

DIAGNOSTIC METHODS OF CARDIOMYOPATHY IN DOGS - OLD AND NEW PERSPECTIVES AND METHODS

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Summary: Dilated cardiomyopathy (DCM) is an important cause of morbidity and mortality especially in large breed dogs. New diagnostic methods have been developed in the past few years to diagnose the disease early and improve chances of survival. Familial predisposition to DCM in some breeds opens possibilities of the early diagnosing by genetic testing and research has been done to find the causative molecular abnormalities. Doppler echocardiography and new sensitive methods like Tissue Doppler Imaging (TDI), a 24 to 48 hours electrocardiography (Holter monitoring), and cardiac biochemical markers such as atrial natriuretic peptide (ANP), B-type natriuretic peptide (BNP), and cardiac troponin I are –among others – the most promising methods in detection of DCM.

Key words: Doberman pinscher dogs; dilated cardiomyopathy; genetics; echocardiography;

Introduction

Cardiomyopathies are diseases of the myocardium associated with cardiac dysfunction. Dilated cardiomyopathy (DCM) is characterized by dilatation and impaired contraction of the left or both ventricles (1).

DCM occurs more frequently in large and giant breed dogs (for example Doberman pinscher, Irish wolfhounds, Saint Bernard dogs, German boxers, Great Danes, German shepherds, Newfoundlands and bull-mastiffs). A relatively high prevalence has been reported in medium sized dogs also (English and American cocker spaniels and Dalmatians) (2, 3, 4). In Slovenia, most affected breeds are: Doberman pinscher, German shepherd, German boxer, Great Dane, and Rottweiler (5).

The most common form of DCM in dogs is idiopathic DCM, because many of the processes that could lead to myocardial injury in dogs remain to be determined. Causes such as genetic factors, toxic factors, immunologic and viral aetiology have been theorised upon and remain to be proved (2).

Most of the available data on the natural course of DCM development have been collected by observing Doberman pinscher dogs. DCM in Doberman pinscher dogs is a slowly progressive primary myocardial disease with a familial predisposition, which develops in two distinct stages: the first phase is a protracted (≥ 2 to 3 years long) occult phase characterised by evidence of echocardiographic and electrical deviations in the absence of clinical signs of heart disease. The echocardiographic abnormalities consist of left ventricular (LV) enlargement in systole and/or diastole that will progress to clinical phase with signs of left sided congestive heart failure (CHF). The electrical abnormality consists of the presence of ventricular premature contractions that can progress to more severe ventricular tachyarrhythmia, leading to sudden death. Approximately 30% of affected dogs die suddenly during the occult phase (2, 3). Screening is recommended for dogs with prevalence of DCM to identify dogs with cardiac abnormalities.

The diagnosis of overt DCM is not problematic, although it requires the exclusion of other cardiac, pulmonary or systemic etiologic factors of heart dilatation and hypokinesis. It is based on history and clinical findings (physical examination, ECG, radiographs, ultrasound) and other clinical tests

like haematology and biochemistry to exclude other primary or concurrent diseases (4).

The therapy and prognosis are determined in relation to the severity of CHF. The onset of clinical signs often means poor prognosis, but therapy usually prolongs life and alleviates symptoms. New studies are therefore oriented towards the early diagnosis of occult DCM.

This article reviews the latest development in the diagnostic methods of DCM in dogs to find out early changes that occur in the preclinical stage of the disease.

Echocardiography

Echocardiography is a non-invasive diagnostic method which provides valuable data concerning cardiac morphology and function. It is a highly operator-dependent diagnostic tool that relies on proper collection and interpretation of results.

Measurements of cardiac dimensions by observing chamber dimensions and wall thickness can reveal changes in geometry and dimensions because of the cardiac disease. Measurements of the left atrium (LA) and left ventricle (LV) give us insight of considerable dilation in diastole and systole. Indices of global LV systolic function, such as fractional shortening (FS) and ejection fraction (EF) can be calculated from the collected data.

The diagnosis of DCM is made on the basis of left ventricular dilatation, a lowered systolic function, and increased LV sphericity, where LV length has decreased. Breed specific echocardiographic data have been published for some breeds: Afghan hounds, beagles, German boxers, Cavalier King Charles spaniels, cocker spaniels (English), corgi (Pembroke), deerhounds, Doberman pinschers, golden retrievers, Great Danes, greyhounds, Irish wolfhounds, Newfoundlanders and miniature poodles (3). In Doberman pinschers, left ventricular diastolic internal dimension (LVIDd) > 45 mm in dogs weighing less or as much as 42 kg, and LVIDd > 49 mm in dogs weighing over 42 kg, were proposed as abnormal by Calvert et al., who have followed these dogs for years (6). Similar observations were made by O'Grady, who suggests that, an LVID at end diastole of greater than or equal to 49 mm or at end systole of greater than or equal to 42 mm, is highly predictive for occult DCM in Doberman pinschers independent of the size of the dog (2). Despite this O'Grady believes that these criteria are not suitable for either small (especially female), or extremely

large (especially male) Doberman pinschers. (2),

LV sphericity is measured so that LV diastolic length (in right parasternal two-dimensional long axis view) is divided by the M-mode diastolic value. An adapted scoring system based on major and minor criteria has been suggested for the identification of animals in the preclinical phase. Major criteria include the LV systolic and diastolic dimensions exceeding 95% confidence intervals of the normal M-mode values relative to breed, height and age, increased sphericity of the LV, FS of less than 20% to 25% (depending on breed specific values) and LVEF less than 40%. The proposed minor criteria include the presence of arrhythmia in predisposed breeds (e.g. Dobermans or boxers), atrial fibrillation, increased mitral valve M-mode E point to septal separation (EPSS), increased pre-ejection period and ejection period ratio (PEP:ET) over 95% confidence intervals, FS in equivocal ranges and left or bi-atrial enlargement (3). The two-dimensional display of left atrial diameter in right short-axis view at the level of the heart base exposes a wider portion of the left atrium and is commonly used measurement in comparison to aortic diameter.

The determination of cardiac function depends on exact measurements of cardiac dimensions. Improper alignment, poor image quality, and inadequate delineation of the endocardial blood pool interface represent technical difficulties that may yield erroneous results.

Fractional shortening (FS) is the major indicator of systolic function in veterinary echocardiography. Values of FS between 20% to 25% in Doberman pinschers are considered equivocal findings, but FS less than 15% suggests strong evidence of DCM, although values from 18% to 22% have been observed in normal Doberman pinschers (2). In humans, an ejection fraction (EF) is more important for the evaluation of the systolic function because FS may be deceptive in a concomitant severe mitral regurgitation. In their proposed guidelines for the diagnosis of DCM, Dukes - McEwan et al. consider less than 40% EF determined by 2D echocardiographic images (modified Simpson's rule) from the right parasternal long axis four chamber view as abnormally low. The end diastolic and end systolic ventricular volumes can be normalised to the body surface area (BSA) and expressed in ml/m² as end diastolic volume index (EDV-I) and end systolic volume index (ESV-I). ESV-I over 80 mls/m² is considered as elevated in regard to the reference <30 mls/m², which is suggested as normal canine ESV-I. The

authors have presumed that the diastolic dysfunction follows the systolic dysfunction. Some authors believe that the diastolic function can be altered and be an early sign of ongoing systolic dysfunction (7). The diastolic function can be assessed with mitral and pulmonary vein Doppler inflow velocity, tissue Doppler imaging of the mitral valve annulus velocity, and colour M-mode imaging of mitral valve opening velocity.

The evaluation of mitral inflow and PVF with pulsed wave Doppler to establish diastolic function is rather used as a prognostic tool than as a screening test. In human medicine, Doppler evaluation of transmitral flow (TMF) and pulmonary venous flow (PVF) is used to evaluate the diastolic filling activity. A restrictive filling pattern is usually present in patients with DCM and is related to a poor prognosis also in dogs, especially with constrained mitral inflow and a short E wave deceleration time (TDe) (<80 ms). The authors have not found any of the standard echocardiographic parameters (FS, mitral EPSS, ESV-I and EDV-I) to be related with survival rate (3).

In a recent study, O' Sullivan et al. investigated the diastolic function by means of combined echocardiographic indices (TMF, IVRT, PVF, Vp, and mitral annular motion) in normal Doberman pinschers and Doberman pinschers with occult and overt DCM. They considered left ventricular flow propagation velocity (Vp) with color mode echocardiography and mitral annular motion by TDI as load independent parameters unlike TMF, IVRT and PVF. They concluded that TMF, IVRT and PVF values vary according to the progression of diastolic dysfunction. TDI can be used to predict time to HF or SD in occult DCM (7).

One of the most significant uses of TDI is the detection of changes in myocardial function that cannot be displayed with conventional methods. It can be used as a complementary diagnostic method in patients with inconclusive echocardiographic results and it represents an important development in the preclinical diagnosis of cardiomyopathies (8).

Early diagnosing of asymptomatic myocardial abnormalities in dogs by TDI was confirmed by Chetboul et al. by dog model of Duchenne's cardiomyopathy (9, 10). Duchenne's muscular dystrophy is a hereditary muscular disease related to the formation of dysfunctional dystrophin, a structural protein of the myocyte. The dystrophinopathy causes not only the dysfunction of the skeletal muscles, but also myocardial alterations, which may be asymptomatic over a variable period of time. TDI parameters of regional myocardial function determined in a short

axis view by applying M-mode TDI, were altered also when global ventricular function (left atrial and LV end-systolic and end-diastolic dimensions, LVFS%, wall thickening and E/A ratio), measured by conventional echocardiographic techniques, was still within normal limits. Systolic and diastolic myocardial velocity gradients (MVG) were lower in Golden Retriever muscular dystrophy (GRMD) dogs than in normal dogs, corresponding to a considerable reduction of systolic and diastolic endocardial velocities. Epicardial velocities were comparable in both groups. The ratio of early to late diastolic MVG was lower in GRMD dogs than in control dogs. According to these findings, systolic MVG was the most reliable parameter for distinguishing GRMD dogs from the control dogs (9).

Golden retriever muscular dystrophy (GMRD) is an inherited neuromuscular disease, similar to the Duchenne dystrophy in humans that eventually leads to GMRD associated DCM. These results in the preclinical phase of the GRMD associated cardiomyopathy confirmed TDI as a possible screening method of DCM (10, 11). Myocardial fibre strain is directly related to left ventricular (LV) contractility. Strain rate can be estimated as the spatial derivative of velocities (dV/ds - difference in velocity/difference in strain) obtained by tissue Doppler echocardiography (TDE). The use of TDI and strain rate imaging (SRI) as diagnostic tools of occult DCM and prognostic tools in dogs with overt DCM has to be evaluated. Recent studies focused on the determination of LVFW radial and longitudinal myocardial contraction velocities in normal dogs and in dogs with DCM revealing intramyocardial radial and longitudinal gradients (12). LVFW velocity gradients in dogs with idiopathic DCM decrease, and LV contractility along the short and the long axis is impaired in systole and in diastole (13).

Introducing new, preload independent parameters may enhance the evaluation of the LVFW diastolic function. Flow propagation velocity (Vp) from a colour M-mode recording and mitral annular motion by PW TDI are measurements that can be added to the Doppler echocardiography which combines transmitral flow (TMF), isovolumic relaxation time (IVRT), pulmonary venous flow (PVF) as preload dependent indices of diastolic function. Doberman pinscher dogs in occult and clinical DCM show altered TMF, reduced systolic to diastolic PVF ratio and reduced Vp. Shorter early TMF deceleration time (DTe) is correlated to the approaching onset of CHF or sudden death (7).

Dobutamine stress echography (DSE) is based on the fact, that increasing myocardial inotropy with dobutamine can reveal occult cardiac dysfunction, which is not evident when the animal is at rest. It can be safely performed as a non-invasive diagnostic method, complementary to conventional clinical examinations. The echocardiographic parameters (morphology and filling pattern) are measured by 2D guided M-mode echocardiography, and colour flow Doppler imaging (14, 15, 16). Minors and O'Grady evaluated echocardiographic parameters in healthy Doberman pinschers and in Doberman pinschers with occult DCM when animals were at rest and under the dobutamine stress. (14) As a result of the study, they were able to detect asymptomatic Doberman pinschers with an early cardiac dysfunction even when the left ventricular end-diastolic dimension and FS were within normal limits. Indices of systolic function when the animals were at rest (left ventricular dimension at end-systole: LVID-S, PEP, and PEP/left ventricular ejection time: LVET ratio) and under DSE (LVID-S, FS, wall stress index at end-systole - WSIS) were reduced early in the course of the disease. Diastolic function in affected dogs was also altered when the animals were at rest (prolonged IVRT) and under DSE (E/A ratio was significantly lower in dobutamine stressed occult DCM dogs than in healthy dogs) (14). New echocardiographic techniques and new software solutions can provide a lot of information regarding the functional status of the myocardium. Parameter values have to be determined to provide a reference for the operators, considering the influence of a breed, body weight, and age on the results. These parameters should be included in screening examination protocols for breeds predisposed to DCM.

Echocardiographic prognostic indicators for dogs with dilated cardiomyopathy have been suggested by Borgarelli et al. Severity of heart failure, ascites, end-systolic index greater than 140 mL/m², EF <25%, and restrictive transmitral flow, significantly affected the survival time period in a negative way. (17)

Electrocardiography

Electrocardiography has proved to be useful in boxers and Doberman pinscher dogs for the identification of dogs prone to developing DCM. As a single ECG recording corresponds to a small fraction of the dog's cardiac rhythm, a 24 to 48 hours ECG (Holter monitoring) is required to assess the heart rhythm over an extended time period (3, 4). The ambulatory

electrocardiography is necessary to quantify heart rates and rhythms, and to identify abnormalities indicating cardiomyopathy. Especially in Doberman pinscher dogs, indications of possible onset of DCM include presence of ventricular premature contractions (VPC) and/or ventricular tachycardia (VT) (6, 18, 19, 20). Heart rate variability is reduced only in dogs with severe myocardial failure and can not provide additional information regarding the severity of LV dysfunction or risk of sudden death (20,21).

Most clinically healthy Doberman pinschers with normal ECG results have no or few VPC/24 h. Most Dobermans that are less than 4 years old have <1 VPC on an ambulatory recording. The number of dogs with detectable VPCs increases with age, but the number of VPC is <10 VPC/24 h. More than 50 VPC/24 h or ≥1 couplet or triplet of VPC/24 h, are predictive of development of DCM (19). In Doberman pinschers, the severity of arrhythmia tends to progress with the degree of myocardial failure, and sustained ventricular tachycardia persisting >30 seconds can be correlated with the risk of a sudden death, whereas less severe arrhythmias are not (3, 20).

Calvert et al. focused their studies in the electrocardiographic evaluation on clinically normal client-owned Doberman pinschers (mean age: 5 to 7 years) with abnormal or equivocal echocardiographic findings (6, 18). The echocardiographic observed were: LVIDd, LVIDs, LVFS, Mitral valve (MV) EPSS. The following values: LVIDd >50mm; LVIDs >40mm; LVFS ≤25% were considered abnormal, and LVIDd 48-50mm; LVIDs 38-40mm; LVFS 26-29% values were considered equivocal (18-20). In these studies, all the dogs with echocardiographic abnormalities (abnormal and equivocal) showed an elevated number of VPC during 24 Holter monitoring (6, 18). A follow-up study confirmed the correlation between the electrocardiographic abnormalities and the possibility to develop dilated cardiomyopathy (19).

The signal-averaged electrocardiography (SAECG) technique involves a computerized analysis of the standard electrocardiogram (ECG). This method allows the operator to detect small electrical impulses that are often covered by skeletal muscle activity and other extraneous sources of "noise" when recording a surface ECG. This low amplitude impulses that follow the QRS segment are defined as ventricular late potentials (VLP) (23). VLP result from regions of myocardial fibrosis. They are related to an increased risk of ventricular tachyarrhythmia and a sudden cardiac death, and occur in patients

with cardiac abnormalities, especially coronary artery disease, or following an acute myocardial infarction (23-26) and have been studied in patients with congenital muscular disorders (27). Calvert et al. in a study, conducted on Doberman pinschers with occult DCM, conclude that dogs with abnormal SAE-ECG results are at higher risk of a sudden death than dogs with normal SAE-ECG results. Despite this, the possibility of a sudden death cannot be excluded in patients with normal SAE-ECG results (24).

Electrocardiography – in particular ambulatory ECG – is an indispensable tool in diagnosing occult DCM, especially in combination with an accurate echocardiographic examination. SAE-ECG is a useful technique to assess the risk of sudden death, and as an index of myocardial dysfunction.

Biochemical markers of cardiac dysfunction

The usefulness of biochemical markers in the diagnosis and prognosis of heart disease is well documented in humans and there is an interest in identifying their relevance in companion animals. The prospect of identifying dogs (and cats) with asymptomatic heart disease via biochemical testing is exciting from several points of view. The introduction of new, simple and standardised laboratory methods for diagnosing heart structural changes would enable the individuals without extensive training in cardiology to identify animals with heart disease more reliably. It is not known how early in the course of a disease the changes can be identified because the data published to date include all animals with advanced disease. Biochemical testing might also help to clarify the status of dogs with equivocal results when evaluated by other diagnostic methods. Other advantages of biochemical testing are of practical nature: sample collection is minimally invasive and easy, the availability of tests is high, and these methods have become quantitative, repeatable, and economically affordable (28).

There are two types of biochemical markers. The first group comprises biochemical markers of myocardial injury and necrosis as cardiac enzymes creatine kinase (CK) and its myocardial fraction CK-myocardial band (CK-MB), aspartate aminotransferase (AAT), lactate dehydrogenase (LDH), and the recently evaluated structural myocardial proteins – troponins. The cardiac enzymes showed a limited ability in detecting myocardial injury due to low specificity and sensitivity, characteristics that are attained by troponins. Myosin light chain 1 (MLC-1) and heart

type fatty acid binding proteins (H-FABP) are newly discovered biochemical markers that have been found in elevated quantities in human patients with myocyte injury, but further investigation is needed to evaluate these markers (29-31). The second group of biochemical markers is used to assess the degree of cardiac dysfunction and is represented by the plasma neurohormones. The most commonly used indicators of neuroendocrine activation are plasma norepinephrine (NE), the atrial natriuretic peptide (ANP), the B-type peptide (BNP), peptides of the renin – angiotensin system (RAS) – vasopressin and aldosterone and plasma big endothelin-1 (32, 33).

The activation of the neuroendocrine system is well known in human patients with congestive HF (32). This finding has been confirmed in veterinary medicine also, and correlated positively with heart failure groups and left atrial size (38). The concentrations of neurohormones are related to the severity of the disease, and could be used in identification of various clinical stages of the disease, or in assessment of a suitable therapy (33, 34). O' Sullivan et al., in a study conducted on Doberman pinscher dogs, conclude that increasing norepinephrine concentrations (1.5 nM in male dogs and 5.8 nM in female dogs respectively, compared to 0.7 nM in normal male dogs and 1.0 nM in normal female dogs respectively) in the advanced phase of overt DCM are predictive of poor prognosis (35).

Endothelin is a 21-amino-acid peptide with a strong vasoconstricting activity, positive inotropy, chronotropy, stimulation of the RAS and sympathetic nervous system (SNS), and with mitogenic effects. It is released from the vascular endothelium and cardiac myocytes in response to cardiac damage in a precursor form (big ET-1) which is cleaved in its biologically active form by the catalytic action of endothelin converting enzyme (ECE) (35, 36). Normal Big ET-1 values range from 4.6 to 9.1 pg/mL averaging at 6.5 pg/mL in male dogs, and from 3.6 to 5.6 pg/mL averaging 4.5 pg/mL in female dogs. Occult DCM male dogs presented 6.9 to 12.5 pg/mL (mean 9.3 pg/mL), and female occult DCM 4.4 to 7.1 pg/mL (mean 5.6 pg/mL), respectively. In the previously mentioned study, O' Sullivan et al. measured Big ET-1 in Dobermans at different stages of DCM. Only the group of Dobermans with overt DCM had increased values of Big ET-1 (10.2 to 14.9 pg/mL – mean 12.3 pg/mL in male dogs, and 11.6 to 35.4 pg/mL – mean 20.2 pg/mL in female dogs), thus adding ET to the biochemical markers of degree of cardiac dysfunction and prognostic indicators (as norepinephrine) (35).

The assessment of natriuretic peptides as biochemical markers of cardiac dysfunction in asymptomatic patients is one of the most attractive methods (37). Natriuretic peptides are natural antagonists of the RAS system. They are released from the myocytes in response to increased cardiac pressure due to compensatory mechanisms. There are two relevant types of natriuretic peptides related to the diagnosis of DCM: the atrial natriuretic peptide (ANP) and the brain natriuretic peptide (BNP) (28).

ANP is mainly released from atrial myocytes in response to the increase in right or left atrial pressure. On secretion, proANP is cleaved to the biologically active 28-amino-acid C-terminal ANP and the 98-amino-acid N-terminal (NT)-proANP. The two peptides are secreted into the circulation in equimolar quantities. NT-proANP has a longer half-life in circulation, it is more stable and more easily measured in laboratory (28, 29, 37, 39). ANP concentrations are known to increase in dogs with mitral regurgitation, heartworm disease, and congestive heart failure. ANP can be used to distinguish cardiac from non cardiac causes of dyspnea in patients with clinical disease (42), although it has been demonstrated that NP assays are not relevant in detection of clinically undetectable mitral valve disease (40). Normal serum ANP values are $0,269 \pm 0,013$ nmol/L, values in occult DCM raise to $0,346 \pm 0,033$ nmol/L (40).

BNP is secreted predominantly by left ventricular myocytes secondary to volume expansion or pressure overload. It is a 32-amino-acid peptide that shares structural and biological similarities to ANP. It is released into the blood as pro-hormone proBNP and it is then cleaved into Nt-proBNP and BNP. Nt-proBNP is more suitable for testing due to its longer half life and higher concentrations. BNP or NT-BNP has been proven to be the most reliable marker of early DCM among all the others (37 – 40) and new studies are oriented in the evaluation of NT-BNP utility to differentiate cardiac and respiratory causes of coughing or dyspnea in dogs (42, 43). Normal values of BNP are 6.51 ± 0.66 pg/mL, whilst 14.35 ± 1.6 pg/mL are indices of a developing heart disease (40). Natriuretic peptide concentrations have been proved to correlate with class of heart failure in dogs and their measurement may allow veterinarians to offer pet owners a more accurate long-term prognosis. Natriuretic peptide assays may also be useful in monitoring the efficacy of therapeutic intervention.

The cardiac troponin complex consists of three subunits (I, T in C), that regulate the excitation-con-

traction coupling of the sarcomeric proteins. CTnI is the inhibitory component that prevents interactions between actin and myosin until intracellular calcium is bound by cTnC. CTnI is normally bound to the actin filament via cTnT, but it detaches in response to sarcomeric injury and is released into the cytosol and extracellular space. Acute and/or chronic cardiac injury induces release of these subunits into the circulation (especially cTnI and cTnT), where their levels are proportional to the severity of myocardial damage. Markers such as cTnI and cTnT are more specific for myocardial damage than previously used enzymatic markers such as lactate dehydrogenase and creatine kinase (28, 40, 44).

Cardiac troponin I (TnI) is a better biomarker of the cardiac injury than cTnT due to its high sensitivity and specificity. The close homology of cardiac isoforms among mammalian species allows using immunoassays developed for humans for rapid and accurate measurements of canine cTnI concentrations (44). Despite this, cTnI is a marker of myocardial injury and its values increase in various cardiac and noncardiac diseases that cause myocardial damage thus limiting the use of cardiac troponin assays to detect myocardial damage and to evaluate its degree. CTnI values <0.07 ng/mL are considered normal, and values >0.07 ng/mL are considered pathologic (40, 44, 46). The use of cTnI as a biochemical marker of myocardial damage and the prognostic tool has been reported in a recent study conducted on female dogs with pyometra (46). According to the case report, high troponin concentrations were a marker of severe myocardial damage following suspected heatstroke (47). Compared with clinically normal dogs, boxers with arrhythmogenic right ventricular cardiomyopathy had a significant increase in serum cTnI concentration (0.142 ± 0.05 ng/mL for boxers with ARVC, 0.079 ± 0.03 ng/mL for control boxers, and 0.023 ± 0.01 ng/mL for control non-boxers) (48). CTnI is used in human medicine to diagnose the acute myocardial ischemia. Even though several studies regard the use of cTnI in veterinary medicine, the diagnostic use is still limited to a potential use (28).

The idea of a simple and routine assessment of cardiac dysfunction is becoming reality thanks to the biochemical markers of cardiac dysfunction. There many variables that changes during a heart disease. In veterinary medicine, however, the natriuretic peptides and cTnI are most promising and useful. New investigation is required to establish the reference values for the biochemical markers

mentioned herein, especially considering physical characteristics (body weight, gender, age).

Genetics

Another interesting field that has been developing rapidly to prevent DCM is based on genetic predisposition and patterns of inheritance. In dogs, familial DCM has been observed in a number of breeds, and in most of them an autosomal dominant mode of inheritance is suspected (50). Boxers and Doberman pinschers are breeds with a certified familial predisposition to DCM (51). A recent study by Meurs et al. proved that DCM in Doberman pinscher dogs is a familial disease with an autosomal dominant mode of inheritance, but further investigation is required to identify the causative gene (52). The latest studies have focused on the evaluation of candidate genes for DCM (53-56). The discovery of the causative genes would enable the practitioners to eliminate the carriers from breeding programs as a definitive diagnostic test for early detection of DCM.

Post mortem histological characterisation of DCM

A histopathologic evaluation of canine DCM established two histologically distinct types of idiopathic canine DCM: the »fatty infiltration-degenerative« type in boxers and Doberman pinscher dogs, and the »attenuated wavy fiber « type of DCM in many giant, large and medium sized dogs, including some boxers and Doberman pinschers (57, 58). A post mortem histopathological evaluation of the heart should be performed in all predisposed dogs to confirm DCM, or to discover changes that were not clinically manifested in order to discover latent carriers of DCM, and to exclude them eventually from the breeding programmes.

Conclusion

Clinically detectable DCM is not difficult to diagnose due to the typical signs of congestive HF, but usually this disease has a poor prognosis. In Doberman pinscher dogs, there is an occult stage of DCM that can be diagnosed in order to determine an early therapy for the affected dog to prevent the onset of HF. A similar pre - clinical phase can be detected in Boxers (59).

New echocardiographic methods, Holter monitoring and the biochemical markers of cardiac dys-

function are to date the most promising methods, not only in the early detection of DCM, but also for the evaluation of the severity of the disease and to estimate the response of the organism to the therapy.

Echocardiographic parameters can be used to detect morphological abnormalities, Holter monitoring can help quantify heart rates and rhythms and to identify abnormalities indicating cardiomyopathy, biochemical markers can provide information about the level of disease exposure, extent of injury, and prognosis.

There are studies that certify the ability of new diagnostic methods for occult DCM, but there are different results among operators, there are different criteria and different conditions. There is still a need to establish reference values, to standardize these methods and make them objective instruments for detecting and evaluating occult DCM. These parameters should be included in screening protocols for predisposed breeds.

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DIAGNOSTIČNE METODE ZA UGOTAVLJANJE DILATACIJSKE KARDIOMIOPATIJE PRI PSIH – PREGLED STARIH IN NOVIH POGLEDOV IN METOD

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Povzetek: Dilatacijska kardiomiopatija (DKM) je pogost vzrok za obolevnost in smrtnost predvsem psov velikih pasem. Številne nove diagnostične metode so bile razvite v zadnjih letih z namenom čim prejšnje diagnoze bolezni in podaljšanja dobe preživetja. Družinska podvrženost DKM pri nekaterih pasmah odpira nove možnosti za zgodnejše odkrivanje bolezni s pomočjo genetskih testov in veliko študij je usmerjenih v iskanje molekularnih nepravilnosti, ki so odgovorne za njen nastanek. Doplerska ehokardiografija in nove občutljive metode, kot so tkivna doplerska ehokardiografija (TDI), 24- do 48-urno elektrokardiografsko snemanje (Holter monitoriranje) in biokemični markerji srca, kot so atrijski natriuretični peptid (ANP), možganski natriuretični peptid (BNP) in srčni troponin I, so najbolj obetajoče metode za zgodnje ugotavljanje DKM.

Ključne besede: dobermani; dilatacijska kardiomiopatija; genetika; ultrazvok; holter monitoring; biokmarkerji.