THORACIC RADIOGRAPHY

Topics
1. Radiographic techniques
2. Assessment of the cardiovascular system
3. Assessment of the respiratory system
4. Recognition of congestive heart failure in dogs and cats
5. Radiographic abnormalities in common cardiovascular disease

Key learning objectives:
At the end of this module delegates should be able to:
- obtain thoracic radiographs of diagnostic quality
- become familiar with interpretation of normal thoracic radiographs
- recognise signs of congestive heart failure
- recognise non-cardiac radiographic abnormalities of the thorax and common artefacts
- become familiar with selective and non-selective angiography
THORACIC RADIOGRAPHY

Thoracic radiography is an important diagnostic aid in cardio-respiratory patients. Interpretation depends not only on the knowledge and experience of the clinician but also on the quality of the image obtained. Assessment of the pulmonary fields, in particular, may be difficult if the quality of the film is not adequate.

Many factors are involved in obtaining good quality radiographs. It is not the intention of this course to fully cover the radiographic examination. Please refer to specialist textbooks for further details.

Digital radiography has dramatically changed modern radiology. One of the major advantages of digital radiography is the ability to process the images after they have been recorded. Various forms of digital processing can be used to change the characteristics of the digital images. Operators can change and optimise the contrast and enhance visibility of detail in some radiographs, in particular vascular and interstitial patterns. Other important advantages of digital radiography, compared to traditional films, include:

1. Rapid storage and retrieval
2. Less physical storage space
3. Ability to copy and duplicate without loss of image quality
4. Possibility to transmit images via internet to specialists for second opinion
5. Possibility to download images for reports and presentations
6. Ability to measure accurately length, area, circumference of thoracic structures and lesions.

Unfortunately, less than 30% of veterinary practices are equipped with digital radiography units at present (year 2010). This is primarily due to the relatively high cost of digital units, although they may become significantly cheaper in the near future.

Practical tips to obtain thoracic radiographs of diagnostic quality (many tips apply to standard [film] radiology):

Short exposure time to minimise motion artefacts
1. Exposure at peak of inspiration (very difficult with tachypnoeic patients)
2. Rare earth intensifying screens (to reduce exposure time)
3. Automatic processing
4. Avoidance of grids (they require longer exposures...but they increase contrast)
5. Sedation may improve the respiratory pattern and reduce anxiety during the procedure
6. Sedation may improve positioning
7. A full set of sandbags, troughs, and foam wedges will improve positioning
8. General anaesthesia is sometimes required to obtain diagnostic images of the lungs.
9. Manual inflation under GA will increase lung details (careful inflation for suspected bullae, emphysema, etc)
10. Ventro-dorsal views are ideal to evaluate lung patterns; however they are difficult to obtain without deep sedation or general anaesthesia.
11. Dorso-ventral (or ventro-dorsal) views should be taken before lateral views to avoid artefacts.
12. Dog’s neck should be extended to avoid “dorsal kinking” of the trachea

Assessment of the cardio-vascular system

Cardiac shape and size
Assessing the cardiac shape and size is one of the most challenging parts of the thoracic radiograph examination. A reliable assessment can be achieved in three ways:
1) “comparison library”
2) “mental library”
3) vertebral heart size, score, system (VHS)

Assessing the cardiac shape and size by “comparison library” means comparing a thoracic radiograph with one obtained in a normal dog of the same breed, age and size. This requires a vast image archive that is not always available in practice. A nice image archive has been published by Boehringer Ingelheim and is available both as hard copy and interactive CD-Rom. Another important use of a comparison library is for monitoring the progression of the disease in the same patient.

A “mental library” is a mental comparison with cases seen previously. This requires a long experience in radiographic reading and is obviously affected by a strong subjective assessment. Nevertheless, experienced operators can reliably assess size and shape of the heart using their “mental library”.

Vertebral Heart Size (VHS) is a number that normalises heart size to body size using mid-thoracic vertebrae as units of measure. Various authors also have called VHS an acronym for vertebral heart...
score, vertebral heart sum or the vertebral heart system. VHS was introduced by Dr Buchanan in 1991 and a peer-reviewed article was published in 1995 (JAVMA 206:194-199). Since then, it has become the standard indicator of radiographic heart size in dogs and cats. VHS should not be affected by breed, age and gender, although variations exist amongst different canine breeds. Normal VHS is < 10.7 [dogs] and < 8.1 [cats].

A thorough tutorial on the use of VHS is available at: www.vin.com/library/general/JB111VHS.htm

It is important to remember that “differences among normal hearts of varying canine breeds or differences between hearts radiographed at inspiration and expiration ARE OFTEN GREATER than the differences among normal and diseased hearts” (Suter & Gomez 1987). In different canine breeds, the heart shape varies depending on their chest morphology. In lateral view, the chest morphology can be classified as normal, shallow and deep and, in dorso-ventral view, as normal narrow and barrel. According to this classification we can observe the following types:

Normal-Normal: eg. Labrador retrievers
Lateral view: the heart is mildly leaning cranially and occupies approximately 2/3 of the height of the chest
   DV view: the heart occupies approximately 2/3 of the width of the chest

Normal-Narrow: eg. Greyhounds
Lateral view: the heart is mildly leaning cranially and occupies approximately 2/3 of the height of the chest
   DV view: the heart occupies more than 2/3 of the width of the chest

Shallow-Normal: eg. Yorkshire terriers
Lateral view: the heart appears globoid in shape and presents an increased sternal contact compared to a normal depth chest.
   DV view: the heart occupies approximately 2/3 of the width of the chest

Shallow-Narrow: Basset hounds
Lateral view: the heart appears globoid in shape and presents an increased sternal contact compared to a normal depth chest.
   DV view: the heart occupies more than 2/3 of the width of the chest
Shallow-Barrel: eg. French Bulldogs
Lateral view: the heart appears globoid in shape and presents an increased sternal contact compared to a normal depth chest.

   DV view: the heart occupies less than 2/3 of the width of the chest

Deep-Narrow: eg. Irish setters
Lateral view: the heart appears in upright position, almost perpendicular to the sternum.

   DV view: the heart occupies more than 2/3 of the width of the chest

Factors affecting findings on thoracic radiography

Effect of age
Possible radiographic variations in old cats (>10y)
   increased sternal contact with no changes in heart size (40%)
   aortic bulge (DV) (30%)
   fat infiltration of the pericardium (fake cardiomegaly)
Possible radiographic variations in old dogs (>8y)
   fat infiltration of the pericardium (fake cardiomegaly)
      bronchial pattern caused by mineral deposition in the bronchial wall
      increased interstitial pattern

Effect of obesity
   Increased interstitial pattern
   Tortuosity of the thoracic aorta
   Elevation of the cardiac silhouette from the sternum

Effect of positioning
   thoracic width is significantly larger on the VD projection than on the DV projection (78% of subjects)
      Angle of divergence formed by the principal bronchi is significantly larger on the VD than DV (80% subjects)
      A cardiac silhouette bulge at 1 to 2 o'clock may be apparent on VD but not on DV (22% of subjects)
Descending aorta is more visible at the 4 to 5 o'clock cardiac silhouette level on the DV projection and laterally at the T8 level on lateral projections.

The CVC is better seen on VD and lateral projections.

The oesophagus is visible as soft tissue opacity in lateral views in large dogs with normal thoracic conformation in 35 per cent of cases.

Flexion of the neck may cause dorsal “kinking” of the trachea in the cranial thorax

*Effect of respiration*

**Inspiration:**
- clear dark lungs
- diaphragm moves caudally
- straight caudal vena cava
- upright heart

**Expiration:**
- hazy denser lungs
- diaphragm moves cranially
- inclined CVC
- rounded heart

**SYSTEMATIC EXAMINATION OF THORACIC RADIOGRAPHS**

Thoracic radiographs should always be examined systematically, following a sort of mental protocol. It is very instinctive to start the analysis from the centre of the film, especially if a cardiac disease is suspected. However, it is more efficient to proceed in the following order:

1) Bones and extrathoracic structures
2) Diaphragm and thoracic wall
3) Pleural cavity and mediastinum
4) Cardiac size and outline
5) Lung fields and any patterns of disease
6) Main airway and bronchi
7) Major blood vessels, oesophagus, liver
Radiography cannot detect a reduction in cardiac output for the needs of the tissue (heart failure) but can provide evidence of pulmonary congestion to suggest congestive heart failure (pulmonary venous engorgement, pulmonary interstitial oedema, and obscuring and enlargement of the cardiac silhouette).

Radiography provides the most readily available means to identify pulmonary oedema and pulmonary venous congestion. Because the vast majority of cases of pulmonary oedema are due to heart failure - then the finding of pulmonary oedema represents a strong evidence of heart failure. Once again, following a sort of mental algorithm can be very helpful:

1) Is there cardiac enlargement? Which chambers are affected?
2) Are pulmonary vessels enlarged? Are they arteries or veins?
3) Is the caudal vena cava enlarged?
4) Is aorta or pulmonary artery enlarged?
5) Is there evidence of interstitial/alveolar pattern suggestive of pulmonary oedema?
6) Is there pleural effusion or ascites?
7) Is there any evidence of pericardial effusion?
8) Is hepatomegaly present?

Since pulmonary venous congestion (distension) will/must occur prior to the development of cardiogenic pulmonary oedema, the presence of pulmonary venous congestion represents a strong indication of congestive heart failure.

Radiographic criteria of pulmonary venous distension (lateral view)
pulmonary veins to the cranial lung lobes are greater than 75% the width of the proximal 1/3 of the fourth rib
pulmonary vein to the cranial lung lobe is obviously larger than its accompanying pulmonary artery (normally they are of equal width)
Pulmonary oedema refers to an abnormal accumulation of fluid in the interstitium and/or the alveoli of the lungs. As fluid weeps out of the capillaries, at first it accumulates in the perivascular and peribronchial interstitial spaces (producing silhouetting of the vessels, and/or peribronchial pattern on radiographs). Continued fluid accumulation results in oedema of alveolar walls and ultimately, alveolar oedema (producing air-bronchograms or coalescent pulmonary densities).

Although alveolar oedema is usually preceded by interstitial oedema, many clinical cases represent a mixture of interstitial and alveolar oedema.

Interstitial oedema - shows a clouding (or silhouetting) of the pulmonary vasculature (perivascular pattern). The walls of the pulmonary vessels are obscured by oedema fluid. A peribronchial pulmonary pattern (the most common sign of interstitial oedema noted in the dog) also may occur as noted.

Alveolar oedema shows as coalescing fluffy densities and/or air-bronchograms.

Many textbooks report that, in dogs, pulmonary oedema appears first in the central peri-hilar area (just caudal to the bronchial bifurcation) progressing outward. However, the author’s experience suggests that a significantly enlarged left atrium is often misinterpreted and classified as peri-hilar oedema. Pulmonary oedema may develop initially in the caudal lung fields, but it can often be recognised also in the cranial part of the thorax, just in front of the cardiac silhouette. In cats: variable distribution often occurring in a patchy, irregular pattern primarily in the caudal lobes.

Radiography can also assist in the diagnosis of:
chamber enlargement
great vessel enlargement
Cardiomegaly can be caused by a single chamber enlargement. The two diagrams reported below indicate a map that can guide through the recognition of single chamber or vessel enlargement.

A uniform generalised enlargement of the cardiac silhouette can be caused by four-chamber enlargement or pericardial effusion. However, the presence of a sharp outline of the cardiac profile in combination with engorgement of the caudal vena cava is more suggestive of pericardial effusion. Conversely, a blurry outline of the cardiac silhouette associated with engorged pulmonary veins and interstitial/alveolar pattern is more suggestive of a four-chamber enlargement (eg. Dilated cardiomyopathy)

Assessment of the respiratory system

Most respiratory diseases produce a mixed pattern and in many cases the distribution of densities may provide useful information as to its cause.

Vascular pattern

Normal pulmonary arteries and veins are seen as being of soft tissue radiopacity with smooth walls and even branching as they extend into the periphery of the lung. Changes in size, shape or number of vessels may help in the differentiation of some diseases. On the lateral views, arteries and veins should have approximately the same size. In lateral view arteries and veins can be assessed on the cranial part of the heart, with the artery dorsal to the vein and the bronchus in between. In DV, the arteries are more external compared to the associated veins that are displayed more medially.

Overcirculation: Left → Right shunts (VSD, PDA)
Left sided heart failure (L-CHF)
(with tortuous vessels): Heartworm disease

Undercirculation: Hypovolaemia, shock, PS, hypoadrenocorticism

NB: vascular pattern is usually more prominent in cats

**Bronchial pattern**

The bronchial wall is thickened and/or irregular because of the presence of fluid, chronic cellular allergic or inflammatory inflammation. In the bronchial pulmonary pattern, bronchi that are not normally visible are seen. Bronchial walls are more prominent or thicker than normal. When seen end-on there is a ring-like appearance in cross-section (“doughnut” sign) because the air within the lumen contrasts with the surrounding bronchial wall thickening or mineralisation. Bronchi may not taper normally into the periphery of the lung creating the so called “tram line” sign in longitudinal section.

*Inflammatory or neoplastic infiltrates*

- Bronchitis and bronchiectasis
- Bronchial calcification

**Alveolar pattern**

The alveolar space (normally air-filled) is filled with fluid and/or cellular debris or are collapsed. There is fluffy, increased opacity of the lung fields, occupying one or more lobes, and often associated with air-bronchograms, where the air-filled bronchus is visible adjacent to fluid-filled or collapsed alveoli.

*Fluid accumulation (oedema, inflammation, exudate, blood, chylous)*

- Atelectasis
- Eosinophilic or interstitial pneumonia
- Lungworm infection

*Near drowning*

**Interstitial pattern**

- Eosinophilic or interstitial pneumonia
- Lungworm infection (nodular pattern)
- Pulmonary fibrosis
**Interstitial pattern**

The interstitium of the lung surrounds and supports alveoli, pulmonary vessels and bronchi. The interstitial pattern results in the filling of the interstitial space with fluid, exudate, fibrosis or metastatic lesions. The interstitial pattern may be classified as nodular or diffuse depending on presentation. The ability to recognise an interstitial pattern depends on the severity and degree of radiopacity. Superimposed subcutaneous nodules, nipples or heterotopic bones (common in some breeds, especially old dogs) should be differentiated from interstitial nodules.

- Normal finding in obese/old dogs (diffuse, unstructured)
- Metastatic tumours
  - Granulomas
- Chronic interstitial lung disease (fibrosis)
- Early stage cardiogenic pulmonary oedema

Other abnormalities can be identified by thorough examination of the chest film, such as tracheal collapse, bronchial or oesophageal foreign bodies, megaoesophagus.

**Characteristic radiographic changes in the most common cardiac diseases**

(Please note that findings on radiography may vary markedly with the severity of the disease)

**Mitral valve disease**

- left atrial enlargement
- splitting of the main bronchi and compression of the left main bronchus on lateral view.
- peribronchial pattern (could be due to concurrent small airway disease or pulmonary oedema of congestive heart failure)
- left ventricular enlargement.
- if CHF present, signs of pulmonary venous congestion, pulmonary oedema.
- pulmonary artery dilation if pulmonary hypertension develops
- if patients present as an acute exacerbation (due to ruptured chordae), severe pulmonary oedema may occur
**Endocarditis**
- Can be normal
- chronic marked left ventricular enlargement will be present if substantive aortic valve insufficiency is present
- evidence of HF would be unusual unless aortic valve insufficiency is present or a ruptured chordae tendinae results in sudden mitral valve insufficiency.

**Pericardial effusion**
- very large globose heart (sharp outline)
- concurrent pleural effusion (common)
- pulmonary metastatic lesions may be present (HSA)
- pulmonary oedema (very unusual, mainly in cats with CM)

**Dilated Cardiomyopathy (DCM)**
- pulmonary venous congestion/pulmonary oedema
- left-side or generalised heart enlargement
- signs of right-sided HF (pleural/peritoneal effusion, hepatomegaly)

**Feline cardiomyopathy (CM)**
- mild to moderate left ventricular enlargement
- moderate to severe left atrial enlargement
- “valentine” cardiac shape is often seen in DV
- the cardiac size may be normal
- pulmonary veins may be engorged or tortuous
- if left HF is present, variable degrees of mixed interstitial and alveolar infiltrate may be seen

**Patent Ductus Arteriosus (PDA)**
- left atrial/ventricular enlargement
- aortic bulge (12 - 1 o’clock on D/V view)
- main pulmonary artery bulge (1 - 2 o’clock on D/V view)
- left auricular bulge (2 - 3 o’clock on D/V view)
- pulmonary venous congestion/pulmonary oedema

**Aortic (sub-aortic) Stenosis (SAS)**
- often normal
- left ventricular enlargement (only observed in moderate/severe cases)
- dilation of the aortic arch particularly on the lateral

**Pulmonic stenosis (PS)**
- may be normal in mild cases
- right ventricular enlargement
- bulge in the main pulmonary artery
- ascites
- hepatomegaly

**Ventricular Septal Defect (VSD)**
- may be normal (especially if mild VSD)
- generalised heart enlargement
- pulmonary overcirculation
- right atrial/ventricular enlargement, pleural effusion, ascites (if right-to-left shunt)

**Tetralogy of Fallot (ToF)**
- right ventricular enlargement
- pulmonary undercirculation
- main pulmonary artery may be small

**Atrio-Ventricular Valve Dysplasia (AVVD)**
- atrial/ventricular enlargement
- possible left-sided / right-sided CHF

**Heartworm Disease**
- enlarged right ventricle
- enlarged main pulmonary artery
- enlarged peripheral pulmonary arteries
- decreased peripheral pulmonary artery taper (i.e. truncation)
- tortuous peripheral pulmonary arteries
- interstitial/alveolar pulmonary pattern with a caudal lobar distribution
References


ENDOCARDIAL DISEASE

Topics
1. Chronic degenerative mitral valve disease
2. ACVIM Consensus 2009
3. Endocarditis

Key learning objectives:
At the end of this module delegates should be able to:
- understand aetiology, pathophysiology and diagnosis of chronic myxomatous valve disease (MMVD)
- become familiar with MMVD staging
- become familiar with clinical management of MMVD
- understand aetiology, pathophysiology and diagnosis of infective endocarditis
- become familiar with clinical management of infective endocarditis
CHRONIC DEGENERATIVE MYXOMATOUS MITRAL VALVULAR DISEASE (MMVD)

The most common cardiac disease in dogs
Mitral valve disease (MVD) is the most common acquired cardiac disease in adult dogs (75% of all cardiac diseases). It is a degenerative (myxomatous degeneration) disorder of the A-V valves, particularly the mitral valve causing thickening and redundancy of the valve leaflets, and thickening and lengthening of the chordae tendineae with subsequent mitral regurgitation (or mitral insufficiency). The free margins of the valve leaflets are usually the most affected areas. Similar changes of the mitral valve are also seen in human beings, horses, and pigs. It can also be seen in cats, although with a much lower prevalence. In people, the condition is more commonly called mitral valve prolapse (MVP) syndrome.

Multiple names for the same disease
• Mitral (and/or tricuspid) endocardiosis
• Myxomatous Atrioventricular Valvular Degeneration (MVD)
• Mitral valve disease
• Chronic valvular disease
• Chronic valvular fibrosis
• Mitral valve prolapse (MVP)

One of the most important causes of death in adult dogs
Approximately 10% of all dogs die or are euthanised because of heart failure before 10 years of age and the percentage might be higher in older dogs.

Anatomy and pathology of the mitral valve
The MV complex comprises the annulus, the leaflets, the chordae tendineae, and the papillary muscles. Also important for its functioning is the left atrial musculature inserting to the leaflets and the myocardium to which the papillary muscles are inserted. Unlike the tricuspid valve which is separated by muscle from its counterpart, the pulmonary valve, the mitral valve is immediately adjacent to the aortic valve.

The septal (aortic or anterior) leaflet has a rounded free edge and occupies a third of the annular circumference, whereas the other (mural) leaflet is long and narrow, lining the remainder of the circumference. The septal leaflet meets the mural leaflet to form a zone of apposition, like two sails that flap in systole under the force of the blood flow, vortices, mechanical vibrations, and tension of
the chordae tendineae. The tension of these “sails” causes an audible “snap” in early systole (first heart sound).

Histologically, the atrioventricular layers present four layers:
1. atrial surface or atrialis (endothelial cells)
2. spongiosa, between atrialis and fibrosa (collagen fibres, fibroblasts, elastic fibres)
3. fibrosa, between spongiosa and ventricular surface (well organised collagen fibres)
4. ventricular surface or ventricularis (endothelial cells)

There are also nerves and muscular fibres in the valve leaflets, which can regulate their tension under autonomic control.

The mitral valve is the most commonly affected valve.

The valvular degeneration involves the mitral valve alone in approximately 60% of cases and both valves in approximately 30% of cases. Tricuspid valvular degeneration alone is rare (~10%). From a pathological point of view, the progression of the disease involves 3-4 phases (some pathologists classify phase 1 and 2 under the same class):
• Phase 1: small lesions, discrete nodules along the margins of the leaflets,
• Phase 2: nodular lesions may merge to form bigger nodules
• Phase 3: thickening of the free edges and some roughening of the chordae tendineae
• Phase 4: gross thickening of the free edges and significant nodular lesions. Redundant tissue is responsible for valvular prolapse. Chordae tendineae are also rough and thickened and chordal ruptures may occur resulting in valve flail.

In the early stages of CVD, histopathology shows earliest changes involve the atrial surface (endothelial proliferation) and the spongiosa (fibroblast proliferation and disorganisation of the elastic fibres). The spongiosa increases in size, while the fibrosa regresses. These changes are responsible for the redundancy and thickening of the valve leaflets, which can be observed both on echocardiography and gross pathology. On histology, the spongiosa appears similar to embryonic mesenchymal tissue (“myxomatous”). Similar changes occur at the level of the chordae tendineae.

Aetiology: myths and facts

Many breeders believe that MVD develops due to endocarditis, secondary to dental disease, with bacteraemia originating from the oral cavity. Another common (mis)concept is that MVD may be a
side-effect of routine vaccination. However, endocarditis is rare in dogs and typically affects large-breed dogs rather than the small-breed dogs.

“Wear and tear” theory
The precise cause of MVD is still unknown. According to an old theory, the repeated impact to the leaflets, especially in the areas of apposition, results in slowly progressive changes. However, not all adult dogs are affected by MVD and therefore some predisposing factors may be necessary for the development of the disease.

Collagen abnormalities
Abnormalities of matrix components (i.e. collagen) have been suggested to predispose to MVD. In people, for example, MVP occurs in association with a variety of connective tissue disorders and thoracic deformities (ie pectus excavatum and shallow chest). A similar association seems to exist in Dachshunds but little is known about other canine breeds. These abnormalities may lead to abnormal valve motion (ie prolapse) and increase the shear stress imposed on the leaflets by abnormal leaflet apposition or by the regurgitant flow.

Endothelial damage
Endothelial damage might be an important factor in the pathogenesis of MVD, because it may lead to an imbalance in local growth-factors produced by endothelial cells, as suggested by the association between disease severity and expression of endothelin receptors and nitric oxide synthase. Furthermore, collagen may become exposed to blood in valvular areas in which the endothelium is damaged, and this exposure is expected to promote thrombosis, although this represents a rare complication in dogs.

Physiopathology
Valvular regurgitation
In dogs, the anatomical changes of the AV valve result in AV valve prolapse (a portion of the valve leaflets protrudes towards the atrium) and incapacity of the valvular edges to coalesce and seal the AV annulus during systole. This abnormality causes valvular regurgitation (valve leaking), characterised by a quantity of blood that flows back into the atrium in systole. Valvular regurgitation is the cause of heart murmur in these patients.

Jet lesions
The regurgitant jet may also cause scar lesions (“jet lesions”) on the atrial endothelial surface. In severe cases, massive enlargement of the atrium and scar lesions can cause atrial tears, with consequent bleeding into the pericardial sac (acute or sub-acute haemo-pericardium).

Chamber dilation
Depending on the severity of the regurgitation (namely the quantity of blood that flows back into the atrium), the disease may cause anatomical changes of the cardiac chambers, such as atrial dilation and, eventually, ventricular enlargement (eccentric hypertrophy). Left atrial and ventricular dilation cause tracheal elevation and, in some patients, compression of mainstem bronchi, resulting in stimulation of the coughing mechanoreceptors (typical dry, “honking” cough). However, this phenomenon seems to occur only in geriatric patients affected by concomitant bronchomalacia, tracheal collapse and/or chronic airway inflammation.

RAAS activation
With mitral regurgitation, as long as the left atrium dilates to accommodate the regurgitant blood volume, the pressure does not increase and pulmonary oedema does not develop. However, the reduced stroke volume (hence cardiac output) is sensed by baroreceptors distributed at the level of the carotid sinus and aortic arch and by the cells of the juxtaglomerular cells-macula densa system in the kidney. This causes the activation of the Renin Angiotensin Aldosterone system (RAAS) sympathetic system, resulting in salt and water retention, vasoconstriction and increased heart rate (compensatory phase). The resultant increase in blood volume increases venous return to the heart, resulting in ventricular volume overload, which eventually causes ventricular dilation (eccentric hypertrophy).

End-point of chamber compliance and venous congestion
With the progression of the disease, the capacity of the ventricle to accommodate volume overload decreases and ventricular diastolic pressure increases. Diastolic atrial pressure also increases because atrium and ventricle communicate in diastole. Left atrium and pulmonary veins also communicate and there are no valves in between. Therefore, increased atrial pressure causes increased pulmonary venous and capillary pressure, which will eventually result in pulmonary oedema (congestive heart failure).

Pulmonary hypertension
In severe advanced cases, the pulmonary arterial pressure will also increase, resulting in pulmonary arterial hypertension, right ventricular pressure overload and right-sided heart failure (jugular pulsation, liver congestion, ascites).

Arrhythmias
Left atrial dilation may also cause the development of atrial arrhythmias (premature atrial contractions and atrial fibrillation)
Left ventricular dilation may cause reduced myocardial perfusion (myocardial ischemia) with consequent ventricular arrhythmias (ventricular premature complexes, ventricular tachycardia, etc.).

Myocardial infarction and fibrosis
Small, often microscopic, intramural myocardial infarctions are common findings secondary to myocardial ischemia. These changes can also affect the papillary muscles, contributing to the misalignment of the valvular architecture.
Uncommonly, macroscopic infarctions are observed on post-mortem.
The coronary lesions responsible for the myocardial ischemia resemble the changes seen in myxomatous valves (hyaline or fibromuscular intramural arteriosclerosis). Intramural arteriosclerosis and myocardial infarcts can predispose to sudden death in 25% of the affected patients. Interestingly, the degree of arteriosclerosis and fibrosis is associated with decreased systolic function and survival time in dogs with MVD and HF.

Epidemiology
A disease of small dogs
MVD is a typical disorder of older small breed animals (possibly small breed animals because they live longer than the large breed animals?) with a net prevalence in Cavalier King Charles spaniels (CKCS). In this breed, the disease is inherited as a polygenic threshold trait, meaning that more than one gene can be responsible for the histological and anatomical changes.
The disease is unusual in dogs younger than five years of age. However, mitral regurgitation might be present in some CKCS less than 12 months of age. Post-mortem studies showed that ALL dogs (of all breeds) older than 12 years have some degree of mitral valve degeneration. Males tend to be slightly over-represented.

...but not only small!
Mitral valve disease is also observed in larger breeds (e.g. German shepherd dogs); however, valvular changes appear different, with a more pronounced laxity of the leaflets and less evident nodular lesions. It has been postulated that MVD in larger breeds may have a different aetiology.

Novelty in Clinical Assessment

Quantification of MR

Diagnosing MVD on echocardiography is relatively simple. Combination of 2-D and M-mode echocardiography allows prompt evaluation of valvular structure and the impact of volume overload on cardiac chambers. A direct evaluation of valvular incompetence can be performed using colour and spectral Doppler. However, a precise quantification of MR requires sophisticated echocardiographic techniques, such as proximal isovelocity surface area (PISA) method, which provides an accurate measurement of the regurgitant orifice and regurgitant factor (the percentage of stroke volume ejected into the left atrium during systole).

Examination of chordae tendineae

Rupture of a first order chorda tendinea may cause devastating complication of MVD, leading to acute pulmonary oedema and death despite aggressive medical therapy. However, rupture of minor chordae can be associated with a better survival time. Therefore, it is important to carefully evaluate these structures on echocardiographic examination.

Prognostic indicators

In a study involving more than 500 dogs belonging to 36 different breeds, Borgarelli et al concluded that mild MVD is a relatively benign condition in dogs (median survival time was 19.5 ± 13.2 months). However, they also identified some clinical and echocardiographic parameters that can identify dogs at a higher risk of death:

(univariate analysis for all causes of death)

- Age>8 years
- Syncope
- HR>140 bpm
- Dyspnoea*
- Arrhythmias
- Class of heart failure (ISACHC)
- Furosemide therapy
- End-systolic volume-index (ESV-I)>30mL/m2
• (LA/Ao)>1.7
• E wave transmitral peak velocity (Emax)>1.2 m/s
• Bilateral mitral valve leaflet engagement

(*) non-significant for cardiac only-related deaths

(multivariate analysis for all causes of death)
LA/Ao>1.7 m/s
Syncope*
Emax>1.2 m/s*

(*) non-significant for cardiac only-related deaths

These variables might be useful to identify individuals that need more frequent monitoring or therapeutic intervention

Novelty in Clinical Management
Diagnosis of MVD is relatively easy, based on signalment (old small dog) and presence of a newly developed systolic heart murmur with a point of maximum intensity over the left apex. This is easy. However, where do we go from here?

Surgical management
Open heart cardiac valve repair or replacement in veterinary cardiology is still limited by prohibitive cost and high surgical risk. In a recent US study, surgical treatment of degenerative mitral valve disease by mitral annuloplasty resulted in median survival of 12 months. In most dogs that had mitral valve replacement, thrombi developed on the valves within 4.5 months, probably because of the device implanted and the complex anticoagulation treatment program used. These data indicate there may still be some room for improvement in the surgical management of mitral valve disease in dogs.

Medical management
At present, there is no medical cure for MVD. Clinical signs of congestive heart failure can be successfully controlled by cardiac medications and provide clinical improvement for many months. However, the disease is inevitably progressive and the dog will eventually die or be euthanised due to refractory heart failure.
Furosemide in the asymptomatic patient
Currently, there is no evidence to support early therapeutic intervention in dogs with asymptomatic MVD. Administration of furosemide in patients that are not in heart failure should be avoided for the risk of dehydration, electrolyte imbalance (especially Mg and K), renal hypoperfusion and stimulation of RAAS.

ACE-inhibitors in the asymptomatic patient
So far, two randomised, double blinded, placebo-controlled studies (that investigated the effect of early intervention in asymptomatic dogs with MVD (SVEP and VETPROOF) failed to demonstrate a significant increase in survival time or a delay in the onset of clinical signs.

Pimobendan in the asymptomatic patient
One study on the use of pimobendan in asymptomatic dogs with MR showed that this drug may increase maximum area and peak velocity of the regurgitant jet and predispose to acute focal haemorrhages, endothelial papillary hyperplasia, and infiltration of chordae tendinae with glycosaminoglycans. This study may suggest that pimobendan is not indicated in asymptomatic dogs.

Is this dog in heart failure?
Many old textbooks still report that coughing is a clinical sign of congestive heart failure. This information is misleading and has been disproven by recent (and currently unpublished) clinical studies. Another common mistake is the identification of “perihilar oedema” which is instead an area of soft tissue opacity caused by an enlarged left atrium.

Conversely, a dog in congestive heart tends to be dyspnoeic/tachypnoeic, lethargic and exercise intolerant. On physical examination a dog in heart failure tends to lose the characteristic sinus arrhythmia, due to sympathetic overdrive.

Natriuretic peptides may add an important piece of information in the clinical assessment, although intrinsic limitations due to test sensitivity and specificity should be considered.

Clinical management of the symptomatic patients

1) Control of the effusion
Loop diuretics (furosemide) are effective in providing symptomatic relief and remain the first line treatment, particularly in the presence of oedema. They should be administered to-effect (radiographic resolution of pulmonary oedema and/or normalisation of the respiratory rate)
2) Counteract the RAAS activation

ACE inhibitors have shown beneficial effects on mortality and quality of life in prospective clinical trials and are indicated in all stages of symptomatic heart failure. Spironolactone is a competitive aldosterone inhibitor. Potassium sparing diuretics have generally been avoided in patients receiving ACE inhibitors, owing to the potential risk of hyperkalaemia. However, the early addition of spironolactone to standard therapy should be considered in all dogs with refractory HF. Indeed, ACE inhibitors can reduce aldosterone production by inhibiting the conversion of angiotensin I into angiotensin II. However, they cannot inhibit “local” aldosterone production (chymase activity in heart and blood vessels). The use of spironolactone seems to significantly reduce the myocardial remodelling. Furthermore, in humans with class IV HF, spironolactone has shown to reduce the risk of death by 30%! The clinical benefits of adding spironolactone to ACE inhibitor therapy has also been demonstrated in dogs, where the addition of this drug improved patient’s quality of life and reduced the risk of mortality by 65%.

3) Improve systolic function and promote vasodilation

Systolic dysfunction in dogs with MVD has been clearly demonstrated, which may justify the routine use of inotrope agents. Pimobendan is a potent inotropic and vasodilatory agent (inodilator) which prolongs time to sudden death, euthanasia for cardiac reasons, or treatment failure in dogs with CHF caused by MVD (Quest study: median survival time 267 days, versus 140 days for benazepril).

4) Control malignant arrhythmias

Atrial fibrillation can be efficiently controlled with digoxin. Class II, III, and IV anti-arrhythmic drugs may also be considered in the control of AF. Malignant ventricular arrhythmias may be successfully controlled with class III anti-arrhythmic drugs.

5) Control pulmonary hypertension

Pulmonary hypertension may cause or exacerbate an already existing right-sided congestive heart failure. Palliative control of pulmonary hypertension can be achieved with administration of phosphodiesterase V inhibitors (i.e. sildenafil). However, it appears that even PD-III inhibition (i.e. pimobendan) can reduce the pulmonary arterial resistance.

Therapy for Stage A

Consensus recommendations:
1. No drug therapy is recommended for any patient.
2. No dietary therapy is recommended for any patient.
3. Potential breeding stock should no longer be bred if mitral regurgitation (MR) is identified early, during their normal breeding age of 6–8 years.

Therapy for Stage B1

Consensus recommendations:
1. No drug or dietary therapy is recommended.
2. Re-evaluation is suggested by either radiography or echocardiography with Doppler studies in approximately 12 months (some panellists recommend more frequent follow-up in large dogs).

Therapy for Stage B2

No consensus could be reached about early use of ACE-inhibitors.

Therapy of Stage C (Acute-Hospital-Based)

Consensus recommendations:
1. Furosemide—The specific dosing of furosemide in a dog with CHF should be related to the severity of clinical signs and the response to initial therapy. Lower or higher doses (eg, 1–4 mg/kg) may be appropriate in specific cases. Repeated IV boluses or a constant rate IV infusion may be indicated for poorly responsive dogs.
2. Allow patient free access to water once diuresis has begun.
3. Pimobendan, 0.25–0.3 mg/kg PO q12h—Although the clinical trial evidence supporting the chronic use of pimobendan in the management of Stage C heart failure from CVHD is stronger than for the acute situation, the recommendation to use pimobendan in acute heart failure therapy is strongly supported by hemodynamic and experimental evidence, as well as the anecdotal experience of the panellists.
4. Oxygen supplementation, if needed, can be administered via a humidity and temperature-controlled oxygen cage or incubator or via a nasal oxygen cannula.
5. Mechanical treatments (eg, abdominal paracentesis and thoracocentesis) are recommended to remove effusions judged sufficient to impair ventilation or cause respiratory distress.
6. Provide optimal nursing care, including maintenance of an appropriate environmental
temperature and humidity, increase in the head on pillows, and placement of sedated
patients in sternal posture.

7. Sedation—Anxiety associated with dyspnea should be treated. Narcotics, or a narcotic
combined with an anxiolytic agent, are most often used by panelists. Butorphanol (0.2–
0.25mg/kg) administered IM or IV was the narcotic most often utilized for this purpose;
combinations of buprenorphine (0.0075–0.01 mg/kg) and acepromazine (0.01–0.03 mg/kg
IV, IM, or SQ) as well as other narcotics, including morphine and hydrocodone, also have
been utilized.

8. CRI of sodium nitroprusside for up to 48 hours is often useful for life-threatening, poorly
responsive pulmonary oedema.

**Therapy for Stage C (Home-Based - Chronic)**

Consensus recommendations:

1. Continue PO furosemide administration to effect. The dosage must be titrated to maintain
patient comfort and with attention to effects on renal function and electrolyte status.

2. Continue or start ACEI. Measurement of serum creatinine and electrolyte concentrations 3–
7 days after beginning an ACEI is recommended

3. Continue pimobendan.

4. Panelists recommend against starting a b blocker in the face of active clinical signs of heart
failure (eg, cardiogenic pulmonary edema) caused by CVHD.

5. Participation in a structured, home-based extended care program to facilitate body weight,
appetite, respiratory, and heart rate monitoring while providing client support to enhance
medication compliance and dosage adjustments in patients with heart failure is encouraged.

6. Maintain adequate calorie intake (maintenance approximately 60 kcal/kg body weight)

7. Specifically address and inquire about the occurrence of anorexia, and make efforts to treat
any drug-induced or other identifiable causes of anorexia that occur.

8. Record the accurate weight of the patient at every clinic visit, and investigate the cause of
weight gain or loss.

9. Ensure adequate protein intake and avoid low-protein diets designed to treat chronic kidney
disease, unless severe concurrent renal failure is present.

10. Modestly restrict sodium intake, taking into consideration sodium from all dietary sources
(including dog food, treats, table food, and foods used to administer medications) and avoid
any processed or other salted foods.
11. Monitor serum potassium concentrations and supplement the diet with potassium from either natural or commercial sources if hypokalemia is identified. Diets and foods with high potassium content should be avoided when hyperkalemia has been identified.

*Therapy for Stage D (Acute - Hospital-Based) (Refractory Heart Failure)*

Consensus recommendations:

1. In the absence of severe renal insufficiency, additional furosemide is administered IV as a bolus at a dosage of 2 mg/kg followed by either additional bolus doses, or a furosemide CRI at a dosage of 1 mg/kg/h until respiratory distress (rate and effort) has decreased, or for a maximum of 4 hours.
2. Continue to allow patient free access to water once diuresis has begun.
3. Fluid removal (eg, abdominal paracentesis, thoracocentesis) as needed to relieve respiratory distress or discomfort.
4. More vigorous afterload reduction in patients that can tolerate arterial vasodilation. Drugs potentially beneficial include sodium nitroprusside (starting at 0.5–1 mg/kg/min), hydralazine (0.5–2.0 mg/kg PO), or amlodipine (0.05–0.1 mg/kg PO). These drugs are recommended in addition to an ACEI and pimobendan.

*Stage D Therapy (Home-Based - Chronic)*

Consensus recommendations:

1. Furosemide dosage should be increased as needed to decrease pulmonary oedema or body cavity effusions, if use is not limited by renal dysfunction, (which generally should be monitored 12–48 hours after dosage increases).
2. Spironolactone, if not already started in Stage C, is indicated for chronic treatment of Stage D patients.
3. beta blockade generally should not be initiated at this stage unless clinical signs of heart failure can be controlled, as outlined in Stage C.
ENDOCARDITIS

Inflammation of the endocardial surface of the heart defines the term endocarditis. Infective endocarditis refers to a microbial infection of the endocardial surfaces of the heart (those in contact with the blood). Vegetative endocarditis is a specific form of endocarditis in which structures (vegetations) composed of platelets, fibrin, microorganisms, and inflammatory cells adhere to the heart valves or cling to the edges of septal defects, chordae tendineae, or to the mural endocardium itself. Endocarditis can be classified as acute or subacute-chronic, based on the duration, rate of progression, and severity of the clinical signs. Endocarditis (both the term and the disease) is pathophysiologically and epidemiologically unrelated to endocardiosis, which is by far the most common form of chronic valvular heart disease in dogs.

Predisposing factors
Congenital aortic valve disease (e.g. subaortic stenosis) and probably other congenital heart diseases that cause disturbances of blood flow and subsequent changes in the endocardium predispose to endocarditis. Steroid use is also an important predisposing factor in dogs, and many cases of endocarditis appear to have a nosocomial origin. Infected intravenous catheters, prosthetic heart valves, open heart surgery, and interventional cardiac catheterization (e.g. aortic balloon valvuloplasty) all appear to enhance the risk of endocarditis. Infection with Ehrlichia sp. may predispose to endocarditis in dogs, and presumably other potentially immunosuppressive organisms similarly enhance the risk. Interestingly, chronic valvular heart disease (endocardiosis) does not appear to predispose to infective endocarditis. There is actually little evidence that periodontal disease is a frequent source of infective endocarditis in dogs, in apparent contrast to humans. Other predisposing factors for endocarditis in dogs include other chronic sources of bacteraemia (e.g. urinary tract infection, diskospondylitis) or systemic illness that facilitates bacterial infection (e.g. diabetes mellitus, Cushing’s disease).

Microbiology
Staphylococci sp., streptococci sp., erysipelothrix sp., corynebacteria sp., and escherichia coli sp. are the most common bacterial isolates in canine infective endocarditis. In recent years, Bartonella sp. have been isolated with increasing frequency from dogs with infective endocarditis. In clinical settings where the index of suspicion for Bartonella sp. is high and facilities for Bartonella culture, reliable serologic investigation, or other means of positive identification (e.g. polymerase chain reaction on tissues) are available, this organism is becoming a frequently recognized cause of infective endocarditis in dogs. A wide variety of other organisms have been cultured from isolated
individual cases, with many nosocomial cases involving Pseudomonas sp., Proteus sp., Bacteroides sp., or other unusual (and often highly antibiotic resistant) isolates.

Clinical recognition
The clinical presentation of infective endocarditis often includes extracardiac manifestations of systemic infection and inflammation. Fever is the most common sign, although it may be intermittent, minimal, or even absent in patients with less virulent organisms (e.g. Bartonella sp., some gram-positive organisms) and in those who are severely debilitated or in congestive heart failure.

The use of anti-inflammatory drugs (steroids or nonsteroidals) may mask fever. Other common systemic signs of subacute infective endocarditis include lethargy, anorexia, weight loss, reluctance to move (back pain, polyarthritis), and intermittent lameness (muscle embolisation, polyarthritis). Almost all patients diagnosed with infective endocarditis have a heart murmur, and presumably most patients with endocarditis have a murmur. The murmur may be new, or may be newly recognized because of changes in intensity, quality, timing, or duration. Many animals with endocarditis have a pre-existing heart murmur, e.g. from mild subaortic stenosis. The presence of a diastolic murmur in a systemically ill animal should dramatically raise the index of suspicion for infective endocarditis. These murmurs of aortic insufficiency are often low intensity, soft, blowing murmurs with a distant quality that makes them difficult to hear in noisy clinical environments. They are often heard best by placing the diaphragm of the stethoscope in the animal’s left armpit with the animal lying on its left side, such that the animal is actually lying on top of the stethoscope.

Diagnostic advances
In part because the presenting complaints of clients whose animals have infective endocarditis tend to be vague and associated with some aspect of systemic illness, endocarditis is often difficult to diagnose. Definitive diagnosis requires the synthesis of clinical, laboratory (microbiologic), and echocardiographic data. The standard clinical data base, including a complete blood count, serum biochemistry panel and urinalysis often reveals abnormalities (e.g. mild anaemia, inflammatory or stress leukogram). Urinalysis results may reveal urinary tract infection or proteinuria, the latter caused by glomerulonephritis associated with chronic antigenic stimulation. These clinical laboratory abnormalities are common with other diseases and therefore nonspecific; they do not contribute independently to the diagnosis of infective endocarditis.

In human medicine, standardized criteria for assessing patients with suspected infective endocarditis have been clinically validated and recently revised by a group at Duke University. These criteria
integrate the presence of known predisposing factors for endocarditis, blood culture results, and echocardiographic findings with other clinical and laboratory information to arrive at a diagnosis. While these criteria are not directly applicable to veterinary medicine for a variety of reasons (different predisposing factors, greater access of human patients to transesophageal echocardiography, different microbiological and anatomic spectrum of human disease, etc), they provide a useful starting point for discussing current veterinary diagnostic criteria. The Duke criteria adaptable to veterinary medicine can be briefly summarized as follows:

**Major Criteria - Microbiologic**
- At least 2 separate blood cultures positive for a typical organism, obtained by separate venipunctures an hour apart (3 cultures are usually recommended if time, money, and patient size permits, at least 2 must be positive).
- In acutely ill patients with apparent sepsis syndrome, 3 blood cultures 5 - 10 minutes apart should be obtained if the patient’s size permits, followed by empiric antibiotic therapy.

**Major Criteria - Echocardiographic Evidence of Endocardial Involvement**
- An oscillating mass at a site of endocardial injury (i.e. a mass near a valve, but separate from the valve, whose movements are distinct from those of the valve -- this criteria excludes valves that are merely thickened, as in endocardiosis).
- Periannular abscess
- New dehiscence of either a prosthetic patch (e.g. VSD patch), or a prosthetic valve.

**Minor Criteria - Known Predisposing Factors**
- Previous proven endocarditis
- Subaortic stenosis
- Prosthetic valve, synthetic intracardiac patch, or transvenous pacemaker
- History of steroid use with any of the above conditions.
- Prolonged IV catheterization, or infected IV catheterization site

**Minor Criteria - Clinical Findings**
- Fever (> 39.7C / 102.5 F), especially recurrent or persistent
- New heart murmur

**Minor Criteria - Microbiologic**
* Single positive blood culture
* Serologic evidence of infection

**Minor Criteria - Echocardiographic**

* Aortic insufficiency (more than just “3-pixel” garden variety common in large dogs)

Definite diagnosis of infective endocarditis in the dog might reasonably require fulfilling 2 major criteria above, or 1 major plus 3 minor criteria, or 5 minor criteria. Dogs with suspected or definite infective endocarditis should have electrocardiograms recorded (and repeated regularly during their clinical course), since the onset of AV or bundle-branch block, particularly in the setting of aortic valve endocarditis, suggests perivalvular extension of the infection. Such extension is a poor prognostic sign, suggesting that current therapy may be insufficient.

When blood cultures from suspected infective endocarditis patients remain sterile after 72 hours of incubation, the laboratory should intensify efforts to grow fastidious organisms such as Bartonella sp. and the clinician should initiate serologic assessment for such organisms if he or she hasn’t already done so. The lysis centrifugation technique allows direct plating to enriched mediums, which speeds the growth and increases the yield of Bartonella sp., which can take up to a month to grow.

**Echocardiography**

Routine transthoracic echocardiography is quick, widely available, non-invasive, and at least in humans has excellent specificity for vegetations when performed by board certified cardiologists (98 percent). The sensitivity of transthoracic echocardiography for vegetations in human patients is substantially less, in the range of 60 percent. For this reason, transesophageal echocardiography is recommended in human patients with suspected endocarditis but a negative transthoracic echo (e.g. a predisposed patient with positive blood cultures). In humans, the sensitivity of transesophageal echocardiography for detecting vegetations is reported to be 75 to 95 percent, while maintaining a specificity of 85 to 98 percent. The sensitivity and specificity of transthoracic or transesophageal echocardiography has not been systematically examined in dogs. In humans, and presumably in dogs, the experience and training of the echocardiographer has a dramatic impact on the accuracy of the test.

**Clinical complications**
Heart failure indicates extensive valve damage and a commensurately guarded long-term prognosis. It is unusual for animals in heart failure secondary to endocarditis to live more than 2 years with this condition, even with effective anti-infective therapy and optimal management for heart failure. Syncope or episodic weakness is an infrequent presenting sign that may be caused by high grade atrioventricular (AV) block (associated with extension of aortic valvular endocarditis into the adjacent tissues, which include the AV node), or less often, sustained ventricular or even supraventricular tachyarrhythmia, or neurologic sequel of bacterial prognosis of infective endocarditis. In dogs as well as humans, aortic valve infection appears to be more often associated with congestive heart failure than mitral-valve infection.

Embolisation of fragments of vegetations can cause acute infarction of a variety of organs, most commonly involving the spleen, liver, kidney, or skin in the dog. Neurologic complications occur in dogs, but generally appear to generally less common (or less visible) in dogs than in people, where the risk of stroke is high in left-sided endocarditis. Polyarthritis, when it occurs, may be immune-complex mediated or may in fact be caused by direct infection of multiple joints with the cultured organism. Endocarditis complicates approximately 20 - 30% of cases of diskospondylitis in dogs, in whom pain or the onset of neurologic signs (caused by spinal cord or nerve root compression) generally signals the presence of disease. Dogs diagnosed with primary diskospondylitis should be screened echocardiographically for evidence of infective endocarditis whenever a heart murmur is detected.

Advances in treatment
Prolonged parenteral administration of a bactericidal antibiotics or combinations of antibiotics is currently recommended for the treatment of infective endocarditis in humans. Such treatment courses are generally prohibitively expensive in dogs. Treatment is usually begun with parenteral antibiotic combinations in hospitalized dogs, but once the fever has resolved and clinical improvement (return of appetite, etc.) is evident (generally not more than 3 - 5 days), treatment is completed on an outpatient basis with oral antibiotics. Treatment is based on blood culture and sensitivity results, but these are not available for the first, often critical, hours or days of therapy. Empiric antibiotic therapy for dogs with a clinical history and echocardiographic findings compatible with infective endocarditis are generally started on a combination of fluoroquinolone and a penicillin-based antibiotics. Parenteral Enrofloxacin (5mg/kg IV q12h) and Amoxicillin (20mg/kg IV q8h) are often chosen. Therapy is generally continued for 12 weeks, and blood cultures are ideally obtained after 10-14 days (on antibiotics), and then again 1 week after stopping antibiotics. If Bartonella sp. are identified by culture or serology, current antibiotic recommendation is
Azithromycin, 5 - 10mg/kg q24h for the first 7 days, then every other day for 6 - 12 weeks. Azithromycin appears to achieve intracellular concentrations approximately 120 times higher than erythromycin.

References
Bruce W. Keene, Recent advances and complications associated with canine endocarditis, Proceedings ACVIM forum, Baltimore 2005
MYOCARDIAL DISEASE

Topics
1. Myocardial disease: general considerations
2. Myocardial disease in cats
3. Myocardial disease in dogs
4. Myocarditis

Key learning objectives:
- At the end of this module delegates should be able to understand aetiology, pathophysiology, clinical signs, diagnosis and treatment of:
  - cardiomyopathy in dogs
  - cardiomyopathy in cats
  - myocarditis
  - other myocardial diseases
FELINE MYOCARDIAL DISEASE

Classification, Pathophysiology, and Clinical Presentation

Introduction

The diagnosis and clinical management of myocardial diseases (or cardiomyopathy) in cats represents one of the most challenging situations in veterinary cardiology. Although several attempts have been made to standardise the classification of cardiomyopathies both in humans and cats, some disagreement still exists amongst cardiologists. Classification criteria are continuously evolving as the aetiology of myocardial disease becomes better understood, especially with the continuous discovery of underlying molecular mechanisms both in people and in cats. It is now widely accepted that, for a given aetiology, there may be a spectrum of phenotypes ranging from restrictive to dilated. The clinical management of cases of feline myocardial disease is an even more controversial topic, especially after the publication of recent clinical studies. These articles will review the various manifestations of myocardial disease in cats and offer a critical, and often controversial, approach to diagnosis and management of these clinical conditions.

Classification

Cardiomyopathy (CM) was initially defined in 1980 by the World Health Organisation (WHO) as heart muscle diseases of unknown cause, in which the dominant feature is cardiomegaly and heart failure. The updated WHO definition in 1995 was “diseases of myocardium associated with cardiac dysfunction” and included the arrhythmogenic right ventricular cardiomyopathy (ARVC) and restrictive cardiomyopathy (RCM) for the first time. In feline medicine, the classification of myocardial diseases follows the WHO
definitions above and guidelines for a standard diagnosis are reported in the literature. However, the common classification of cardiomyopathy as hypertrophic (HCM), restrictive (RCM) and dilated (DCM) forms presents important limitations because it mixes anatomic designations (i.e. hypertrophic and dilated) with functional ones (e.g. restrictive). Consequently, confusion may arise because the same disease could appear in two categories. Furthermore, a myocardial disease secondary to valvular, ischaemic or inflammatory conditions may share a final common pathway with a primary CM. In fact, there is a substantial overlap in the remodelling and compensatory mechanisms in the failing heart, which justifies a wider use of the term CM. Another criticism to the current classification of CM is that it should include not only altered contractility or impaired diastolic function, but also myocardial electrical diseases, such as rhythm disturbances and enhanced arrhythmogenicity. Finally, cardiac remodelling may cause some myocardial conditions to evolve from one form to another during their natural clinical course. For example, HCM may progress from a non-dilated and hyperdynamic state to a dilated form with systolic dysfunction and failure. At present, the diagnosis and classification of CM is primarily based on echocardiographic criteria. However, phenotypic variability is substantial, even within the same form of CM, and this often causes subjective interpretations of echocardiographic diagnosis, especially by inexperienced echocardiographers. Pathology is an alternative approach to diagnosis and classification of cardiomyopathy (figure 1) but this is less relevant to practical clinical considerations.
Hypertrophic cardiomyopathy (HCM)

This condition represents the most common myocardial disease in cats and accounts for nearly two thirds of the CM cases seen in this species. It is characterised by increased cardiac mass associated with a hypertrophied, non-dilated left ventricle. The myocardial hypertrophy usually presents with a wide phenotypic variability, as it can affect different portions of the interventricular septum (IVS) and/or left ventricular free wall (LVFW). According to Fox et al., myocardial hypertrophy in feline HCM can present in four different patterns:

1) Diffuse and substantial concentric hypertrophy, involving portions of IVS as well as the contiguous LVFW (one third of cases).

2) Diffuse and substantial asymmetric hypertrophy, affecting preferentially the IVS or the LVFW (one third of cases).

3) Segmental hypertrophy confined to one left ventricular segment (IVS or LV)

4) Segmental hypertrophy affecting non-contiguous segments of IVS and LV

These lesions are often accompanied by left atrial (LA) dilation, aneurismal thinning of the LV apex, and focal myocardial infarction.
In addition to the lesions reported above, right ventricular (RV) hypertrophy and right atrial (RA) enlargement can also be observed.

Primary HCM is an inheritable condition in people with eleven mutated sarcomeric genes presently associated with the disease. Due to an elevated inter- and intra-genetic diversity, more than 400 individual mutations have been identified so far. Familial HCM has also been described in Maine coon cats with an autosomal dominant mode of inheritance. A similar inheritance may also be present in other pedigrees, such as Ragdolls and British shorthair breeds. A causative mutation for HCM has been recently identified in the sarcomeric gene for the cardiac myosin binding protein C (MYBPC3) both in Maine coons and Ragdolls. However, the mutation in the two breeds appears in different regions of the same gene (between domains C0 and C1 of the protein in Maine coons and domain 6 in Ragdolls). Other mutations are likely to be identified in the near future.

Secondary myocardial hypertrophy can be caused by ventricular pressure overload (i.e. outflow obstruction, systemic hypertension), hypersomatropism and hyperthyroidism. However, the LV concentric hypertrophy commonly observed in hyperthyroid people presents less commonly in feline hyperthyroidism. In a study involving 23 hyperthyroid cats, Connolly et al observed only a modest septal hypertrophy and a reduction of the fractional shortening. A mild septal hypertrophy accompanied by clinical evidence of congestive heart failure was also been observed in cats after administration of methylprednisolone acetate. Other forms of myocardial hypertrophy have been described in feline muscular dystrophy and infiltrative myocardial tumours (e.g. lymphomas) which can induce echocardiographic changes analogous to HCM both in people and cats. Finally, a number of other diseases occurring in people are associated with LV hypertrophy and they may resemble or mimic primary HCM (i.e. glycogen storage disease, Noonan syndrome).
Restrictive cardiomyopathy (RCM)

Cardiac conditions characterised by a myocardial stiffness and diastolic dysfunction (restrictive pathophysiology) represent the second most common form of CM in cats (approximately 20% of feline CM cases). Restrictive CM can present with a spectrum of clinical manifestations and pathologic phenotypes even wider than that observed in HCM. Restrictive cardiomyopathy should be differentiated from constrictive pericarditis, which is also characterised by a normal or nearly normal systolic function and abnormal ventricular filling. However, in a practical clinical setting, such differentiation can be very difficult because it requires cardiac catheterisation and/or endomyocardial biopsy. Furthermore, cases of constrictive pericarditis have not been reported in the cat, although a thorough pathological examination of the feline pericardium is seldom performed.

There are two types of RCM described in the human literature, the myocardial and the endomyocardial form, and this classification may also be suitable to describe RCM in cats. Feline myocardial RCM is a non-infiltrative disease characterised by restrictive filling, normal or mildly thickened LVFW or IVS, preserved systolic function and severe, often bilateral, atrial enlargement. The endomyocardial form of feline RCM is characterised by extensive reparative fibrosis at the level of endocardium or endomyocardium. Fibrotic lesions affect primarily the LV and they can present as large scars bridging the ventricular lumen from the LVFW to the IVS and causing obstruction of the mid to apical LV chamber and often turbulence of the blood flow. It is very likely that the previously described “moderator band cardiomyopathy” or “excessive moderator band” are simply lesions associated with endomyocardial RCM. Furthermore, the moderator band (or trabecula septomarginalis) is a muscular band of myocardium located in the right ventricle. Therefore the use of “moderator band” in the above reports is a misnomer.
In the “obliterative” form of RCM, extensive fibrosis markedly reduces the LV lumen. In general, the abnormal fibrous tissue can cause chamber deformity at different levels, including the mitral valve apparatus, which may ultimately result in mitral regurgitation. Myocardial infarction is sometimes observed in the LV, presenting as focal, depressed and hypokinetic areas. The presence of significant fibrotic lesions and focal areas of myocardial hypomotility may facilitate the echocardiographic recognition of RCM.

In people, approximately 50% of the RCM cases result from specific clinical disorders, primarily genetic and acquired infiltrative amyloidosis, while the remaining 50% of RCM cases are of unknown nature (idiopathic). Other causes of myocardial RCM described in people are sarcoidosis, inheritable metabolic disorders (Fabry disease, Gaucher disease, glycogenosis, mucopolysaccaridosis), haemochromatosis, glycogen storage disease, and diabetes. Endomyocardial types of RCM can result from Löffler endocarditis (hypereosinophilic syndrome), endomyocardial fibrosis (EMF, typically found in populations of equatorial Africa), endocardial fibroelastosis (EFe, described in foetuses and infants) and carcinoid syndrome (metastasis of carcinoid tumours from the intestine to the heart). To the best of the author’s knowledge, an aetiological sub-classification of RCM has not been reported in cats, although myocardial damage followed by reparative fibrosis might be associated with hypereosinophilia, viral or immune-mediated diseases.

Dilated cardiomyopathy (DCM)

Dilated cardiomyopathy is characterised by a severely dilated LV chamber and hypocontractile myocardium. This CM had represented the second most common form of feline cardiac disease until 1987, when Pion et al reported the association between taurine deficiency and DCM and the normalisation of LV function after oral taurine supplementation. Consequently, taurine content in feline diets was adequately increased, resulting in a dramatic
reduction in the prevalence of feline DCM (approximately 10% of all cases of feline CM). Taurine deficiency may also cause central retinal degeneration in cats, which seems to persist even when plasma taurine level is restored. However, not all cats fed taurine-deficient diets develop DCM, indicating that other pathophysiological mechanisms might be involved, like taurine depletion associated with potassium-deficient diets or genetic predisposition. The rare cases of taurine-associated feline DCM observed nowadays are generally the consequence of a non-traditional diet (ie, vegetarian/vegan diets or canine diets). Finally, sporadic cases of DCM can still be seen in cats with normal plasma taurine levels. These forms of DCM could represent the end-stage of an undiagnosed valvular disease (i.e. mitral dysplasia) or an ischemic myocardial disease. They could even be related to sustained tachycardia (tachycardiomyopathy) or unrecognised episodes of toxicity or viral infection.

Arrhythmogenic right ventricular cardiomyopathy (ARVC)
The hallmark of ARVC is a markedly enlarged RV and RA. The right myocardial free wall appears very thin and hypokinetic, and the presence of aneurysm is also common. Mild tricuspid regurgitation is usually present, while the LV appears minimally involved and preserves its main morphology and functions. In people, ARVC is a familial disease characterised by progressive myocardial atrophy caused by injury (myocyte death and patchy myocarditis) and subsequent repair by fibro-fatty replacement. Potential pathogenetic mechanisms include apoptosis (programmed cell death), genetically determined atrophy (dystrophy), inflammatory and immune-mediated processes. In people, ARVC accounts for 20% of sudden cardiac death, especially in young athletes, due to paroxysmal ventricular tachycardia progressing into ventricular fibrillation. Cats with ARVC may also present with arrhythmias, including ventricular tachycardia, atrial fibrillation, supraventricular
tachycardia, ventricular premature complexes, right bundle branch block and atrioventricular block.

*Unclassified cardiomyopathy (UCM)*

In people, unclassified cardiomyopathies include all cases that do not fit readily into any other group of CM. Similarly, a significant number of feline myocardial diseases show features that are not typical of any other commonly recognised CM and are therefore described as “unclassified”. The pathogenesis of UCM is unclear. However, this condition could represent an early or late stage of another recognised form of CM. Furthermore, some segmental myocardial changes accompanied by ventricular dysfunction could be secondary to myocardial ischemia and infarction. End-stage myocardial remodelling of HCM, in particular, presents with relative thinning of the LVFW and IVS and with dilation of the ventricular lumen, decreased fractional shortening, and progression to heart failure both in humans and cats. Finally, myocardial remodelling may result from unrecognised or undiagnosed valvular or pericardial abnormalities. Therefore, it is unlikely that UCM represents an individual pathological entity and a very careful approach should be taken in classifying cardiac conditions under this group.
Myocarditis

Inflammation of the myocardium (myocarditis) represents another important myocardial disease in cats. Although several cases of feline myocarditis have been reported in the literature, this condition is surprisingly underestimated. In a recent study conducted by Meurs et al., myocarditis was identified on histopathology in nearly two thirds of a randomly selected population of cats with idiopathic CM (hypertrophic, dilated and restrictive), whereas control cats showed a normal myocardium. Approximately one third of cardiomyopathic cats were found positive for panleukopenia viral DNA by polymerase chain reaction (PCR) technique, but resulted negative for herpes virus, calici virus, and corona virus. This remarkable study suggests a possible role of viral myocarditis in the pathogenesis of feline CM. Myocarditis in cats can also been associated with protozoal infections, such as toxoplasmosis (T. gondii) and sarcocystosis (S. felis), and bacterial

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<th>Cause</th>
<th>Myocardial lesion(s) commonly observed</th>
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<tr>
<td>Hyperthyroidism</td>
<td>Modest septal hypertrophy and a reduction in fractional shortening</td>
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<tr>
<td>Administration of methylprednisolone acetate</td>
<td>Septal hypertrophy accompanied by clinical evidence of congestive heart failure</td>
</tr>
<tr>
<td>Hypersomatotropism</td>
<td>Concentric left ventricular hypertrophy</td>
</tr>
<tr>
<td>Left/right outflow obstruction</td>
<td>Concentric left/right ventricular hypertrophy</td>
</tr>
<tr>
<td>Systemic hypertension</td>
<td>Concentric left ventricular hypertrophy</td>
</tr>
<tr>
<td>Myocardial tumours (eg, lymphomas)</td>
<td>Concentric left ventricular hypertrophy and hypokinesis</td>
</tr>
<tr>
<td>Dystrophin-deficient hypertrophic feline muscular dystrophy</td>
<td>Concentric left ventricular hypertrophy and hypokinesis, hypertrophic endocardium and hypertrophic and slightly enlarged papillary muscles</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Depressed and hypokinet myocardial areas, ventricular chamber dilation</td>
</tr>
<tr>
<td>Tricuspid dysplasia</td>
<td>Right ventricular and right atrial chamber dilation resembling ARVC</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>Concentric left/right ventricular hypertrophy</td>
</tr>
<tr>
<td>ARVC = arrhythmogenic right ventricular cardiomyopathy</td>
<td></td>
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</tbody>
</table>
streptococcal infection (*S. canis*). In all these cases, myocardial lesions resembled echocardiographic features of CM.

**Pathophysiology of feline myocardial disease**

*Left Ventricular Outflow Tract (LVOT) obstruction*

Many human patients affected by HCM present a variable degree of dynamic LVOT obstruction. This obstruction is primarily caused by systolic anterior motion (SAM) of the mitral valve and mid-systolic contact with the ventricular septum. Similarly, SAM is present in approximately 50% of cats affected by HCM. The main characteristic of SAM is an abrupt movement of the elongated anterior leaflet of the mitral valve towards the IVS. Since the LVOT is constituted by this valvular leaflet and the proximal part of the IVS, such an abnormal movement causes narrowing of the tract and interferes with the LV outflow in mid-systole. The magnitude of the outflow gradient can be reliably estimated with Doppler interrogation and is directly related to the duration of the contact between the valvular leaflet and the proximal IVS. Under these conditions, the mitral valve does not completely seal the atrio-ventricular annulus and mitral regurgitation will follow. The resulting combination of flow turbulence in the LVOT and mitral regurgitation explain the presence of an audible systolic murmur on auscultation in these patients (figure 2 and 3). Dynamic obstruction and systolic murmurs can be present at rest or can become audible when the heart rate and cardiac contractility increase, like during stress or excitement.

The mechanism of SAM is not fully understood and several hypotheses have been suggested. However, deformation of the mitral valve architecture (leaflets, chordae tendineae, papillary muscles) and the hyperdynamic state caused by the concomitant myocardial hypertrophy seem the most plausible explanations. Intrinsic valvular disease (i.e. endocardiosis or dysplasia) may also play a role in some patients with SAM, especially when accompanied by
severe mitral regurgitation. Surprisingly, Rush et al observed that cats with SAM live longer than cats without this echocardiographic finding. It should also be noted that, despite a widespread belief amongst clinicians, SAM is not pathognomonic of myocardial hypertrophy, having been convincingly documented in human and canine patients in the absence of significant LV hypertrophy.

Myocardial ischemia
Regional myocardial ischemia is commonly recognised in human and feline patients with all forms of CM and it is often followed by replacement fibrosis. The cause of ischemia is not fully understood but it is likely related to intramural coronary arterial disease caused by the myocardial hypertrophy or distension. The significant elevation of troponin I in cats with HCM might indicate an ongoing myocardial damage, possibly secondary to a concurrent myocardial infarction. Ischemia and infarction will induce regional myocardial abnormalities characterised by systolic dysfunction (dyssynchrony, hypokinesis and dyskinesis), diastolic impairment, ventricular remodelling and malignant ventricular arrhythmias.

Diastolic dysfunction
Abnormality in the ventricular relaxation (diastolic dysfunction) is present in almost all cases of CM. In HCM patients, the reduced ventricular compliance is predominantly caused by myocardial hypertrophy, although interstitial fibrosis and loss of cellular architecture may also contribute to the loss of compliance. The diastolic dysfunction in RCM is primarily caused by myocardial fibrosis, infiltration, or scarring of the endomyocardial surface. Similarly, loss of compliance can be present in all the other manifestations of myocardial disease accompanied by fibrotic lesions, including DCM.
Tachycardia may also exacerbate the diastolic dysfunction by reducing diastolic time, hence the time available for ventricular filling. Furthermore, since coronary blood flow occurs in diastole, fast heart rates may aggravate myocardial ischemia.

Diastolic dysfunction will cause increased filling pressure. Left atrial enlargement will initially compensate for this until the point of its maximal compliance, which is followed by pressure increase in the atrial chamber. The absence of valves between the LA and pulmonary veins will result in pulmonary venous hypertension and eventually pulmonary ooedema and/or pleural effusion (congestive heart failure, CHF). Dynamic outflow obstruction (SAM) and mitral regurgitation also contributes to increase LV and LA pressure.

*Systolic dysfunction*

Reduced myocardial contractility is the primary pathophysiological mechanism in DCM and ARVC with a predominant involvement of the LV and RV respectively. However, systolic impairment was also demonstrated in HCM cats by using pulsed tissue Doppler imaging (TDI) technique. In this study, the systolic dysfunction did not appear related to the presence of left ventricular outflow tract obstruction and congestive heart failure. Systolic dysfunction may occur in any myocardial disease accompanied by significant ischemia and replacement fibrosis (i.e. RCM, UCM, myocarditis). Systolic dysfunction will result in reduced stroke volume and increased ventricular filling pressure, due to increased end-systolic ventricular diameter, which will eventually lead to CHF.

*Neuro-hormonal activation (RAAS, Sympathetic activation, αTNF, endothelin)*

Reduced stroke volume caused by lower end-diastolic volume (diastolic dysfunction) or reduced myocardial contractility (systolic dysfunction) is sensed by baroreceptors (distributed at the level of the carotid sinus, aortic arch and afferent renal arterials) and by the cells of the
juxtaglomerular system in the kidney. This induces the activation of the Renin-Angiotensin-Aldosterone-System (RAAS), resulting in vasoconstriction and salt and water retention (compensatory phase). The resultant increase in blood volume increases venous return to the heart, leading to increased myocardial wall stress.

Stimulation of baroreceptors also determines the activation of the sympathetic nervous system, which has deleterious effects since it promotes vasoconstriction, induces further activation of the RAAS, and increases heart rate and myocardial contractility with a final exacerbation of myocardial wall stress.

Circulating concentrations of the cytokine tumour necrosis factor alpha (αTNF) are increased in many feline patients with CHF and this could be implicated in the development of endothelial abnormalities.

Finally, endothelin (ET), a potent vasoconstricting peptide produced by endothelial cells and other tissues, is significantly increased in cats with myocardial disease and may have an important pathogenetic role in feline CM by inducing cell proliferation, vasoconstriction, activation of the sympathetic system and cardiac remodelling.

**Arterial thromboembolism (ATE)**

The presence of a thrombus in one of the cardiac chambers and subsequent ATE represent a relatively common and dramatic sequel in the pathophysiology of feline CM. Intracavitary thrombi may be identified incidentally during echocardiography and whether their formation is correlated to severe LA dilation remains controversial. The thrombus formation may be facilitated by intracardiac blood stasis, altered coagulability or endothelial injury secondary to αTNF release. Interestingly, only 50% of feline ATE cases present with a concurrent CM and not all cats with echocardiographic evidence of intracavitary thrombi develop ATE.
However, it should be taken into consideration that thrombi can also induce blood flow obstruction.

**Clinical presentation**

The clinical presentation of these cats does not differ significantly amongst the various groups. Therefore, it is more practical to approach all these patients simply as cardiomyopathic. Furthermore, criteria for diagnosis, classification, and treatment of different forms of CM have changed over the years and the data provided in the above study for individual forms of CM may not apply to the current trends in feline cardiology. The median age of cats when diagnosed with a form of CM is 5.5 years (range 4 months to 16 years). The disease appears equally distributed between males and females and amongst different breeds, although genetic predisposition of some pedigrees should be taken into consideration (i.e. Maine coons, Ragdolls, Norwegian Forest cats).

Cardiomyopathic cats present with a wide variety of clinical signs. Abnormal heart sounds are the most common clinical sign. They include heart murmurs (approximately 60% of CM cats), gallop sounds (nearly 20% individuals) and muffled heart sounds (5% of CM cats). The heart murmur is primarily a consequence of mitral regurgitation and/or dynamic LVOT obstruction. However, tricuspid regurgitation may also be present, especially in severe forms of right ventricular dilation (ARVC, DCM, pulmonary hypertension secondary to left-sided CHF). Gallop sounds are characterised by the presence of diastolic sounds (S3 and/or S4), which become audible due to a reduced compliance of the myocardium. This may occur secondary to ventricular wall hypertrophy, myocardial infiltration, fibrosis, tachycardia or a combination of these factors. Muffled heart sounds would indicate the presence of pleural and/or pericardial effusion.
**Dyspnoea** is another common clinical sign, which suggests a concomitant congestive heart failure (pulmonary oedema and/or pleural effusion). It is common for many clinicians to have observed cats developing CHF acutely after a stressful event (e.g. car journey, hospitalisation) or after simple clinical procedures (e.g. restraint, forced recumbency for radiographic examination). The sudden onset of CHF in these cases is attributable to a rapid release of catecholamines, which induces generalised vasoconstriction and increased cardiac output (increased stroke volume and heart rate). The result of these combined effects is a ventricular pressure overload, increased atrial pressure and, eventually, pulmonary capillary hypertension, pulmonary oedema and/or pleural effusion. Hence, patients suspected of having or known to have CM should always be examined gently and cautiously and considerations given to the risks of any procedure borne in mind.

*Heart rate higher than 200 bpm* is present in approximately one third of cardiomyopathic cats and it is likely caused by sympathetic stimulation. Although there is no consensus available to define a heart rate threshold for tachycardia in cats, most cardiologists would agree that fast heart rate can potentially worsen the clinical presentation by affecting the myocardial diastolic function and reducing coronary blood flow.

*Limb paresis/paralysis* associated with arterial thromboembolism (ATE) is seen in approximately 10% of cats with myocardial disease. Bilateral hindlimb paresis represents the most common presentation (71% of all ATE cases), followed by unilateral hindlimb (14%) and unilateral frontlimb (12%) paresis. The lack of a palpable pulse is suggestive of ATE. However, occlusion of the internal iliac artery or more distal arteries can still induce paresis with a concomitant palpable femoral artery (figure 4).

Significant hypothermia is observed in the majority of cats with CM and this appears particularly pronounced in cases complicated by ATE.
Cardiac arrhythmias and hypotension (systolic blood pressure < 120 mmHg) are observed in approximately 10% and 15% of CM cats respectively. Many arrhythmias can be paroxysmal in these patients and they may not be detected during physical examination or standard electrocardiographic recording. Severe paroxysmal arrhythmias can be responsible for episodes of syncope (nearly 10% of cases) and sudden death (5% of cases) that occur in cats with myocardial disease. Hypotension is believed to be the result of a significant reduction of the cardiac output, which is usually observed in the most severe cases. Ascites is also observed in feline myocardial disease (around 10% of CM cases) and this suggests the presence of right-sided-failure, more likely associated with ARVC, DCM, RCM or complicated forms of HCM or myocardial ischemia (figure 5).
<table>
<thead>
<tr>
<th>Clinical finding</th>
<th>Approximate incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart murmur</td>
<td>60</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>50</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>30</td>
</tr>
<tr>
<td>Lethargy</td>
<td>20</td>
</tr>
<tr>
<td>Gallop rhythm</td>
<td>20</td>
</tr>
<tr>
<td>Hypotension</td>
<td>15</td>
</tr>
<tr>
<td>Poor body condition</td>
<td>10</td>
</tr>
<tr>
<td>Ascites</td>
<td>10</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>10</td>
</tr>
<tr>
<td>Collapse</td>
<td>10</td>
</tr>
<tr>
<td>Abnormal respiratory sounds</td>
<td>10</td>
</tr>
<tr>
<td>Hindlimb paresis</td>
<td>7.5</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>5.5</td>
</tr>
<tr>
<td>Muffled heart sounds</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Adapted from Ferasin et al (2003)⁷
Figure 1. Various phenotypic manifestations of feline myocardial disease. Legend: RV=right ventricle; LV=left ventricle; (white bar = 1.0 cm)

a) Left ventricular hypertrophy with reduced lumen of the chamber in a cat with hypertrophic cardiomyopathy; b) fibrotic lesion bridging the left ventricular lumen (black arrowhead) and affecting the papillary muscles (“interpapillary muscle sinueia”) (white arrowhead) in a cat with restrictive cardiomyopathy; c) bi-ventricular enlargement in a dilated form of feline cardiomyopathy

d and e) LV enlargement in a cat affected by hypertrophic cardiomyopathy; f) bi-ventricular enlargement in a dilated form of cardiomyopathy
g) atrial myocardium in a normal cat; h) bi-atrial wall hypertrophy and chamber dilation in a subject affected by hypertrophic cardiomyopathy; i) bi-atrial dilation and wall thinning in a cat affected by dilated cardiomyopathy.

j) severe RV dilation in a cat affected by ARVC; k) histological cross section of the same heart showing massive right ventricular dilation and thinning of the RV wall.
Figure 2  Dynamic left ventricular outflow obstruction. The picture on the left side shows a normal laminar flow in the LVOT (depicted as blue arrow) during systole with both mitral valve leaflets coalescing and sealing the AV ostium. The picture on the right side shows a motion of the AML and contact with the IVS (systolic anterior motion or SAM). This abnormal movement of the AML causes narrowing of the left ventricular outflow tract and mitral valve insufficiency and consequently blood flow turbulence both in the LVOT and LA (depicted as colour melange arrows). Legend: LVOT= left ventricular outflow tract; Ao= aorta; LA= left atrium; LV= left ventricle; AML= anterior mitral leaflet; PML= posterior mitral leaflet; IVS= inter-ventricular septum
Figure 3  Echocardiographic features of systolic anterior motion (SAM) in a cat affected by an obstructive form of hypertrophic cardiomyopathy (HOCM). The abnormal movement of the anterior mitral valve leaflet towards the interventricular septum in early-mid systole causes dynamic interference of the left ventricular outflow and turbulence in the outflow tract. Since the mitral valve remains partially open during this phase, mitral regurgitation is also observed. The two simultaneous turbulent flows are characteristic of this phenomenon (figure 3A). Repeated contacts of the anterior mitral leaflet with the proximal part of the interventricular septum in mid-systole can cause a fibrotic lesion that appears as a septal hyperechoic area (white arrow, figure 3B). The abnormal movement of the anterior mitral leaflet towards the septum can be easily observed on m-mode scanning of the mitral valve leaflets (figure 3C). Increased gradient and “scimitar-like” shape of left outflow caused by the contact between the valvular leaflet and the proximal interventricular septum.
Figure 4 Post-mortem specimen of a case of arterial thromboembolism (ATE) in a cat presented with hindlimb paresis and echocardiographic evidence of a restrictive myocardial disease. Both femoral pulses were palpable at presentation. The subject was later euthanised due to development of complete paralysis.

a) A 2 x 1 mm thrombus is lodged at the trifurcation of the internal iliac arteries and sacral arteries (black arrowhead), possibly responsible for the initial paresis. A 6 x 3 mm fibrinous thrombus is present at the bifurcation of the deep femoral and femoral arteries (white arrowhead) and little to no intra-arterial blood downstream the occlusion. This was the possible cause of the later clinical complication.

b) Extensive areas of pallor and softness affecting the gastrocnemius; c) similar lesions at the level of the lateral digital extensor and flexors and muscles.
Figure 5 Clinical features of right-sided congestive heart failure in a cat affected by arrhythmogenic right ventricular cardiomyopathy (ARVC). Distended abdomen caused by ascites and prominent subcutaneous veins are caused by hypertension at the level of the caudal vena cava.

Diagnosis, Prognosis and Clinical Management

Introduction

Diagnosis, prognosis and clinical management of feline myocardial disease (cardiomyopathy, CM) represents one of the most controversial topics in veterinary cardiology. Diagnosis is challenging, due primarily to the complex classification of feline CM, which is based on a variety of structural and functional phenotypes. It is further complicated by the occurrence of myocardial changes that are secondary to other diseases, such as systemic hypertension, hyperthyroidism, and lymphoma. Even the most sophisticated echocardiographic examinations present important limitations because they do not necessarily identify the primary cause of the disease or recognise the precise origin of an end-stage myocardial disease. Similarly, prognosis is strongly dependent on the underlying aetiology and stage of
the disease, which are often difficult to accurately define. The disagreement regarding classification of feline CM emphasises the importance of a thorough clinical evaluation of the patient and understanding of the underlying pathophysiological mechanisms in order to select the most appropriate treatment and provide the highest standard of care.

**Diagnosis**

_Echocardiography_

Echocardiography is the most important diagnostic tool for identification of myocardial disease in cats, and has become widely available in veterinary practice to provide a non-invasive assessment of cardiac anatomy and function. Learning how to perform a basic echocardiographic examination is very intuitive, and examiners can quickly recognise basic patterns of myocardial disease. However, clinicians should be aware that some echocardiographic changes may result from intra- and inter-operator variability, which mainly depends on the operator skill and experience. Most cats tolerate a full echocardiographic study without sedation. However, sedation may become necessary when the examination is made difficult by a restless patient or a stress-induced tachycardia. Although sedation may affect some echocardiographic measurements, the magnitude of observed changes in sedated cats is usually insufficient to affect the diagnosis. Furthermore, Campbell et al recently observed that sedation with acepromazine and hydromorphone does not affect 2D and M-mode echocardiographic measurements. Propofol appears to induce only a mild reduction of myocardial systolic velocity but does not alter diastolic function on tissue Doppler studies.

_M-mode echocardiography_ allows accurate measurement of myocardial thickness and ventricular chamber diameter during the different phases of the cardiac cycle. Systolic anterior motion (SAM) is also documented on M-mode interrogation of the mitral valve as
abnormal movement of the septal leaflet towards the interventricular septum (IVS) in early-mid-systole. Superimposition of colour Doppler to the M-mode interrogation of the mitral valve can document the blood flow turbulence during SAM. Left atrial (LA) size can also be measured on M-mode, although it is difficult to align the cursor through the body of the atrial chamber.

Hypertrophy of the myocardium is defined as diastolic wall thickness ≥6mm, and it is often accompanied by increased LV fractional shortening (FS). Left ventricular diameter ≥14 mm in end-systole is consistent with dilation and, in cases of systolic dysfunction, also accompanied by reduced FS (≤ 28%). However, a diagnosis of CM should never be based solely on these findings, since thickness of LV myocardium can increase with dehydration and tachycardia (pseudo-hypertrophy) and FS can vary significantly in other conditions, such as mitral valve insufficiency, hyperthyroidism, sympathetic stimulation and over-hydration.

A significant overestimation of myocardial thickness can result from an erroneous position of the cursor across the papillary muscles, which can be very difficult to avoid when papillary muscles are prominent. Conversely, M-mode studies can fail to demonstrate regional hypertrophy and do not provide any information on abnormal blood flow, patchy fibrotic lesions or valvular insufficiency. Finally, assessment of right ventricular (RV) morphology and function is almost impossible on M-mode studies.

Despite these severe limitations, there is still a widespread tendency to concentrate on M-mode measurements and fail to notice other cardiac abnormalities that could be observed on a more careful two-dimensional examination, such as right sided changes, valvular and pericardial abnormalities, or regional reduced hypokinesis.

Two-dimensional (2D) echocardiography allows overall assessment of myocardial function and identification of various phenotypical expressions of myocardial disease (figure 1). Diastolic measurements of the LV myocardium should be taken in four different wall
segments in order to identify regional hypertrophy. Diagnosis of LV hypertrophy can be made when the hypertrophic segment of the myocardium (≥6 mm) occupies more than 50% of its area.

Papillary muscles can be measured on two-dimensional echocardiography; their size is generally greater in cats with concentric myocardial hypertrophy.

Global bi-ventricular function should be always assessed on 2D in order to identify regional dyssynchrony, hypokinesis or dyskinesis that could be related to a myocardial insult (i.e. ischemia and reparative fibrous infiltration). Paradoxical motion of the septum would suggest the presence of RV volume overload and/or pressure overload, such as severe tricuspid insufficiency, pulmonary hypertension, atrial septal defect or arrhythmogenic right ventricular cardiomyopathy (ARVC).

Based on the limitations of M-mode studies listed above, left atrial size should be measured on 2D echocardiography. The LA diameter in normal cats is approximately 10 mm, both in short and long axis view and, when indexed to the aortic diameter, should have a ratio of less than 1.5. However, volume depletion and over-zealous fluid administration can lead to significant variation of LA size with potential erroneous interpretation of the echocardiographic findings. Increased LA size accompanied by an abnormal arching of the atrial septum towards the right atrium (RA) is suggestive of increased atrial pressure that can lead to pulmonary venous congestion and pulmonary oedema and/or pleural effusion. The presence of an echo-dense structure in the LA lumen or auricle can indicate a thrombus, which could predispose to aortic thromboembolism (ATE). Similarly, spontaneous echo-contrast (“smoke”) observed in the cardiac chambers indicates red blood cell aggregation and altered blood flow and may be considered a potential marker of left atrial thrombus or previous thromboembolism. Finally, 2D echocardiography allows the identification of RV
enlargement, pericardial effusion and myocardial fibrotic lesions that can accompany different forms of CM.

**Colour Doppler** allows the identification of flow turbulence and facilitates spectral interrogation. The presence of simultaneous turbulence in the left ventricular outflow tract (LVOT) and LA during early-mid systole suggests dynamic LVOT obstruction and mitral regurgitation, which is consistent with systolic anterior motion (SAM). Accurate colour Doppler setting (i.e. pulse repetition frequency, gain, filters) is mandatory to avoid misleading artefacts.

**Spectral Doppler** interrogations of all four cardiac valves should always be performed to identify abnormalities that could mimic myocardial disease, such as mitral or tricuspid regurgitation, aortic or pulmonic stenosis. Left dynamic outflow obstruction caused by SAM should always be suspected when the aortic peak velocity exceeds the normal reference range and the shape of the Doppler recording presents an abrupt acceleration in mid-systole, producing a concave, asymmetrically shaped waveform (figure 3D, above). Sometimes, SAM occurs only during stress or excitement and a simple method to detect the abnormality is to excite the cat by increasing the speaker volume during Doppler interrogation of the LVOT. A significant change in shape and peak velocity of the aortic wave would be consistent with dynamic LVOT obstruction. Pulsed-wave Doppler (PW) can be used to study mitral and pulmonary venous inflow patterns and isovolumetric relaxation time (IVRT), which provide a non-invasive assessment of impaired diastolic function in a variety of myocardial diseases. (Figure 2). An important limitation to the mitral inflow study is represented by the fusion of the E and A waves at heart rates above 160 bpm, which makes it difficult to characterise the different inflow patterns. Recently, PW Doppler has been used to measure LA appendix flow velocity, which appears decreased in cats with cardiomyopathy.
and can stratify patients at increased risk of spontaneous echo contrast and possible thromboembolism.

**Tissue Doppler imaging (TDI)** is a technique that allows non-invasive quantification of regional myocardial function. TDI provides a reliable evaluation of the systolic and diastolic myocardium and is independent of changes in preload in the diseased state. Pulsed TDI show lower early diastolic velocities, acceleration, and deceleration in cats with HCM, especially along the longitudinal axis of the heart. Systolic impairment has also been documented by TDI in HCM cats, irrespective of the presence of LVOT obstruction and congestive heart failure. Colour TDI provides estimation of the myocardial velocity gradient and mean myocardial velocity and it has been demonstrated to be a useful tool in the investigation of different myocardial diseases of humans. Interestingly, diastolic impairment has been detected in Maine Coon cats before the occurrence of hypertrophy both with pulsed TDI and colour TDI, although it is unclear whether it would be a sensitive enough screening test for detection of genotypically affected cats with no hypertrophy.

**Radial strain and strain rate** are novel techniques that provide non-invasive assessment of LV function and may have a potential utility in the early detection of myocardial dysfunction in cats.
**TABLE 1** General guidelines for echocardiographic classification of feline CM

<table>
<thead>
<tr>
<th>CM type</th>
<th>Two-dimensional and M-mode echocardiographic abnormalities</th>
<th>Doppler echocardiographic abnormalities</th>
</tr>
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<tbody>
<tr>
<td>HCM</td>
<td>Diastolic wall thickness ≥ 6 mm&lt;br&gt;Enlarged papillary muscles&lt;br&gt;End-systolic cavity obliteration&lt;br&gt;Increased fractional shortening&lt;br&gt;Left atrial enlargement&lt;br&gt;Right ventricular hypertrophy&lt;br&gt;Right atrial enlargement</td>
<td>Prolonged IVRT&lt;br&gt;Mitrail inflow: increased E wave amplitude, prolonged DT and increased A wave amplitude; E:A ratio &lt; 1&lt;br&gt;Pulmonary vein flow: reduced D wave and increased AR&lt;br&gt;Reduced left atrial appendix flow</td>
</tr>
<tr>
<td>HOCM</td>
<td>As above + systolic anterior motion (SAM)</td>
<td>As above + eccentric mitral regurgitation + abrupt aortic acceleration (simitar-like shape), consistent with dynamic obstruction</td>
</tr>
<tr>
<td>RCM</td>
<td>Marked left atrial (or bi-atrial) dilation&lt;br&gt;Absence of significant myocardial hypertrophy&lt;br&gt;Areas of increased endomyocardial echogenicity&lt;br&gt;Lesions consistent with fibrous tissue sometimes bridging the ventricular lumen</td>
<td>Decreased IVRT&lt;br&gt;Mitrail inflow: increased E wave velocity, shortened DT and decreased A wave velocity&lt;br&gt;Pulmonary vein flow: increased AR (AR duration &gt; transmirtal A duration)&lt;br&gt;Mitrail regurgitation&lt;br&gt;Flow turbulence caused by fibrotic lesions</td>
</tr>
<tr>
<td>DCM</td>
<td>Increased end diastolic left ventricular diameter&lt;br&gt;Increased end systolic left ventricular diameter (≥ 14 mm)&lt;br&gt;Fractional shortening ≤ 28%</td>
<td>Mitrail inflow parameters may vary depending on left ventricular diastolic pressure and loading conditions&lt;br&gt;Mitrail regurgitation&lt;br&gt;Tricuspid regurgitation</td>
</tr>
<tr>
<td>ARVC</td>
<td>Right ventricular dilation ± aneurism (thinner myocardial wall)&lt;br&gt;Right ventricular hypokinesia&lt;br&gt;Right atrial enlargement</td>
<td>Mild tricuspid regurgitation</td>
</tr>
<tr>
<td>UCM</td>
<td>Abnormalities that do not readily fit into any of the above classifications (e.g., regional myocardial abnormalities such as hypokinesia, thinner and hyperechogenic myocardium, etc)</td>
<td>Mitrail regurgitation&lt;br&gt;Tricuspid regurgitation</td>
</tr>
</tbody>
</table>

NB. A definitive diagnosis of CM should never be based solely on these echocardiographic findings since some echocardiographic parameters may vary in different physiological and pathological conditions. HCM = hypertrophic cardiomyopathy, HOCM = hypertrophic obstructive cardiomyopathy, DCM = dilated cardiomyopathy, UCM = unclassified cardiomyopathy. For explanations of IVRT, DT, E:A ratio and AR, see box on page 186.
Thoracic radiography

Thoracic radiographs are invaluable for recognition of cardiomegaly, pulmonary vein congestion and interstitial/alveolar pattern consistent with congestive heart failure. The distribution of alveolar infiltrate can be diffuse or patchy, in contrast to the more consistent perihilar location of cardiogenic pulmonary oedema observed in dogs (figure 3). Thoracic radiographs can also allow identification of pleural effusion and ascites. Cardiomegaly is not always present in myocardial diseases, especially when they are not accompanied by a significant LV or LA enlargement or pericardial effusion. The classic “valentine-shaped” heart on dorso-ventral (or ventro-dorsal) view is caused by severe bi-atrial enlargement, which would be expected in all advanced stages of feline myocardial diseases, and not only HCM as it has been reported in the past.

Cardiac magnetic resonance (cMRI)

Cardiac MRI is a relatively novel diagnostic test that allows quantification of ventricular mass and ventricular function. In human medicine, cMRI is becoming extensively used in patients with specific myocardial disorders, such as ARVC, endocardial fibroelastosis, and myocarditis. Cardiac MRI is also an important tool in the quantification of LV mass in HCM patients and differentiation of infiltrative and inflammatory CM. Recent studies have demonstrated that cMRI is an accurate method to identify changes in LV mass in HCM cats but it is not useful for identifying diastolic dysfunction in these patients. The use of general anaesthesia, long duration of scanning (approximately 1 hour), ECG cardiac gating and high costs represent important limitations for the widespread use of cMRI in feline cardiology. However, it is possible that availability of new technologies will overcome these problems in the future.

Radionuclide imaging
In people, radionuclide ventriculography can be useful to identify ischaemic myocardial injury and can elucidate the nature of regional wall motion abnormalities. Positron emission tomography (PET) and single photon emission tomography (SPECT) can provide combined molecular, functional and morphological image data of the cardiovascular system. In feline cardiology, PET scan has been used to measure coronary flow reserve in healthy cats and cats affected by HCM, demonstrating a lower flow in the latter group. High costs and limited availability of this technology represent an important constraint for routine use of PET scan, although it may become more accessible and affordable in the future.

*Electrocardiography (ECG)*

Cats with myocardial disease may present with a variety of ECG abnormalities, including morphological changes consistent with chamber enlargement, arrhythmias and conduction abnormalities, the most common being left anterior fascicular block (LAFB), which is observed in approximately 20-30% of CM cats. Although ECG can be unremarkable at presentation in many CM cats, in the author’s experience ventricular arrhythmias, including paroxysmal ventricular tachycardia, can be documented on 24h-ECG (Holter) recording in almost all cats with myocardial disease. This suggests that standard ECG is a relative insensitive diagnostic test in cats with myocardial disease.

*Histopathology*

Post-mortem histopathology can identify a variety of myocardial lesions in CM cats. These include: myofibre hypertrophy and disarray, focal to multifocal or extensive myocyte necrosis and degeneration, interstitial fibrosis, and fibrous or fibro-fatty myocyte replacement. Major or intramural coronary arteries can show medial and intimal thickening associated with increased connective tissue elements. In some cases occlusive fibrinous thrombosis can be observed. Signs of endomyocarditis are often indicated by
endomyocardial infiltrates of mononuclear cells, macrophages, and occasional neutrophils. (Figure 4)

Although some histological changes can be indicative of one particular form of CM, they are unlikely to be pathognomonic. Fibrous or fibro-fatty myocyte replacement, for example, is a common sequel of myocardial ischaemia and tissue necrosis, frequently observed in all forms of cardiomyopathy.

Ante-mortem identification of infiltrative and inflammatory changes can be obtained by transvenous endomyocardial biopsy. However, its use is highly controversial due to the risk of RV perforation and malignant ventricular arrhythmias evoked by the procedure. Furthermore, patchy myocardial lesions may be missed by the random biopsy sampling.

Genetic tests

Genetic mutations responsible for HCM have been identified both in Maine Coons and Ragdoll cats although not all Maine Coons or Ragdolls with HCM show this particular mutation. However, the mutation in the two breeds is located in different regions of the same gene and other mutations are likely to be identified in the future. Studies are in progress to identify similar mutations in other predisposed breeds, such as Norwegian Forest Cat and Sphinx. Genetic tests can identify predisposed individuals for that particular mutation and may be useful for screening programs. However, the disease can still originate from a different mutation which has not been identified yet.

Biomarkers

Cardiac troponin-I (cTn-I) is a sensitive and specific marker of cardiac myocyte injury and its plasma concentration is increased in a variety of cardiac diseases, including HCM in cats. Elevated cTn-I level is not pathognomonic of HCM but simply indicates ongoing myocardial damage, which may be present in all forms of myocardial disease. However, this assay may serve as useful adjunctive assessment to help determine diagnosis and/or prognosis.
Natriuretic peptides ANP and BNP are found in higher concentrations in the heart of cats with HCM. Similarly, their level is increased in the circulation of cats with cardiac disease. Natriuretic peptides measurement can be clinically useful as an initial screening test for cats with suspected cardiac disease. The N-terminal fragments of ANP and BNP, namely NT-proANP and NT-proBNP respectively, are more stable, have a longer half-life and are therefore easier to analyse. In particular, NT-proBNP concentrations are positively correlated with left atrial size and pressure, indicating its utility for assessing cardiac disease severity and, potentially, prognosis.

**Prognosis**

Median survival time of cats with HCM that survived the first 24h after initial examination has been reported as 732 days, 709 days and 596 days. Patients affected by ATE and concurrent myocardial disease carry a worse prognosis (184 days). Other forms of CM carry a less favourable prognosis with a median survival time of 132 days for RCM and 11 days for DCM. Identification of a primary cause is a critical element that affects survival time since some forms of CM, such as taurine-deficiency, hyperthyroidism or sustained tachycardia, can potentially be corrected with subsequent reversed remodelling and resolution of the myocardial function.

Many clinical features have been suggested to identify risk factors and establish an accurate prognosis in cats with myocardial disease.

In one study, HCM cats with heart rate ≥ 200 bpm appeared to have a reduced survival compared to HCM cats with lower heart rates. However, a later study reported no statistical association between heart rate and survival time and whether or not tachycardia may represent a negative prognostic factor remains controversial.
Presence of clinical signs associated with CHF represents a negative prognostic factor in cats with HCM in two retrospective studies. In the study of Rush et al, LA size, age, subjective evidence of RV enlargement and performed thoracocentesis were negatively associated with survival time but only LA size and age were significant predictors in multivariate analyses. In the same study, LA and LV diameter were also associated with a higher incidence of ATE, in contrast with that observed by Smith et al. in a retrospective study on 127 ATE cases. However, in none of the above articles did the authors specify the method used to measure LA dimensions. It is well documented that M-mode measurements of the LA have inherent limitations and tend to produce different values when compared to 2D evaluations. For this reason, the association between LA dimension and risk of ATE remains controversial.

Coagulation markers TAT complex, D-dimers and FDP have shown that 45% of HCM cats are in a hypercoagulable state. However, coagulation results are not correlated with LA size and an association between hypercoagulability and risk of thrombosis has yet to be documented in cats with HCM.

The major limitation of retrospective studies to establish prognostic factors is represented by different management of patients following diagnosis, different severity of the cardiac disease at presentation and euthanasia. In addition, cases are managed by a number of different clinicians who may choose different drugs and doses. Additionally, criteria for classification of myocardial disease change over time and are affected by several subjective evaluations.
Clinical management

Ideally, treatment of feline cardiomyopathy should be aimed at resolving all the underlying pathogenic mechanisms of the disease, such as diastolic and systolic dysfunction, dynamic outflow obstruction, ischaemia, arrhythmias, neuro-hormonal activation, and hyper-coagulability status. In reality, with the only exception of taurine in cats with taurine-deficient DCM, such ideal treatment is not available and no drug at present has convincingly demonstrated to improve survival and/or quality of life in cats with myocardial disease.

The asymptomatic patient

Whether or not an asymptomatic cat with CM should be treated is a very controversial topic. Anecdotal reports claim improvement of physical activity in asymptomatic cats with HCM treated with diltiazem or beta-blockers. In addition, a recent pilot study has demonstrated a possible reduction of myocardial damage in cats with compensated HCM following daily administration of atenolol, as suggested by a significant reduction of circulating cTn-I. However, randomised placebo-controlled studies are still lacking and clinical utility of diltiazem or beta-blockers in asymptomatic cats has still to be proven.
The use of ACE-inhibitors has also been advocated in cases of HCM, both in asymptomatic and symptomatic cats. In that retrospective study, significant changes in cardiac dimensions where identified echocardiographically together with an improvement of life expectancy after administration of enalapril. Unfortunately, recent prospective, controlled study studies have failed to demonstrate significant effects of ACE-inhibitor (benazepril and ramipril) in cats with sub-clinical forms of HCM.

The potassium sparing agent spironolactone has shown anti-remodelling properties in human patients with asymptomatic cardiac disease, as well as in patients with mild CHF (NYHA class I and II). It might be naïve, but it is not unrealistic, to believe that spironolactone may produce a similar effect in cats with asymptomatic CM, although controlled clinical studies are necessary to confirm this hypothesis. Regrettably, a recent study failed to demonstrate improvement of diastolic function and LV mass in Maine Coon cats with HCM treated with spironolactone for 4 months. Furthermore, in that study, one third of the treated cats developed severe ulcerative facial dermatitis. However, to the best of the author’s knowledge, this side effect that has never been reported in Europe.

Cats with asymptomatic forms of CM but with echocardiographic evidence of intra-cavitary thrombi, spontaneous echo-contrast or severe LA dilation may benefit from anti-thrombotic prophylaxis to reduce the risk of ATE. This could theoretically be achieved by administering low-dose aspirin, clopidogrel or a combination of the two drugs, although such combination has not shown clinical benefit in humans. However, results of controlled prospective studies are necessary to prove the prophylactic efficacy of these treatments.

The symptomatic patient

Cats presenting clinical or radiographic signs of CHF should be treated accordingly. In cases of acute respiratory distress, stress should be minimised and cage-rest and oxygen
supplementation should be instituted promptly. Pulmonary oedema is generally controlled by intravenous administration of furosemide every 4-6 hours, until a normal respiratory rate is achieved. Dyspnoea secondary to pleural effusion can be successfully managed by thoracocentesis. Sedative medication with acepromazine and butorphanol may contribute to alleviate the respiratory distress. In extreme cases, where the patient does not respond to acute diuresis, airway suctioning and mechanical ventilation can be considered. Once pulmonary oedema is sufficiently controlled, furosemide can be given orally and at the lowest effective dose. A similar approach should be taken in chronic and non-acute cases, in order to reduce the negative side-effects of diuresis that can include reduced ventricular preload, hypotension, pre-renal azotaemia and hypokalaemia, which can predispose to anorexia and severe ventricular arrhythmias. The risk of hypokalaemia could be reduced by concomitant administration of potassium sparing agents, such as spironolactone although sufficient data of its clinical efficacy in cats are not available.

Calcium channel blockers have been advocated as effective treatment for symptomatic feline HCM for many years. Diltiazem has a lesser effect on the systemic vasculature and inotropic state than verapamil, and it is generally the calcium channel blocker of choice in the treatment of feline HCM. The claimed beneficial therapeutic effects of diltiazem are due to its positive lusitropic and coronary vasodilating properties and include increased LV filling, reduced heart rate, increased venous oxygen tension, improved echocardiographic parameters and resolved radiographic abnormalities. However, due to its pharmacokinetics, diltiazem needs to be administered every 8 hours, and many clients struggle to comply with this dosing frequency, administering the drug only once or twice daily. Unfortunately, the administration of the extended release formulation is accompanied by significant side-effects.

Beta blockers have also been suggested as useful treatment of feline CM, since they can provide heart rate and arrhythmia control, relieve LVOT obstruction and lessen myocardial
oxygen demand. Atenolol, a selective beta-1 agonist, is generally preferred over other beta-blockers (i.e. propranolol) because it reduces the risk of bronchospasm. Furthermore it can be administered only once or twice daily versus the recommended three times daily administrations of propranolol.

Recently, interim results of a prospective double-blinded, multicentre, controlled study comparing the clinical efficacy of atenolol, diltiazem and enalapril in cats with diastolic heart failure were presented. According to these results, cats receiving atenolol and furosemide survived for a significantly shorter time than cats treated with furosemide alone. Similarly, patients receiving diltiazem survived less than cats on furosemide alone, while cats in the enalapril group did as well or better than the placebo group. However, these differences were not found to be statistically significant. Therefore, a prudent approach should be taken when recommending any of these drugs, in addition to furosemide, for chronic treatment of feline CM.

Taurine-deficient DCM cases can be successfully treated with taurine supplementation, in addition to supportive treatment to control the clinical signs of CHF, and echocardiographic evidence of improved systolic function is generally seen within 6 weeks of supplementation. Other cats with echocardiographic evidence of systolic dysfunction not related to taurine deficiency may benefit from positive inotropic drugs. Dobutamine infusion can be considered in severe cases, especially those accompanied by severe hypotension. Less severe cases, may benefit from an oral positive inotropic medication. Digoxin, for example, has been used for many years in cats but careful dosing and periodic plasma measurements are necessary to reduce the risk of toxicity. Pimobendan can also be considered in all cases of feline CM accompanied by systolic dysfunction. Although this drug is not licensed for use in cats, its administration is well tolerated in this species, and induces significant improvement in the demeanour and appetite of the treated cats in association with resolution of clinical signs. In
addition to its positive inotropic property, pimobendan has a positive lusitropic effect, which may also have benefits in other forms of feline myocardial disease. However, further studies are necessary to confirm this hypothesis.

Finally, whenever a primary cause of myocardial disease is suspected or recognised, every attempt should be made to manage it directly. For example, sustained tachycardia can induce systolic dysfunction (tachycardiomyopathy) but the myocardial lesions can be reversible if the arrhythmia is successfully controlled. Similarly, corticosteroids may control the inflammatory changes in cases of myocarditis and, where the cause is bacterial (e.g. *Bartonella*) or protozoal (e.g. *Toxoplasma*), antimicrobial treatment may eliminate the aetiological agent.
### TABLE 3

<table>
<thead>
<tr>
<th>Drug</th>
<th>Trade name</th>
<th>Class</th>
<th>Pharmacological action</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enalapril⁴⁰</td>
<td>Enacard (Morita)</td>
<td>ACE inhibitor</td>
<td>Promotes vaso- and arteriolar dilatation (reduced ventricular preload and afterload); decreases Na and water retention; depresses sympathetic activation</td>
<td>0.25–0.5 mg/kg PO SID or BID</td>
</tr>
<tr>
<td>Benazepril⁴⁰</td>
<td>Fortekor (Novartis)</td>
<td>ACE inhibitor</td>
<td>As above</td>
<td>0.25–0.5 mg/kg PO SID or BID</td>
</tr>
<tr>
<td>Ramipril</td>
<td>Vasotop (Intervet)</td>
<td>ACE inhibitor</td>
<td>As above</td>
<td>0.5 mg/kg PO SID</td>
</tr>
<tr>
<td>Irdapril</td>
<td>Pritium (Vetquionil)</td>
<td>ACE inhibitor</td>
<td>As above</td>
<td>0.25 mg/kg PO SID</td>
</tr>
<tr>
<td>Dilatazem</td>
<td>Hyercard* (Dechra)</td>
<td>Benzothiazepine</td>
<td>Reduces heart rate and myocardial contractility; vasodilation (cardiac vessels and peripheral arteries)</td>
<td>10 mg/cat PO TID</td>
</tr>
<tr>
<td>Atenolol</td>
<td>Atenolol (non-proprietary)</td>
<td>β₁ receptor selective antagonist (β-blocker)</td>
<td>Reduces heart rate and myocardial contractility; induces mild vasodilation</td>
<td>6.25–12.5 mg/cat PO SID</td>
</tr>
<tr>
<td>Pimobendan</td>
<td>Vetmedin (Boehringer Ingelheim)</td>
<td>Ca sensitizer and PDEIII inhibitor</td>
<td>Induces myocardial contractility and vasodilation (inotrope). Promotes myocardial relaxation (positive lusitrope)</td>
<td>0.1–0.3 mg/kg PO BID</td>
</tr>
<tr>
<td>Furosemide†</td>
<td>Dimazion (IV†)</td>
<td>Loop diuretic</td>
<td>Promotes diuresis by inhibiting Na reabsorption</td>
<td>0.5–2 mg/kg PO or IV SID to TID</td>
</tr>
<tr>
<td>Spirotonolactone</td>
<td>Prilactone (Orov)</td>
<td>Potassium-sparing diuretic</td>
<td>Promotes diuresis by inhibiting aldosterone action. Might reduce cardiac remodelling</td>
<td>2–4 mg/kg PO SID</td>
</tr>
<tr>
<td>Taurine</td>
<td>Taurine (non-proprietary)</td>
<td>Amino acid</td>
<td>Essential ion for myocardial mechanical function</td>
<td>125–250 mg PO BID</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Asprin (non-proprietary)</td>
<td>NSAI</td>
<td>Inhibition of platelet aggregation</td>
<td>81 mg/cat q 3 d or 5 mg/cat q 3 d</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>Plavix (Sanofi-Aventis)</td>
<td>Antiplatelet drug</td>
<td>Inhibition of platelet aggregation</td>
<td>18.75 mg/cat SID</td>
</tr>
</tbody>
</table>

*Licensed in the UK for the clinical management of feline primary HCM. †Licensed in the UK for the clinical management of feline CHF.
PO = orally, IV = intravenously, SID = once daily, BID = twice daily, TID = three times daily, q 3 d = every three days, PDEIII = phosphodiesterase III, NSAI = non-steroidal anti-inflammatory drug

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Figure 1  Phenotypical expressions of myocardial disease on B-mode echocardiography. Legend: RA= right atrium; RV= right ventricle; LA= left atrium; LV= left ventricle; Ao= aorta; IVS= interventricular septum; FW= free wall

a) Myocardial hypertrophy of the IVS, RV and LV free wall and LA dilation; b) severe LA dilation with hyperechoic subendocardial lesions (arrow) suggestive of fibrous replacement

c) Echodense structure bridging between the proximal and mid-IVS (arrow); d) similar lesion crossing the lumen of the LV (arrow); these lesions are probably constituted by fibrous tissue

e) Dilation affecting all four cardiac chambers; f) dilation affecting primarily the right side of the heart (RV and RA)
Figure 2  Pulsed Doppler derived measures of left ventricular diastolic function

**Normal pattern:** Laminar flow, with peak velocities usually < 1 m/sec. E wave represents the early diastolic filling that follows the myocardial relaxation. E wave acceleration is directly determined by LA pressure and inversely related to myocardial relaxation. The rate of fall in velocity is represented by the deceleration time (DT), which becomes shorter when LV compliance decreases. There is an inverse relationship between the mean LA pressure and DT. During atrial contraction, LA pressure determines a second flow peak (A wave). In normal heart, the E/A ratio is used to assess LV diastolic function and is > 1.

The normal pulmonary vein flow pattern is usually biphasic with a predominant systolic forward flow (S wave) and a less prominent diastolic forward flow wave (D wave) which reflects the transmitral E wave. A retrograde flow wave into the pulmonary vein (AR wave) occurs during atrial contraction and its amplitude and duration are related to LV diastolic pressure, LA compliance and heart rate.

**Abnormal myocardial relaxation** (with normal diastolic LA and LV pressures; e.g. early HCM). Prolonged IRVT, decreased E wave amplitude, prolonged DT and increased A wave amplitude (E/A ratio is < 1), reflecting compensatory increase in atrial contribution to ventricular filling in late diastole.

The pulmonary venous flow velocity pattern may show a diminished diastolic (D) wave due to reduced early diastolic filling and an increased reversed wave during atrial contraction (AR) when the LV end-diastolic pressure is elevated.

**Pseudo-normalisation** (increased diastolic filling pressure due to decreased LV compliance). This pattern represents a transition between abnormal relaxation and restrictive pattern. The mitral inflow resembles a normal pattern but there is increased amplitude and duration of the AR wave.

**Restrictive pattern** (severely compromised LV compliance). Increased E wave velocity, shortened DT and lower A wave velocity. Atrial contraction results in increased flow reversal into the pulmonary veins (AR duration is much longer than the transmitral A duration).

Legend: Red: mitral inflow; Blue: pulmonary vein inflow.

(modified from Garcia and Thomas).
Figure 3  Thoracic radiographs (dorso-ventral view) from a cat affected by myocardial disease; a) cardiomegaly and bi-atrial enlargement (Valentine-shaped heart) and patchy alveolar opacity (arrows) consistent with focal pulmonary oedema. b) resolution of pulmonary oedema after intravenous administration of furosemide
Figure 4. Various histopathological lesions that can be observed in feline myocardial disease.

a & b) Interstitial fibrosis, lympho-plasmacytic infiltration and myocyte hypertrophy with fibre disarray in the left ventricle of a cat affected by hypertrophic cardiomyopathy (H.E)

c & d) Focal area of coagulation necrosis and degeneration in the atrial myocardium of a cat affected by hypertrophic cardiomyopathy (H.E.)

e) Severe fibrosis of the endocardium with formation of an “interpapillary muscle sinechia” in a cat affected by restrictive cardiomyopathy (blue area). Interstitial fibrosis is also observed (Trichromic stain); f) Intramural coronary artery obliteration (arrowheads) in the right ventricle of a cat affected by cardiomyopathy and complicated by arterial thromboembolism (H.E.)

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g) Thin and elongated myocytes with degeneration and vacuolisation and (h) subendocardial areas on a papillary muscle with myocyte hypertrophy in the left ventricle of a cat affected by dilated cardiomyopathy (H.E.)

i & j) Fibro-fatty infiltration (black arrow) with replacement and myocyte atrophy (red arrow) in the right ventricle of a cat affected by arrhythmogenic right ventricular cardiomyopathy (H.E.)

k & l) Necrosis and interstitial oedema in the gastrocnemius muscle of a cat affected by a form of cardiomyopathy complicated by arterial thromboembolism (H.E.)
CANINE MYOCARDIAL DISEASE

Introduction

The definition and classification of cardiomyopathies have been extensively reported in the previous chapter (feline myocardial disease). The phenotypical presentation of CM in dogs is usually more consistent, with the dilated form (DCM) representing the most common cardiomyopathy in this species. In certain breeds, such as Doberman pinschers and Great Danes, DCM is considered the most common cause of morbidity and mortality. In a study conducted at the University of Purdue, DCM has been reported to have an overall prevalence of 0.5%. This only included dogs with clinical signs referable to heart disease, particularly congestive heart failure. Further analysis showed higher prevalence in pedigree dogs (0.65%) compared with cross-breeds (0.16%), and prevalence in certain specific breeds was very high (e.g. Deerhounds 6.0%; Dobermanns, 5.8%; Irish Wolfhounds, 5.6%; great Danes, 3.9%; Boxers, 3.4%; Newfoundlands, 1.3%). Large and giant breed dogs are most predisposed to develop DCM, with the exception of spaniel breeds (especially Cocker Spaniels (English and American)). Prevalence increases with age, and males are usually reported as being overrepresented in the population of dogs with congestive heart failure. Prevalence rates are much higher in prospective studies screening for the presence of DCM, when dogs without clinical signs may be detected (e.g. Dobermanns, 63.2%11; Irish Wolfhounds, 24.2%12; Newfoundlands, 17.6%13). It should, however, be noted that concentration on certain family lines in these studies may over-estimate actual population prevalence. In these prospective studies, there is not usually a marked sex-predisposition reported, although male dogs may show an earlier onset of congestive heart failure.
Aetiology

In the previous chapter on feline CM, DCM has been defined as a morphologic diagnosis, with the only exception of taurine deficiency. The heart has a limited number of responses to many potential myocardial insults. Thus, the morphologic response called DCM provides no insight as to the myocardial insult(s) that contributed to this outcome. Therefore the diagnosis of idiopathic DCM in dogs, relatively common in veterinary practice, may sometimes represent a “misdiagnosis” of a primary causative myocardial insult, such as myocardial ischemia, previously undiagnosed congenital defects, tachycardiomyopathies, etc. The most common causes of DCM in people include familial/genetic, viral or immunologic, and toxic factors. Recognised causes of DCM in the dog include genetic factors, tachycardia, toxic factors, and, possibly, carnitine and/or taurine deficiency, although the scientific evidence that supports these nutritional aetiologies is very weak. Although there is substantial evidence to support a viral etiology in some cases of DCM in people, such correlation has never been demonstrated in canine medicine, with the only exception of parvovirus infection in puppies. Several studies have also failed to demonstrate a convincing immunological aetiology, with poor correlations observed between presence of canine DCM and abnormal circulating antibodies. However, these findings do not exclude completely the possibility of an immunologic reaction directed against other myocardial proteins, including contractile, regulatory, and cytoskeletal matrix as well as extracellular matrix or membrane.
Clinical presentation

Most of the natural history data available concerning DCM applies to Doberman Pinschers, with many studies and observations conducted by Dr Mike O’Grady (University of Guelph, Canada). It has also been postulated that the natural course of DCM in Dobermans might be different from that observed in other breeds. Indeed, the progression of DCM to CHF (overt stage) and death is more rapid in this breed. However, the rate of progression of the occult stage in other breeds compared to Dobermans is not well determined.

The natural progression of DCM can be described by three distinct stages/phases (see timeline below).
Stage I  morphologically and electrically normal heart and no evidence of clinical signs of heart disease.

Stage II  evidence of morphologic or electrical derangement in the absence of clinical signs of heart disease ("Occult DCM"). This is characterised by LV enlargement (systole and/or diastole) and/or electrical abnormalities (presence of VPCs).

Stage III  presence of clinical signs of heart failure ("Overt Stage"). Because most dogs are non-working, evidence of exercise intolerance is usually unobserved until the onset of CHF.

According to the available literature the occult stage in Dobermans can last 2 to 4 years before the onset of clinical signs (respiratory distress, syncope, and sudden death). Multiple syncopal episodes are rare and most dogs will die during their first event. Sudden death in Dobermans with DCM may occur in approximately 30% of affected dogs, most likely as a result of paroxysms of ventricular tachycardia that progress into ventricular fibrillation.

In a small study of the natural history of DCM in Dobermans (28 m follow-up) involving 103 dogs, 100% of the dogs that demonstrated at least 1 PVC on a 3-minute ECG, 100% of the dogs with LVIDs > 38 mm, and 85% of the dogs with an LVIDd > 46 mm developed clinical especially for DCM. However, these criteria for occult DCM may be a little too vague,
especially for very small or extremely large individuals. Other studies suggest that an LVIDd ≥ 49 mm or at LVIDs ≥ 42 mm has a high positive predictive value for identifying Dobermans with occult DCM, independent of the size of the dog. With respect to the presence of ventricular ectopies, a number ≥ 1 VPCs per minute on a resting ECG may provide evidence of occult DCM. A 24-hour Holter examination has been recommended to identify Dobermans with occult disease and a number ≥ 50 VPCs in 24h has been suggested as indicative of occult DCM. The use of echocardiographic fractional shortening (FS) in Dobermans free of clinical signs as a discriminating marker for the presence or absence of DCM is unreliable. Although a low FS (eg ≤ 15%) is highly suggestive of occult DCM; there are normal dogs with values in the range of 18% to 22% that will never develop any clinical signs. It is extremely difficult in these cases to establish whether these values are attributable to an abnormal myocardial function or simply a phenotypical manifestation of an athletic heart.

Atrial fibrillation (AF) represents another important confounding factor. In an European study, involving 500 Irish Wolfhounds, 49 were diagnosed with occult DCM based on echocardiographic criteria. AF was detected in 73% of these occult dogs and was also detected in 11 dogs that did not meet the criteria for occult or overt DCM. It is possible that compensated dogs, previously occult, decompensate with the development of AF. However, it is also true that AF might be the cause of tachycardiomyopathy, which appears echocardiographically as a DCM case. For these reasons, owners of Dobermans and Irish Wolfhound should be advised to consider annual screening in the form of an echocardiogram and/or Holter examinations.

The prognosis after the onset of CHF is generally poor, although variable. Sudden death as a result of arrhythmias, death caused by severe pulmonary oedema, and euthanasia due to refractory CHF are the most common outcomes of canine DCM.
In dogs, few studies have been conducted to characterise prognostic indicators in those with DCM, with pulmonary oedema, pleural effusion, age, dyspnoea, ascites, AF, and bilateral HF representing the best independent parameters associated with significantly shorter survival times. Ascites also represents a useful clinical prognostic indicator. However, stratified analysis shows that ascites has no effect on survival in dogs with a restrictive pattern. In his study published in JVIM 2006, Borgarelli et al did not find any effect of age or dyspnoea on survival. Median survival time observed in the 76 dogs used in their study (671 days) was longer than those reported in other studies. One explanation for this finding is that they included dogs with asymptomatic or mildly symptomatic disease. Another possibility is that their dog population was substantially different from what had been previously reported.

Functional class of HF is considered a prognostic indicator in people, and results in dogs agree with such an observation. In Borgarelli’s study no dogs with ISACHC class 1 HF died during the study period, whereas dogs with class 2 and 3 disease had significantly worse prognoses.
Fig 1. Survival curves of 63 dogs with dilated cardiomyopathy according to class of heart failure (HF). All dogs with class 1 HF survived during the observation time. Median survival time for dogs with class 2 HF was not determined (lower 95% confidence limit, 233 days). Median survival time for dogs with class 3 HF was 350 days (95% confidence interval, 93–193 days). $P < .001$ for class 1 (dashed line) vs class 2 (dotted line) and class 3 (continuous line). $P < .05$ for class 2 vs 3.

Fig 3. Survival curve of 39 dogs with dilated cardiomyopathy with and without restrictive transmitral flow pattern (dashed line). The median survival time for the nonrestrictive group was not determined; the median survival time for the restrictive group was 114 days (95% confidence interval, 54–208 days; $P < .001$).
Fig 2. Survival curve of 63 dogs with dilated cardiomyopathy with an end-systolic volume index (ESV-I) greater than or less than 140 mL/m² (dashed line). Median survival time for dogs with an ESV-I less than 140 mL/m² was not determined (lower 95% confidence limit, 458 days). Median survival time for dogs with an ESV-I greater than 140 mL/m² was 208 days (95% confidence interval, 74–671 days; \( P < .001 \)).

Table 3. Effect of heart failure class, atrial fibrillation, end-systolic volume index, and ejection fraction on median survival time in 28 dogs with restrictive transmitral flow.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median (95% CI) (days)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascites</td>
<td>58 (27–193)</td>
<td>.4</td>
</tr>
<tr>
<td>No ascites</td>
<td>164 (74–208)</td>
<td>.4</td>
</tr>
<tr>
<td>AF</td>
<td>58 (27–193)</td>
<td>.4</td>
</tr>
<tr>
<td>No AF</td>
<td>164 (74–208)</td>
<td>.4</td>
</tr>
<tr>
<td>Class 3 HF</td>
<td>80 (42–193)</td>
<td>.32</td>
</tr>
<tr>
<td>Class 2 HF</td>
<td>114 (74–208)</td>
<td>.61</td>
</tr>
<tr>
<td>ESV-I &gt;140 mL/m²</td>
<td>58 (42–193)</td>
<td>.15</td>
</tr>
<tr>
<td>ESV-I ≤140 mL/m²</td>
<td>114 (74–208)</td>
<td></td>
</tr>
<tr>
<td>EF ≥25%</td>
<td>80 (54–208)</td>
<td></td>
</tr>
<tr>
<td>EF &lt;25%</td>
<td>114 (11–233)</td>
<td></td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; CI, confidence interval; EF, ejection fraction; ESV-I, end-systolic volume index; HF, heart failure.
In a much larger study involving 369 cases, Martin et al (JSAP 2009) found a significant higher prevalence of DCM in males (ratio of 2.7:1 [male: female]). In this study there were some differences in the clinical presentation between breeds, for example in boxers collapse (70%) was the most common presentation, in golden retrievers reduced appetite (60%) and in great Danes weakness (55%) was the most common.

Atrial fibrillation was present in 45%, VPCs in 31% and SVPCs in 9% of dogs. AF was most common in the giant and large breed dogs: IWH(94%), great Dane (79%), Newfoundland (77%), GSD (73%) and Saint Bernard (72%) and least common in cocker spaniels (8%). VPCs were most common in boxers (53%) and Dobermans (44%). SVPCs were most commonly seen in boxers (25%) and GSDs (14%). Only 11 per cent of dogs did not demonstrate an arrhythmia, and of these, all had either QRS enlargement pattern consistent with cardiomegaly or ST depression.

The survival analysis was performed on 354 dogs; 180 (51%) dogs were euthanased for cardiac reasons, 142 (40%) died for cardiac reasons and nine (3%) died or were euthanased for non-cardiac reasons. The median survival time (to death or euthanasia) for all dogs with DCM was 19 weeks (4 - 60 weeks) and the mean survival (SD) was 50 weeks (827). The survival rate at one year was 28 per cent and at two years was 14 per cent (Figure below).
FIG 3. Kaplan-Meier survival curve in dogs diagnosed with dilated cardiomyopathy. The graph shows the percentage of dogs surviving (not reaching the endpoint of death or euthanasia) versus time since referral.
Making a diagnosis of DCM

Ante-Mortem

Other congenital, acquired and systemic conditions must initially be excluded, as listed in the table below.

<table>
<thead>
<tr>
<th>Congenital and other acquired heart diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachyarrhythmias which may result in a tachycardia induced cardiomyopathy</td>
</tr>
<tr>
<td>Systemic hypertension</td>
</tr>
<tr>
<td>Pericardial diseases (not mild pericardial effusion that may be secondary to heart failure)</td>
</tr>
<tr>
<td>Systemic diseases that may affect cardiovascular function (e.g. hypothyroidism)</td>
</tr>
<tr>
<td>History of use of drugs known to affect cardiac function (e.g. doxorubicin)</td>
</tr>
<tr>
<td>Metabolic deficiency (e.g. taurine, L-carnitine)</td>
</tr>
<tr>
<td>Presence of atrial fibrillation with a fractional shortening &gt; 25% (mean of 5 to 10 beats)</td>
</tr>
</tbody>
</table>

Note, these criteria can be simply and practically excluded in the living dog. At post mortem, other criteria should actively excluded, such as myocardial infarction, other coronary vascular disease, myocarditis etc. The authors recommend that, wherever possible, post-mortem examination is carried out.

The ECVIM task-force for the study of canine DCM recommends the following guidelines for an accurate diagnosis of DCM:

1. Left ventricular dilation (especially in systole but also in diastole).
2. Depressed systolic function.
3. Altered geometry of the left ventricle (increased sphericity).

A subjective assessment is often made, but a quantitative method is preferred. The ECVIM task-force proposes that a ratio of LV diastolic length (from right parasternal (RPS) long axis four chamber view) to the M-mode LV diastolic dimension (LVIDd) <1.65 represents increased sphericity13 (Figure below).
In addition, the following features are commonly identified in confirmed overt DCM:

4. Left or bi-atrial enlargement

5. Increased mitral valve M-mode E point to septal separation (EPSS).

6. Arrhythmias recorded on the simultaneous ECG through the echocardiographic examination or during routine ECG or Holter recording are supportive of the presence of DCM. Arrhythmias are more important as a criterion for the diagnosis of DCM in certain breeds, especially ventricular arrhythmias in Dobermanns and Boxers and atrial fibrillation in Irish Wolfhounds.

In dogs presenting with CHF or other manifestations of DCM, it is normally possible to meet these criteria and to make an unequivocal diagnosis (although subsequent post-mortem confirmation is recommended). However, veterinary cardiologists are increasingly being presented with dogs with more equivocal findings, perhaps from breed schemes screening for DCM. Therefore, the authors of the ECVIM task force propose a scoring system which may be of use in determining whether a particular patient is likely to have pre-clinical DCM or echocardiographic abnormalities which may precede pre-clinical DCM. Such a scoring system may be of use in serial evaluation or longitudinal screening of a population of dogs in ascertaining the presence of progressive disease, as expected in DCM.

**Major criteria**

1. Left ventricular M-mode systolic or diastolic dimensions exceeding 95% confidence intervals for the individual based on regression equations or predicted reference values, or outside other established breed-specific reference ranges. Account should also be paid to the influence within specific breeds of body surface area, gender or age where these data are available and applicable.

2. Increased sphericity: LV length: M-mode LV diastolic dimensions is decreased.
The ECVIM-Task Force authors propose that a ratio of LV diastolic length (from RPS long axis four chamber view) to the M-mode LV diastolic dimension <1.65 represents increased sphericity.

3.a. EITHER:
M-mode fractional shortening of <20% or 25% (depending on breed-specific reference values).

3.b. AND / OR:
Left ventricular ejection fraction less than 40%.

It is important that breed specific reference ranges are generated or consulted if available.
The authors urge particular caution in assessing extreme breeds, or very athletic breeds (which, at rest, often have a low measured fractional shortening).

**Minor criteria**

1. The presence of an arrhythmia in a specific breed where the arrhythmia has been shown to be strongly associated with DCM (e.g. increased ventricular ectopy in Dobermanns or Boxers). Other (cardiac or systemic) causes for ventricular ectopy should be actively excluded.
2. Atrial fibrillation.
3. Increased mitral valve M-mode E point to septal separation (EPSS).
4. PEP:ET ratio increased over 95% confidence intervals (e.g. over 0.4)
5. M-mode fractional shortening in equivocal range (depending on breed-specific references).
6. Left or bi-atrial enlargement

It must be emphasised that other cardiac or systemic disease, including systemic hypertension, must be excluded as far as possible before a firm diagnosis of DCM may be made. The presence of persistent tachyarrhythmias, such as atrial fibrillation, which may
result in myocardial failure, must also be considered. They may be the cause or the consequence of myocardial dysfunction and careful consideration of their presence is required prior to making a diagnosis of DCM.

If major criteria score 3 points and minor criteria score 1 point each, a total score of SIX or more should identify dogs with DCM but this must be assessed for various breeds prospectively. Further refinements with number loading of some criteria are possible in certain breeds.

The authors emphasise that the identification of one or more of these major or minor criteria should prompt the cardiologist to serially examine that animal for evidence of progression, which should be identified over some years if DCM is genuinely present. The score should increase over time. Prospective evaluation of screened dogs is recommended by a number of centres to evaluate the usefulness of our proposed criteria in screening for DCM. At this stage, these criteria should be assessed for the diagnosis of DCM, and should not be interpreted as being breeding guidelines.

*Post-mortem diagnosis*

Gross pathology examination of dogs with DCM generally shows dilatation of either all four cardiac chambers or predominant dilatation of the left chambers. Myocardial eccentric hypertrophy, rather than true dilatation, is evidenced by increased heart weight: body weight ratio, together with a decreased ratio of the left ventricular thickness to chamber diameter.
An example of histology from the normal canine myocardium is shown in the figure below.

![Figure 1A - Histology specimen from the myocardium of a dog which had no evidence of cardiac disease. Haematoxylin & Eosin stain. Size bar = 100 μm.](image)

Some studies on histopathological findings in the myocardium of dogs with the clinical diagnosis of DCM report non-specific findings. This is consistent with the histopathological findings of human idiopathic DCM, where the degree of fibrosis, degeneration and fibre attenuation may be variable. In dogs, however, two distinct histopathological forms of DCM have been described by various authors:

The attenuated wavy fibre type of DCM has been described by several authors in a total of 119 dogs of many giant-, large- and medium-sized breeds (including some boxers and Dobermanns). The myocardial lesions associated with the attenuated wavy fibre type of DCM consist of myocytes that are thinner than normal (< 6 μm in diameter) with a wavy appearance, comprising at least half of the thickness of the myocardial specimens from the upper and lower portions of the left ventricular wall. The myocytes are separated by a clear
space, indicating oedematous fluid that is generally free from cellular infiltrates (Fig. below).

![Histology specimen from the myocardium of a dog with attenuated wavy fibre type of canine idiopathic DCM. The myocytes are thinner than normal and have a wavy appearance. The myocytes are separated by a clear space, indicating oedematous fluid, which is generally free from cellular infiltrates. Haematoxylin & Eosin stain. Size bar = 200 μm.]

There may also be diffuse subendocardial fibrosis present. The presence of myocardial lesions associated with the attenuated wavy fibre type of DCM was found to have a very high sensitivity (98%) and specificity (100%) for DCM in a study of 70 dogs with the clinical and echocardiographic diagnosis of DCM, when final diagnosis was made post mortem. As attenuated wavy fibres were not found in the myocardium of dogs with cardiac dilatation caused by heart disease other than DCM, this myocyte abnormality does not seem to be induced by chronic volume overload and stretching of the myocyte, as has been suggested. Atrophy or attenuation of myofibres without a wavy appearance has also been described. Finally, some pathologists would argue about the reliability of wavy fibres as a diagnostic marker, since they might also be caused by processing artefacts.

**AF causing DCM or vice-versa??**
Further controversies are also introduced in this asymptomatic period. For example, dogs may be identified with atrial fibrillation without any significant echocardiographic changes. Atrial fibrillation may be an early indicator of the presence of myocardial disease, and the typical echocardiographic appearance of DCM later develops. This has been suggested in Irish Wolfhounds. It is possible that underlying myocardial disease is responsible for AF, such as focal atrial cardiomyopathy or myocarditis recognised on atrial endomyocardial biopsy samples in people with recurrent paroxysmal lone. Conversely, lone atrial fibrillation may result in secondary systolic dysfunction and chamber dilatation due to tachycardia induced cardiomyopathy (in a similar manner to pacing induced models of dilated cardiomyopathy). True lone AF in humans is not associated with any specific chamber enlargement or abnormalities in systolic and diastolic function. However, patients with AF and systolic dysfunction, or those initially considered to have DCM, may show significant improvement in systolic function and diminution of chamber dilatation, with conversion to sinus rhythm or appropriate rate control. In dogs also, a similar possibility exists; since tachyarrhythmias may also result in a dilated, hypokinetic heart, similar to paced models for DCM, is this AF the cause of myocardial failure, or is it an early marker of incipient disease? Therefore the presence of AF is only a minor criterion in the ECVIM scoring system, despite the strong association of atrial fibrillation and DCM in breeds such as the Irish Wolfhound. It is highly recommended that in dogs with AF and systolic dysfunction, systolic function should be re-evaluated once the ventricular rate has been normalised (e.g. with medical therapy), before a presumptive diagnosis of DCM is made. Until recently in humans with atrial fibrillation, restoration of sinus rhythm has been seen as a major goal and more emphasis on rhythm control has been urged in the dog. However, two large human studies, comparing rate control with rhythm control in patients with AF, show that controlling the
ventricular response to atrial fibrillation is far from inferior and may be associated with fewer pharmacological side effects.
Treatment of canine DCM

Treatment of Occult dilated cardiomyopathy:

Management of the occult stage of DCM involves identifying the cause, identifying factors that can precipitate the acute progression to CHF, and instituting nonspecific measures to delay progression of DCM from the occult stage to the overt stage.

The most precipitating factor involves the development of ventricular and/or supraventricular arrhythmias. The presence and complexity of VPCs in Doberman Pinschers suggest that these individuals are at risk for sudden death, so efforts to reduce arrhythmias and the risk of sudden death are indicated. At present, no studies have been conducted to address the potential to reduce the risk of sudden death in this cohort of dogs. In human medicine the antiarrhythmic agents used to reduce the risk of sudden death showed to be ineffective or, even more, some of these antiarrhythmic agents increased the risk of sudden death in people. Thus, it is important to note that even if we control ventricular arrhythmias with drugs does not mean we are able to reduce the risk of sudden death. Additionally, some dogs die suddenly without having any of these arrhythmias documented. If treatment is warranted the most promising antiarrhythmic agents are amiodarone and sotalol but no controlled studies have been conducted in dogs with DCM.

Although the goals of treatment include decreasing the number of VPCs, decreasing symptoms and decreasing the risk of sudden death, the ability of any antiarrhythmic to reach these goals has not been well studied yet.

ACE inhibitors have been investigated in the setting of occult DCM in Doberman Pinschers, observing a modest delay in the onset of the overt stage in patients treated with ACE inhibitors versus untreated patients. Although this study was limited to evaluation of Doberman Pinschers, the use of ACE inhibitors for other breeds with occult DCM might be considered.
More recently, a randomized placebo-controlled study (PROTECT Study) on preclinical DCM in Doberman pinschers showed that administration of pimobendan in this group of dogs can prolong the time to the onset of clinical signs and extends survival. Treatment of dogs in the preclinical phase of this common cardiovascular disorder with pimobendan can lead to improved outcome.

Treatment of Overt dilated cardiomyopathy:

Most dogs present with moderate-to-fulminant pulmonary oedema. Signs of poor perfusion may also be seen. The primary aim of acute therapy is to reduce pulmonary oedema formation and improve oxygenation. Thoracic radiographs may be obtained if they can be done without stressing too much the patient. Drug therapy to reduce pulmonary venous congestion and oedema is based on IV furosemide (2-4 mg/kg every 1-4h) and nitroprusside. Nitroprusside decreases pulmonary capillary wedge pressures, it must be administered in IV infusion and blood pressure should always be monitored when using it. Initial rate at 2.5μg/kg/min and increase it until patient is stabilized or mean blood pressure falls below 70 mmHg. Dobutamine can also be used in order to give an inotropic support.

When the patient is stabilized, IV drugs can be discontinued and start chronic oral treatment with pimobendan, furosemide and ACE inhibitors. Pimobendan is a phosphodiesterase III and V inhibitor with calcium-sensitizing properties that acts as a positive inotrope, as well as vasodilator (inodilator). Pimobendan has balanced vasodilatation and positive inotropic effects and has been shown to increase survival (median of 130 days versus a median of 14 days for the placebo in one study) in Doberman Pinschers with DCM when given at a dose of approximately 0.25 mg/kg orally every 12 hours.
**Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)**

(“Boxer cardiomyopathy”)

ARVC is a relatively uncommon disease of the myocardium predominantly affecting the right ventricle, which appears markedly dilated and hypokinetic. Right atrial enlargement, signs of right-sided congestive failure and arrhythmias are commonly observed. This CM has been described in many dog breeds but its aetiology is not fully understood. ARVC and Boxer CM (or familial arrhythmic disease of Boxers) may represent the same pathological entity, clinically characterised by severe and life-threatening episodic ventricular arrhythmias (often diagnosed only on 24h Holter recording). According to Harpster’s classification, Boxer CM can present in three forms (based on 24h Holter recording).

- **Type 1**: affected subjects present a significant ventricular arrhythmia (at least more than 500 VPCs/day) but they are asymptomatic.
- **Type 2** is characterised by syncopal patients with confirmed ventricular arrhythmia. Both type 1 and 2 do not present echocardiographic changes.
- **Type 3** are syncopal Boxers with arrhythmia and signs of CHF (or at least significant echocardiographic changes).

Severe right ventricular and right atrial enlargement are the most obvious gross lesions. The RV free wall appears significantly thinner than normal.

Histopathological changes may be present in the myocardium of all four free walls and the interventricular septum, but they are most marked in the right ventricular free wall. The changes comprise endocardial fibrosis, with infiltration of the myocardium by fibrous tissue and adipose tissue and degeneration or replacement of myocytes. Mild infiltrate of mixed inflammatory cells can also be observed.

In most cases, diagnosis is based on electrocardiographic abnormalities (ventricular ectopics) detected on 24h (Holter) recording, even in the absence of echocardiographic changes.
Canine Myocarditis

Myocarditis is an inflammatory process of the myocardium and may be caused by different aetiologies:

Infectious aetiologies

Lyme disease
- bacterial infection caused by Borrelia burgdorferi (borreliosis) transmitted by tick bites.
- characterised by pyrexia, lethargy, lameness, severe arthritis, lymphoadenopathy
- complete AV block and endocarditis are possible sequelae

Parvovirosis
- viral infection caused by canine parvovirus may cause myocarditis in young puppies.
- sudden onset, usually accompanied by fulminating death

Babesiosis
Cardiac troponin I is elevated and represents a marker of myocardial injury in canine babesiosis, and the magnitude of elevation of plasma troponin I concentrations appears to be proportional to the severity of the disease. ECG changes in babesiosis are similar to the pattern described for myocarditis and myocardial ischaemia and together with histopathological findings indicate that the heart suffers from the same pathological processes described in other organs in canine babesiosis, namely inflammation and hypoxia. On cardiac histopathology from dogs that succumbed to babesiosis, haemorrhage, necrosis, inflammation and fibrin microthrombi in the myocardium were documented, all of which would have resulted in ECG changes and elevations in cardiac troponin. Myocardial damage causes left
ventricular failure, which will result in hypotension and an expansion of the plasma volume due to homeostatic mechanisms

Trypanosomiasis (Chagas’ disease)
- protozoal infection caused by Trypanosoma cruzi (Southern USA, Central and South America, Africa) T. cruzi is transmitted by triatomine (reduviid, "kissing," or "assassin") bugs. While biting, infected bugs deposit faeces containing metacyclic trypomastigotes on the skin. These infective forms enter through the bite wound or penetrate mucous membranes.

  - dogs younger than 2 years are more affected
  - clinical signs of infectious disease and CHF
  - diagnosis requires demonstration of parasitaemia by culture or serodiagnosis

Non-infectious aetiology
Ischaemic heart disease
- coronary embolism (rare in dogs and cats), secondary to infective endocarditis, septicaemia, pulmonary neoplasm, GDV and pancreatitis
- MIMI are common in patients with pre-existing valvular heart disease and are located in the left ventricle, around the papillary muscle. MIMI may contribute to dysrhythmias

Physical injury
- traumatic myocarditis (RTA, heat stroke, electric shock)
- undetected cardiac trauma may result in sudden death in 12-24 hours after the accident

ECG may include ST elevation/depression and arrhythmias
References


