardiographic tracings during echocardiographic examination.

Diagnosis of mitral regurgitation

Dogs were diagnosed as having echocardiographically documented mitral regurgitation (MR_{echo}) if an eccentric systolic jet or multiple systolic jets were documented within the LA in the right parasternal long axis four-chamber view or left apical three or four chamber views using color Doppler mapping. Single, narrow, central regurgitation jets that extended to less than approximately 10% of the LA were not classified as MR_{echo}. Presence or absence of MR_{echo} was recorded, but no attempt to quantify MV structural changes or MR_{echo} severity was included in this study. The echocardiographic images were reviewed at a separate time point and without knowledge of the dog's identity by a single observer (RLS) blinded to the dog's identity and auscultation results at the time of echocardiographic analysis.

Statistics

Descriptive statistics were used to characterize the total population and a subset representing animals in a breeding age population. Values are presented as median [range]. Age was recorded in months, and reported in years, with <24 months of age categorized as '1 year old', ≥24 months but <36 months categorized as '2 years old', up to the '12 years old' group. Dogs ≥13 years were grouped due to low numbers (13 years, n = 4, 14 years, n = 3, 15 years, n = 3). The prevalence of MR_{echo} was calculated as the number of dogs with MR_{echo} as a proportion of the total number of dogs and by 2-year age grouping. Sensitivity, specificity, positive and negative predictive value and likelihood ratio for the presence of a left apical systolic murmur to identify MR_{echo} and the effect of murmur intensity on these parameters were calculated. Non-parametric test methods were used for all comparisons (Fisher's exact test or Mann−Whitney *U* test between groups) and data are presented as median [range]. Spearman rank correlation was used to test the relationship between age (2-year groups) and prevalence of MR_{echo}. Significance was defined as values where $p<0.05$.

Results

Two hundred dogs had complete information available for analyses. Median age of all dogs was 4 [1−15] years and median weight was 15 [9−22] kgs. One hundred four dogs out of 200 (52%) were intact (n = 79) or spayed (n = 25) females. Ninety-six dogs (48%) were intact (n = 79) or neutered males (n = 17). Left-sided systolic heart murmurs were detected in 185/200 (92.5%) of dogs examined and no murmur was heard in 15 dogs (7.5%). Left apical systolic murmurs (L_{apex}) were detected in 57/200 (29% overall, 31% of dogs with murmurs) of dogs and left basilar systolic murmurs (L_{base}) were detected in 128/200 (64% overall, 69% of dogs with murmurs). Median intensity of L_{apex} was 3/6 [1−6/6] and median intensity of L_{base} was 2/6 [1−4/6].

Seventy-six (38%) dogs in this population had MR_{echo} according to the echocardiographic criteria used in this study. Dogs with MR_{echo} were older (8 [1−15] years) than dogs without MR_{echo} (4 [1−15] years, $p<0.0001$, Fig. 1). Male/neutered male dogs were more likely to have MR_{echo}, with 50/96 (46%) male dogs affected vs. 32/104 (31%) female/spayed female dogs ($p=0.03$), but there was no difference in median age between male (4 [1−14] years) and female (2 [1−15] years, $p=0.043$) groups. Prevalence of MR_{echo} was closely correlated with age by 2 year groups ($r = 0.96$, $p=0.0028$, Fig. 2); MR_{echo} was present in 15% of dogs ≤2 years of age, in 59% of 7−8 year old dogs and in 80% of all dogs aged 13 years or older.

Detection of L_{apex} of any intensity in the population studied (n = 200) predicted the presence of MR_{echo} with sensitivity of 65%, specificity of 94%,

[d] Acuson Cypress™ System, Siemens Medical Solutions USA, Inc., Mountain View, CA 94043, USA.

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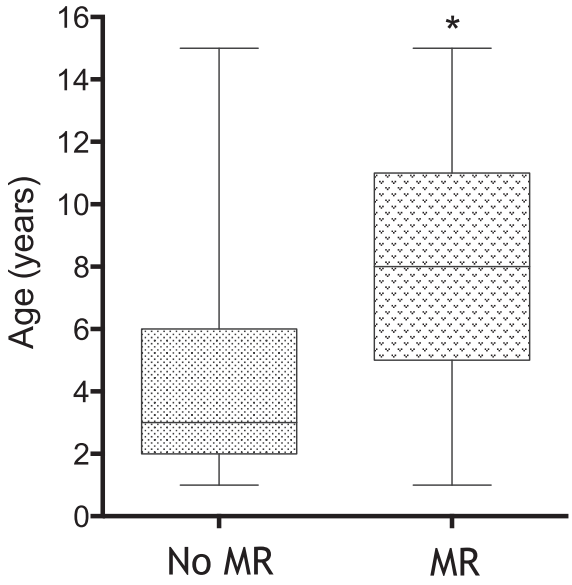

Figure 1 Box-whiskers graph showing an age comparison of dogs with and without echocardiographically documented mitral regurgitation (MR). Median (bar), interquartile range (box) and range are represented. Asterisk denotes significant difference, $p<0.0001$.

positive predictive value (PPV) of 86%, negative predictive value (NPV) of 81%, and likelihood ratio (LR) of 10.0 (Table 1). Overall concordance of findings (auscultation categorized dogs correctly as either 'MR_{echo}' or 'no MR_{echo}') was 83%. Fourteen of the 15 dogs (93%) with no murmur were correctly categorized as 'no MR_{echo}' by auscultation. Higher intensity L_{apex} (≥grade 3/6, n = 41) predicted MR_{echo} with sensitivity 93%, specificity 84%, PPV 93%, NPV 84%, and LR 5.9. Any murmur of greater intensity (≥grade 3/6) was more likely to be an accurate detector of presence or absence of MR_{echo}; when all dogs with L_{apex} or L_{base} ≥ grade 3/6 were considered (n = 61), concordance improved to 90%.

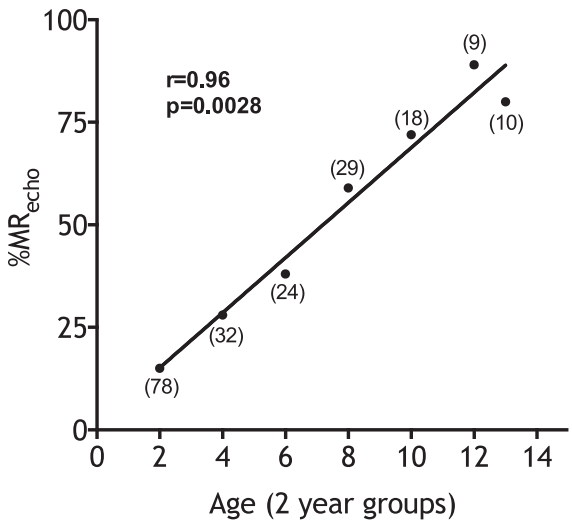

Figure 2 Spearman rank correlation of prevalence of echocardiographically documented mitral regurgitation (MR_{echo}) with age in 200 clinically healthy North American Whippets, by 2-year age groups. Numbers in parentheses indicate the total number of dogs in each 2-year age group. Highest age group, identified as 13 years, contains dogs ≥13 years (n = 4), 14 years (n = 3) and 15 years old (n = 3).

In order to assess test characteristics in a population likely to be presented for pre-breeding examination, dogs of typical breeding age (2–5 years, n = 85) were considered as a subset. Median age in this group was 3 (range: 2–5) years and 46/85 (54%) were female (n = 50) or spayed female (n = 4). There were 26 males and 5 neutered males. Six dogs (7%) did not have a heart murmur detected (Table 1). Median murmur grade in the dogs with murmurs (n = 79) was grade 2/6 [1–4/6]; 70/85 (82%) of dogs had L_{base} (2/6 [1–3/6]); and 9/85 (11%) dogs had L_{apex} (3/6 [2–4/6]). MR_{echo} was present in 18/85 dogs (21%) and there was no difference in prevalence of MR_{echo} between female/spayed female and male/neutered male dogs (p=0.46). L_{apex} predicted MR_{echo} with sensitivity 35%, specificity 98%, PPV 89%, NPV 80%, and LR 21.6 (Table 2). None of the six dogs with no murmur had MR_{echo}. Of the dogs with no murmur or L_{base} (n = 76), auscultation correctly categorized 61/76 (80%) dogs without MR_{echo}, but miscategorized 15/76 dogs (20%) with MR_{echo}. Detection of L_{apex} correctly categorized 8/9 (89%) of dogs with MR_{echo}. Overall concordance of auscultation and echo findings in this group was 81%.

Discussion

Screening programs for myxomatous mitral valve disease depend on reliable detection of true abnormality in a population at risk, and in the case of MMVD, abnormalities may be detected via auscultation, phonocardiographic examination, Doppler-echocardiographic examination, or some combination of these [4,10,12,13]. The prevalence of the disease in the population is a crucial part of the evaluation, allowing estimation of the PPV and NPV of a test as applied to a specific population, e.g. a specific breed of dog, or a specific age group. Highly sensitive detectors of MR (i.e. phonocardiography, Doppler echocardiography) may lead to overdiagnosis of MMVD when small, central MR jets are documented, even though the risk associated with these jets are unknown

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Table 1 Prevalence of heart murmurs and mitral regurgitation detectable by Doppler echocardiography in 200 healthy Whippets.

Dog group (n)	Any murmur	No murmur	L_{base} murmur	L_{apex} murmur	MR_{echo}
All dogs (200)	185 (92.5%)	15 (7.5%)	128 (64%)	57 (29%)	76 (38%)
Breeding age dogs (85)	79 (93%)	6 (7%)	70 (85%)	9 (11%)	18 (21%

L, left; MR_{echo}, mitral regurgitation detected by Doppler echocardiography.
Data is presented as number of dogs (% of group) affected.

Table 2 Test characteristics of auscultation to detect echocardiographically confirmed mitral regurgitation (MR_{echo}) in clinically normal Whippets.

Population (n)	Sensitivity	Specificity	PPV	NPV	LR	Concordance of results	*p*-Value
All dogs (200)	65%	94%	86%	81%	10.0	83%	$p<0.0001$
Murmurs $\geq$ 3/6 (61)	93%	84%	93%	84%	5.9	90%	$p<0.0001$
Breeding age[a] dogs (85)	35%	98%	89%	80%	21.6	81%	$p<0.0001$

PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.
Presence of any intensity of left apical systolic murmur was considered to be a positive test result to reflect MR_{echo}. Concordance indicates the percentage of dogs in which the results of auscultation and Doppler-echocardiographic examination agreed regarding the presence or absence of MR_{echo}.
[a] Breeding age: 2—5 years.

[12,14]. Higher intensity systolic heart murmurs are more likely to accurately detect MR_{echo} [12,13], but accurate diagnosis via auscultation may be affected by presence of concurrent abnormalities [15], observer experience, environmental noise, circulatory dynamics, ease of auscultation [12], and in some types of dogs, the prevalence of ejection, or non-pathological murmurs [6,10]. The presence of non-pathological (functional) murmurs may lead to misdiagnosis of MR if auscultation alone is used for examination, or may obscure MR murmurs if the MR murmur is less intense than concurrent functional murmurs.

The prevalence of left-sided systolic murmurs in this study population was high, with only a small proportion of examined Whippets having no heart murmur detected. A previous study of 105 European Whippets without MR found a prevalence of 'innocent' murmurs of approximately 58% [10]. The prevalence of L_{base} murmurs (64%) in our population was comparable. The overall prevalence of left-sided heart murmurs was higher because we deliberately did not exclude dogs with MR from analysis. Other study population differences that may have had an effect include differences in population size, weight, athletic conditioning or genetic background, since our study dogs were exclusively North American and generally larger than the population previously reported by Bavegems et al. in a previous echocardiographic study of a European population [16]. As is the case in other Sighthounds [6], the body conformation and general ease of auscultation of Whippets may increase the probability of detection of soft murmurs. The finding that left basilar murmurs in this study were generally of lower intensity than L_{apex} murmurs is in agreement with other studies of physiologic murmurs in dogs[c] [6,10,12] and in people, where higher intensity murmurs are more likely to be disease-related rather than functional [15].

The prevalence of MR_{echo} in the population studied was 38%, and 21% in the subset of dogs of breeding age (2—5 years). Reported prevalence of MR varies by breed, but few studies have addressed the prevalence of MR documented by echocardiography in larger populations of dogs. In previous studies, prevalence has been expressed as the percentage of dogs with typical murmurs by certain ages; 50% of dachshunds had MR murmurs by 9.4 years of age [2] and in a study of Cavalier King Charles spaniels, 50% had MR murmurs by 7.5 years of age [17]. In the current study, findings were comparable; prevalence of MR_{echo} exceeded 50% (59%) in 7 to 8-year old dogs and 72% of 9 to 10-year old dogs studied had MR, and the breeding age population prevalence of 21% reflected their younger age. Since this was a cross-sectional study and severity of MR_{echo} was not examined, the severity of the MR_{echo} and changes over time were not analyzed. The relationship between male sex and presence of MR_{echo} was significant in the general population and agrees with previous studies [9,17].

Median age of dogs with MR_{echo} was significantly higher than dogs without MR_{echo} and there was a

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relevant and close relationship between age by 2-year group and prevalence MR_{echo} ($r = 0.96$, $p=0.0028$). Age is correlated to presence of MR in many breeds, with some breeds prone to development of MV changes at earlier ages [2,17]. In our Whippet population, 15% of 78 dogs $\leq$2 years old and 21% of the 'breeding age' population had MR_{echo}, suggesting that some dogs have an early onset of MR_{echo} and age alone cannot be used to exclude the possibility of MR in this breed.

Detection of any intensity of L_{apex} murmur predicted had MR_{echo} with sensitivity of 65%, specificity of 94%, PPV of 86% and NPV of 81%. These diagnostic test characteristics are similar to those reported in a human auscultation study, in which MR_{echo} was predicted by the detection of a typical murmur with a sensitivity of 70% and a specificity of 70% [15]. In another human study of both functional and disease-related heart murmurs, the concordance of findings for auscultation and Doppler echocardiography was 77.9%, comparable to our diagnostic concordance of 82.5% [18]. The PPV of L_{apex} murmurs to detect MR_{echo} in our study improved when only more intense murmurs (grade $\geq$ 3/6) were analyzed, as did concordance of findings. Dogs in the breeding age group had a prevalence of ausculted murmurs (93%) that was similar to the overall prevalence, but the prevalence of L_{base} was much higher at 85% vs. the general population. Similarly, the prevalence of MR_{echo} was lower in the breeding age population (21% vs. 38% of overall population). In this population of breeding age animals, MR_{echo} is less likely but cannot be excluded on age alone. The low prevalence of MR_{echo} in this group renders a high PPV (89%) when L_{apex} is detected. No attempt was made in this study to quantitate the severity of MR_{echo}, so the clinical importance of any MR_{echo} detected in these dogs remain unknown; it is possible that the dogs with MR_{echo} that had L_{base} identified by auscultation (discordant findings) had MR_{echo} that was too mild to be heard or accurately localized by auscultation. If the intention of screening programs for breeding animals is to exclude dog with any degree of MR_{echo}, Doppler echocardiography would be required to detect all affected animals. When applied to the general population, our findings suggest that absence of any heart murmur is likely to indicate absence of MR_{echo} and left-sided systolic murmurs of $\geq$3/6 are likely to be localized correctly, whether they indicate the presence of MR_{echo} or the presence of a functional murmur. Further studies are necessary to investigate the severity of MR_{echo} that is clinically important or likely to reflect truly affected animals.

There are limitations in this study. The prevalence of MR_{echo} was determined in a population of clinically normal Whippets that were brought to a national show as show/performance competitors or as companions; this population may not reflect the general Whippet population. This is especially important when considering the older age groups —lower numbers of enrollees in these groups may indicate that fewer dogs in the age group are 'clinically normal' or considered healthy enough by the owners to be brought to a show. Examination of greater numbers of older dogs may have resulted in a more accurate estimation of MR_{echo} prevalence in these age groups but it remains unknown if the prevalence would have been higher or lower.

The 'gold standard' for diagnosis of MR in this study was Doppler-echocardiographic findings of an eccentric systolic jet or multiple systolic jets documented within the left atrium. Doppler echocardiography is considered to be highly sensitive for detection of MR [14], but MR jets may be more visible in either the right or left views in a given animal. We attempted to minimize this error by imaging animals from both right and left views. In people [15] and dogs [12], concern has been expressed that Doppler echocardiography may be too sensitive in detecting small MR jets that may be inconsequential. This concern may be important in Whippets in general, a breed often competing in athletic events like lure coursing or agility at national shows, but especially pertinent in the breeding age population, since younger dogs are more likely to be enrolled in highly competitive athletic events. Intensively trained human athletes have been found to have a higher prevalence of MR_{echo} than matched sedentary subjects [19,20] and these MR jets were significantly smaller (filling less than 20% of LA area) than in control subjects in one study [20]. In the current study, dogs with small, central systolic jets filling less than 10% of the LA were not classified as having MR_{echo} to limit false positive results in this athletic population, since controversy remains regarding the prognostic importance of such jets in athletic dogs with a possible breed predisposition for MMVD. No analysis of valve morphology was included in this study; addition of such information may have improved diagnosis of MV abnormalities, but our aim was to detect regurgitant mitral valve jets rather than anatomic changes that may precede MR [21]. In the setting of 'pre-breeding screening', diagnosis of disease in these patients may result in unnecessary restriction of the genetic pool [12]. Conversely, it is unknown if young animals with small, eccentric MR_{echo} jets without visible valve

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abnormalities are truly affected or have changes due to mitral valve dysplasia; thus, our estimates of prevalence must be considered indications of the prevalence of Doppler-echocardiographic abnormalities rather than disease per se. The echocardiographic gold standard for diagnosis of MMVD remains undetermined, although various criteria have been suggested [21—23].

Color Doppler mapping is setting-dependent and recognition of regurgitant jets relies on obtaining consistent views and analyzing color mapping images consistently. We attempted to minimize variability by having a single operator to obtain all images, and a different single operator to analyze all images. Finally, although ejection murmurs based on blood turbulence in the aortic root may occur whether or not MR_{echo} is present, the accuracy of categorization of dogs in this study may have been hampered by study design. Dogs with any MR_{echo} were considered 'positive' for MR, so if the loudest detected murmur was indeed an ejection murmur at the left heart base, and the LA murmur was not the loudest murmur, the dog would have been miscategorized.

The effect of auscultator experience on the accuracy of findings in differentiating disease-related and non-disease related heart murmurs has been explored [12,15,24]. A single, experienced cardiologist performed all auscultations in this study; results may vary with experience and abilities of other examiners in a similar situation [12]. No attempt was made to track or limit intraobserver variability and a 'training' effect of the auscultator or variability in auscultation conditions cannot be ruled out.

Murmurs may be miscategorized for multiple reasons: unusual jet direction may cause turbulence to be directed toward and detected at the location of the aorta [15], physiologic murmurs may vary with state of excitement or cardiac output and patients may be difficult to examine based on behavior [12]. Variations in excitement or stress level in dogs affect auscultation findings and echo findings [12,24]. In this study, owners were present to comfort the dogs during both auscultation and echocardiography, but differences in the dogs' stress level during these two procedures may have caused some variability in murmur grade or MR_{echo} appearance on Doppler examination.

All findings in this study are limited to time of a given dog's individual examination and the effect of findings on prognosis was not studied; longitudinal studies of individual dogs are needed to document the natural history of MMVD changes in Whippets.

Conclusions

Systolic murmurs are very common in North American Whippets and there is a high prevalence of MR_{echo} with a relatively early onset and close association with age in this breed. Whippets with non-clinical MR_{echo} may not be identifiable by auscultation alone due to the high prevalence of functional systolic murmurs. Auscultation alone may not be sensitive enough to differentiate murmurs indicative of MR_{echo} from functional murmurs with confidence, and Doppler-echocardiographic examination may be required to exclude a diagnosis of MR_{echo} in dogs with low intensity left-sided systolic heart murmurs. Detection of a systolic murmur of grade 3/6 or higher increases the likelihood of accuracy when differentiating murmurs reflecting MR_{echo} from functional murmurs in this population. In a breeding age population, lack of heart murmur or detection of L_{apex} may be considered fairly accurate to rule out or suspect MR_{echo}, but detection of L_{base} in Whippets aged 2—5 years does not rule out the possibility of MR_{echo}. The prognostic significance of MR_{echo} jets in young dogs requires further study.

Conflicts of Interest Statement

The authors do not have any conflicts of interest to disclose.

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References

[1] Borgarelli M, Häggström J. Canine degenerative myxomatous mitral valve disease: natural history, clinical presentation and therapy. Vet Clin Small Anim 2010;40:651—63.

[2] Olsen LH, Fredholm M, Pedersen HD. Epidemiology and inheritance of mitral valve prolapse in Dachshunds. J Vet Intern Med 1999;13:448—56.

[3] Swenson L, Häggström J, Kvart C, Juneja RK. Relationship between parental cardiac status in Cavalier King Charles Spaniels and prevalence and severity of chronic valvular disease in offspring. J Am Vet Med Assoc 1996;208:2009—12.

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[4] Atkins C, Bonagura J, Ettinger S, Fox P, Gordon S, Häggström J, Hamlin R, Keene B, Luis Fuentes V, Stepien R. Guidelines for the diagnosis and treatment of canine chronic valvular heart disease. J Vet Intern Med 2009;23:1142–50.
[5] Stepien RL, Hinchcliff KW, Constable PD, Olson J. Effect of endurance training on cardiac morphology in Alaskan sled dogs. J App Physiol 1998;85:1368–75.
[6] Fabrizio F, Baumwart R, Iazbik MC, Meurs KM, Couto CG. Left basilar systolic murmur in retired racing greyhounds. J Vet Intern Med 2006;20:78–82.
[7] Constable PD, Hinchcliff KW, Olson J, Hamlin RL. Athletic heart syndrome in dogs competing in a long-distance sled race. J App Physiol 1994;76:433–8.
[8] Côté E, Edwards NJ, Ettinger SJ, Luis Fuentes V, MacDonald KA, Scansen BA, Sisson DD, Abbott JA. Management of incidentally detected heart murmurs in dogs and cats. J Vet Cardiol 2015;17:245–61.
[9] Thrusfield MV, Aitken C, Darke P. Observations on breed and sex in relation to canine heart valve incompetence. J Small Anim Pract 1985;26:709–17.
[10] Bavegems VC, Duchateau L, Polis IE, Van Ham LM, De Rick AF, Sys SU. Detection of innocent systolic murmurs by auscultation and their relation to hematologic and echocardiographic findings in clinically normal Whippets. J Am Vet Med Assoc 2011;238:468–71.
[11] Moise NS, Fox PR. Echocardiography and Doppler imaging. In: Fox PR, Sisson D, Moise NS, editors. Textbook of Canine and Feline Cardiology. 2nd ed. Philadelphia: WB Saunders; 1999. p. 131–71.
[12] Pedersen HD, Häggström J, Falk T, Mow T, Olsen LH, Iversen L, Jensen AL. Auscultation in mild mitral regurgitation in dogs: observer variation, effects of physical maneuvers, and agreement with color Doppler echocardiography and phonocardiography. J Vet Intern Med 1999;13:56–64.
[13] Ljungvall I, Ahlstrom C, Höglund K, Hult P, Kvart C, Borgarelli M, Ask P, Häggström J. Use of signal analysis of heart sounds and murmurs to assess severity of mitral valve regurgitation attributable to myxomatous mitral valve disease in dogs. Am J Vet Res 2009;70:604–13.
[14] Perry GJ, Bouchard A. Doppler echocardiographic evaluation of mitral regurgitation. Cardiol Clin 1990;8:265–75.
[15] Jost CA, Turina J, Mayer K, Seifert B. Echocardiography in the evaluation of systolic murmurs of unknown cause. Am J Med 2000;108:614–20.
[16] Bavegems V, Duchateau L, Sys SU, De Rick A. Echocardiographic reference values in whippets. Vet Radiol Ultrasound 2007;48:230–8.
[17] Häggström J, Hansson K, Kvart C, Swenson L. Chronic valvular disease in the Cavalier King Charles Spaniel in Sweden. Vet Rec 1992;131:549–53.
[18] Bloch A, Crittin J, Jaussi A. Should functional cardiac murmurs be diagnosed by auscultation or by Doppler echocardiography? Clin Cardiol 2001;24:767–9.
[19] Macchi C, Catini C, Catini CR, Zito A, Urbano F, Miniati B, Molino Lova R, Brizzi E. A comparison between the heart of young athletes and of young healthy sedentary subjects: a morphometric and morpho-functional study by echo-color-Doppler method. Ital J Anat Embryo 2001;106:221–31.
[20] Douglas PS, Berman GO, O'Toole ML, Hiller WD, Reichek N. Prevalence of multivalvular regurgitation in athletes. Am J Cardiol 1989;64:209–12.
[21] Olsen LH, Martinussen T, Pedersen HD. Early echocardiographic predictors of myxomatous mitral valve disease in dachshunds. Vet Rec 2003;152:293–7.
[22] Zoghbi WA, Enriquez-Sarano M, Foster E, Grayburn PA, Kraft CD, Levine RA, Nihoyannopoulos P, Otto CM, Quinones MA, Rakowski H, Stewart WJ, Waggoner A, Weissman NJ. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 2003;16:777–802.
[23] Sargent J, Connolly DJ, Watts V, Mõtsküla P, Volk HA, Lamb CR, Luis Fuentes V. Assessment of mitral regurgitation in dogs: comparison of results of echocardiography with magnetic resonance imaging. J Small Anim Pract 2015;56:641–50.
[24] Höglund K, French A, Dukes McEwan J, Häggström J, Smith P, Corcoran B, Kvart C. Low intensity heart murmurs in Boxer dogs: inter-observer variation and effects of stress testing. J Small Anim Pract 2004;45:178–85.

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