Canine cardiomyopathies: aetiology and breed characteristics

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DEFINITION

Cardiomyopathy, or heart muscle disease, describes a group of heterogeneous conditions that affects the heart muscle functionally and/or structurally or morphologically.

By definition:

- **Primary cardiomyopathies** are idiopathic, and no underlying disease can be identified.
- **Secondary cardiomyopathies** are a consequence of an underlying pathology and the term cardiomyopathy should preferably not be used in this setting. The use of the inciting cause in the nomenclature would be more appropriate (e.g. carnitine deficiency cardiomyopathy, doxorubicine cardiotoxicity, tachycardia-induced myocardial failure).

CLASSIFICATION

Canine cardiomyopathies can be classified, as in human medicine, using the World Health Organisation (WHO) classification (Table 1). However, in veterinary medicine an aetiological classification into the primary (idiopathic) and secondary forms may be more appropriate (Table 2).

TABLE 1: World Health Organisation classification

IDIOPATHIC (I)
Dilated cardiomyopathy (IDCM)
Hypertrophic cardiomyopathy (IHCM)
Restrictive cardiomyopathy (IRCM)
Arrhythmogenic right ventricular cardiomyopathy (ARVC)
SPECIFIC
Hypertensive cardiomyopathy
Endocrine cardiomyopathy
Metabolic cardiomyopathy
Ischaemic cardiomyopathy

The **dilated form of cardiomyopathy** (DCM) is characterised by impaired systolic function (loss of contractility) of the ventricular myocardium leading to progressive dilation of first the ventricle(s) and later the atria. Some degree of diastolic dysfunction can be present (Fig. 1).

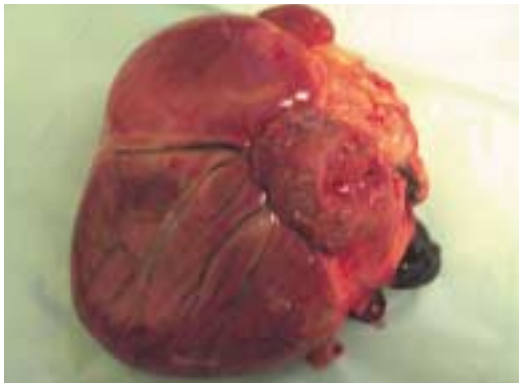

Fig. 1: *Post-mortem specimen of the heart of a Newfoundland dog with DCM.*

Hypertrophic cardiomyopathy (HCM) is a disease of mostly (but not only) the left heart characterised by inappropriate symmetrical or asymmetrical concentric hypertrophy of the ventricular myocardium (Fig. 2). In some subcategories hypertrophy of the interventricular septum can cause dynamic obstruction of the left ventricular outflow tract (**hypertrophic obstructive cardiomyopathy**) (HOCM).

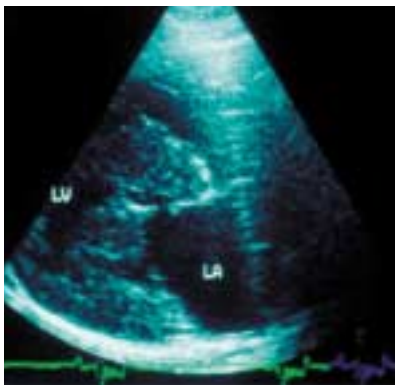

Fig. 2: *Echocardiographic image of a hypertrophied left ventricle (LV) with left atrial dilation (LA).*

Restrictive cardiomyopathy (RCM) indicates that ventricular restriction causes diastolic dysfunction. It is so rare that it is not recognised as a separate entity in dogs. **Endocardial fibro-elastosis** for example is an extremely rare cause of RCM in the dog.

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is characterised by partial or total fibrous and/or fatty replacement of the right ventricular and atrial wall, and in

TABLE 2: Veterinary classification of canine myocardial diseases

PRIMARY IDIOPATHIC (I)	
Dilated cardiomyopathy (IDCM)	Breed characteristics: Dobermann, Great Dane, Boxer, Irish Wolfhound,…
Hypertrophic cardiomyopathy (IHCM)	Obstructive (HOCM) Non-obstructive
Restrictive cardiomyopathy (RCM)	Endomyocardial fibrosis
Unclassified cardiomyopathy (UCM)	Arrhythmogenic right ventricular cardiomyopathy (ARVC) Atrioventricular cardiomyopathy (Persistent atrial standstill)
SECONDARY FORMS (S)	
Genetic	X-linked Duchenne's muscular dystrophy (SDCM)
Metabolic	systemic hypertension (SHCM) tachycardia/bradycardia induced (SDCM) uraemic (SDCM) chronic volume overload (SDCM)
Endocrine	hypothyroidism (SDCM)/hyperthyroidism (SHCM) diabetes mellitus (SDCM) acromegaly (SHCM) phaeochromocytoma (SHCM)
Nutritional	carnitine deficiency (SDCM) taurine deficiency (SDCM) Vit. E/Selenium (SDCM)
Infiltrative	neoplasia (lymphoma SHCM, SDCM) glycogen storage diseases (SDCM) mucopolysacharidoses (SHCM)
Ischaemic	atherosclerosis (extremely rare) (SDCM) septic coronary embolism (myocarditis) (SDCM)
Infectious	Parvovirus, Distemper, Herpes (myocarditis) (SDCM) Toxoplasmosis, Trypanosoma Cruzi (myocarditis, often right-sided SDCM) Bartonella species (myocarditis) (SDCM) Borrelia burgdorfi (Lyme disease myocarditis) (SDCM,)
Inflammatory	myocarditis (SDCM) trauma (road traffic accident) (SDCM) heat stroke (SDCM) electrocution (SDCM)
Drugs and toxines	doxorubicine (SDCM) catecholamines (SDCM)

a lesser extent the interventricular septum and the left ventricular wall. Often ventricular arrhythmias originating from the right side of the heart (Fig. 3) and bundle branch blocks are present.

Atrioventricular cardiomyopathy is characterised by progressive destruction of the atria associated with atrial standstill. Occasionally the ventricle is affected. Some dogs will have a poorly defined muscular dystrophy.

AETIOLOGY

In people with **DCM**, mutations in the genes coding for cytoskeletal and sarcomeric proteins have been identified.

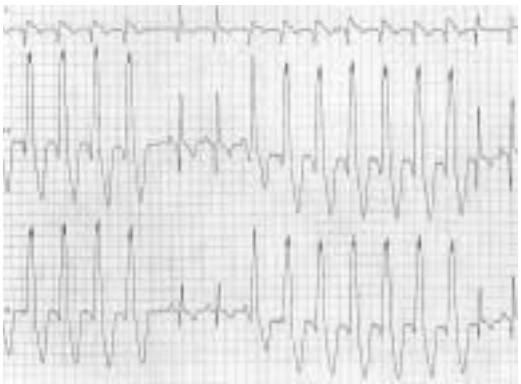

Fig. 3: *An ECG showing a sinus rhythm with paroxysmal ventricular tachycardia originating in the right ventricle in a dog with ARVC.*

TABLE 3: Breed characteristics of idiopathic DCM

BREED	CHARACTERISTICS	AGE AND SEX	PROGNOSIS	GENETICS
German Shepherd Dogs **Golden Retrievers** **Labradors** **Old English Sheepdogs** **St Bernards** **Deerhounds**	Biventricular congestive heart failure Atrial fibrillation is often associated with clinical signs	Male > female	Slower progressive course with survival up to 1-2 years after diagnosis	Familial or genetic basis suspected
Dobermann	Sudden onset left-sided congestive heart failure Ventricular arrhythmias Often they do not show severe left ventricular enlargement on RX but there is always marked left atrial enlargement	Male (7.5 y) > Female (9.5 y) Recently a juvenile form has been described (10d-4w)	Most dogs die within 6 months of diagnosis Extremely poor if atrial fibrillation 20% die suddenly	Suspected autosomal dominant with reduced penetrance
Boxer	**Cat I:** Ventricular arrhythmias only	No sex predilection	Prognosis guarded (>2y)	
	Cat II: severe ventricular arrhythmias	Average 8 y (6 m-15 y)	Most commonly sudden death but can go into heart failure	Autosomal dominant trait
	Cat III: myocardial failure and ventricular arrhythmias		Congestive heart failure reason of death (<6 m)	
	L-carnitine supplementation has been beneficial in a family of Boxers in the USA			
Newfoundland	Congestive heart failure at advanced age AF more common than ventricular arrhythmias Can be associated with hyperthermia Systemic taurine deficiency has been reported	Male > female Older age	Slow progression Biventricular congestive heart failure most common reason of death	Suspected autosomal dominant
Great Dane	Congestive heart failure and AF In UK ventricular arrhythmias and sudden death prior to clinical signs of DCM	Male > Female Also in very young animals	Relatively slow progression of DCM In the V arrhythmia group sudden death without congestive heart failure is not uncommon	X-linked recessive trait suspected
Irish Wolfhound	AF common (AF at slow rate can proceed overt signs of DCM for years) Left anterior fascicular block in some families Pleural effusion and chylothorax	Male > Female	Survival longer than other breeds, except for the younger animals	Suspected autosomal dominant
Irish Water Spaniel	Vomiting and lethargy before fulminant congestive heart failure	Juvenile form	Death soon after diagnosis	Autosomal recessive trait

TABLE 3: Breed characteristics of idiopathic DCM (continued)

BREED	CHARACTERISTICS	AGE AND SEX	PROGNOSIS	GENETICS
Dalmatian	Has been associated with U/D and taurine deficiency	Male > Female	Prognosis fair	Suspected hereditary
American Cocker Spaniel	Has been associated with U/D and taurine deficiency in the US			
English Cocker Spaniel	Slow progression Pulsus alternans	Male > Female Average age 5-6y	Can live up to 5 years post diagnosis Survival worse for males	Hereditary, pattern unknown
English Springer Spaniel	Fast progression	Probably female>male Average age 27m	Prognosis poor	?
Weimaraner	Ventricular arrhythmias are common		Rapidly progressive form Sudden death reported	Familial or genetic basis suspected

In dogs more than 90% of the dilated forms of cardiomyopathy are thought to be idiopathic. However many secondary forms are recognised (see Table 3: SDCM) giving myocardial failure and secondary eccentric hypertrophy and dilation.

The cause of **primary HCM** in dogs remains unknown. In people several sarcomeric gene mutations have been identified. Multiple secondary forms are recognised (see Table 3: SHCM) often giving mild symmetrical ventricular hypertrophy.

In humans with **ARVC** the discovery of a deletion in the plakoglobin (=key component of desmosomes and adherens junctions) gene has suggested that the proteins involved in cell-cell adhesion may play an important role in myocyte dysintegrity and hence cell death and fibro-fatty replacement.

The aetiology of **atrioventricular cardiomyopathy** remains unknown.

In **endocardial fibro-elastosis** the age of presentation suggests a congenital abnormality but the exact inciting factor remains unknown.

PREVALENCE

Idiopathic DCM (IDCM) is the most frequently diagnosed primary cardiomyopathy in the canine species. IDCM is, after mitral valve endocardiosis (or chronic degenerative mitral valve disease), the second most frequent acquired cardiac condition in the dog. The prevalence is estimated around 0.5%. Many breeds are predisposed to **IDCM** (mainly large and giant pure-bred dogs (Fig. 4) with exception of the Spaniels). Young animals can be affected but the disease is most commonly diagnosed in middle-aged animals. Male predominance is seen in most but not all affected breeds (Table 3).

Fig. 4: *Breeds predisposed to DCM (St Bernard and Irish Wolfhound).*

Idiopathic hypertrophic cardiomyopathy is extremely rare in the dog. It has been diagnosed mainly in young male dogs of different breeds (German Shepherd Dog, Rottweiler, Golden Retriever). It is hereditary in Pointers.

Restrictive cardiomyopathy and ARVC are very rare. ARVC has been reported in multiple related Boxers in the UK (Fig. 5).

Atrioventricular cardiomyopathy is very uncommon and has mainly been reported in English Springer Spaniels and Old English Sheepdogs.

Fig. 5: *A Boxer diagnosed with ARVC.*

BREED CHARACTERISTICS OF IDIOPATHIC DILATED CARDIOMYOPATHY

IDCM has a very different natural history depending on the breed (Table 3). Animals can present in congestive heart failure, with arrhythmias or with a combination of both. Unfortunately in certain breeds (Boxer, Doberman, Great Dane) syncope and sudden death are often the first, and last, clinical signs that indicate the presence of cardiomyopathy.

In dogs IDCM is often familial which indicates that a certain mode of inheritance is suspected (Table 3).

CHARACTERISTICS OF SOME SECONDARY FORMS

Taurine deficiency can cause or contribute to the development of myocardial failure in a small group of dogs (e.g. American Cocker Spaniels, Newfoundland). The lowest whole blood taurine concentrations are seen in dogs fed lamb and rice diets. The exact mechanism of the secondary cardiomyopathy remains unknown but taurine's beneficial action has been related to its modulatory effects on angiotensin II, its stimulatory function on salt and water excretion and its direct positive inotropic and lusitropic mechanisms. **Carnitine deficiency** occasionally causes myocardial failure in dogs. Carnitine has a major role in the fatty acid transport and hence the mitochondrial energy production. Cystinuria is a possible risk factor for carnitine deficiency.

IDCM HAS A VERY DIFFERENT NATURAL HISTORY DEPENDING ON THE BREED

Doxorubicine induced myocardial failure is a cumulative cardiotoxicity. The accepted cumulative dose is 180 mg/m^2 and cardiotoxicity may occur months to years after treatment. Life-long monitoring might be necessary. The exact mechanism remains elusive. The most thoroughly studied mechanism is the free radical hypothesis. Doxorubicine (Fig. 6) induces free radical liberation to which the heart is very vulnerable due to its lack of protective enzymatic defences. Very rarely doxorubicine induces acute cardiotoxicity after the first administration, characterised by dangerous ventricular arrhythmias.

Fig. 6: *Doxorubicine, also called the 'red death'.*

Experimental pacing will induce myocardial failure (**tachycardia induced myocardial failure**) after a pacing rate of 200 beats per minute for only 2-6 weeks. It causes dilation of all chambers with wall thinning. The myocardial failure is usually rapidly reversible.

Myocardial failure has been reported in dogs with **hypothyroidism**. Decreased myocardial function with increased left ventricular end-systolic diameter and decreased ventricular wall thickness in systole can be observed at echocardiography. Congestive heart failure solely secondary to hypothyroidism has not been reported until very recently in dogs. It is the author's opinion that congestive heart failure does occur in hypothyroid dogs.

FURTHER READING AND REFERENCES

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CPD CONTINUING PROFESSIONAL DEVELOPMENT SPONSORED BY MERIAL

These multiple choice questions are based on the above text. Readers are invited to answer the questions as part of the RCVS CPD remote learning program. Answers appear on the inside back cover. In the editorial panel's view, the percentage scored, should reflect the appropriate proportion of the total time spent reading the article, which can then be recorded on the RCVS CPD recording form.

1. Which statement is false regarding Idiopathic DCM in the dog:

a. Young animals can be affected but the disease is most commonly diagnosed in middle-aged animals.
b. It is characterised by impaired systolic function (loss of contractility) of the ventricular myocardium leading to progressive dilation of first the ventricle(s) and later the atria.
c. The most frequently diagnosed acquired cardiac disease.
d. Some degree of diastolic dysfunction can also be present.
e. Male predominance is seen in most but not all affected breeds.

2. Which statement is false regarding Idiopathic HCM in the dog:

a. It is a very common disease.
b. It is a disease of mostly the left heart characterised by inappropriate concentric hypertrophy of the ventricular myocardium.
c. The cause of primary HCM in dogs remains unknown.
d. In some subcategories hypertrophy of the interventricular septum can cause dynamic obstruction of the left ventricular outflow tract.
e. It was proven to be hereditary in Pointers.

3. Which statement is false regarding Idiopathic DCM in the Newfoundland dog:

a. They develop congestive heart failure often at advanced age.
b. Atrial fibrillation is more common than ventricular arrhythmias.
c. It can be associated with hyperthermia.
d. Systemic taurine deficiency has recently been reported.
e. Sudden death is very common cause of death.

4. Which statement is false regarding Idiopathic DCM in the Doberman:

a. They have a fulminant form of DCM with sudden onset left-sided congestive heart failure.
b. Ventricular arrhythmias are a sign of DCM.
c. Most animals die suddenly.
d. Often they do not show severe left ventricular enlargement on RX but there is always marked left atrial enlargement.
e. A juvenile form has been described (10d-4w).

5. Which statement is false regarding Idiopathic DCM in the Boxer:

a. There is no sex predilection.
b. The average age is around 8 years.
c. It is often characterised by ventricular arrhythmias without signs of decreased contractility.
d. All Boxers with DCM are carnitine deficient.
e. Sudden death is a very common cause of death.