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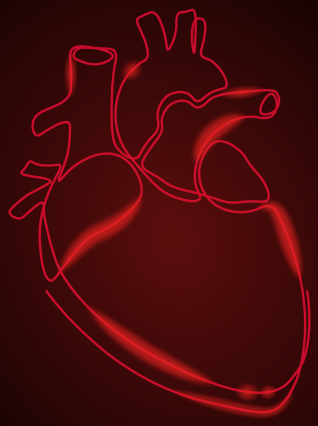

CARDIAC DISEASE

How Nutrition can make the difference

PURINA® PRO PLAN® VETERINARY DIETS VIRTUAL SYMPOSIUM

2nd November 2020

ECVIM-CA ONLINE CONGRESS

INTRODUCTION TO PURINA SYMPOSIUM 2020

Cardiac disease is a common disease in dogs, as about 1 in 10 dogs is diagnosed with it. Specifically, myxomatous mitral valve disease accounts for the 75% of heart disease in dogs. This Symposium tackles the ever-growing topic area of cardiac disease mainly in dogs, but also in cats. This is an opportunity to learn from leading experts, discover new research and refresh your outlook on cardiac disease in pets.

Purina knows that the research and development in this area is key to provide our pets with a better quality of life, and is committed to it, undertaken extensive studies on how nutrition can support cardiac health. These studies have been possible thanks to the collaboration between internal and external experts, which have helped to further strengthen Purina´s research capabilities and pave the way toward impactful scientific discoveries for the cardiac research area. Purina research and the transfer of knowledge allows for constant improvement, so we progress and move forward in our quest to benefit both humans and their pets.

Purina has always been a strong supporter of veterinary education, and we are very proud to have organized this Purina Symposium to contribute to the dissemination of knowledge and allow for network building in the global veterinary community.

I hope you enjoy the Purina Pro Plan Veterinary Diets Virtual Symposium on **"Cardiac Disease, how nutrition can make the difference".**

Rosa Carbonell
Head of the Veterinary Channel

ECVIM-CA
ONLINE CONGRESS

*Historical collaboration with ECVIM-CA.
This year, considering the pandemic situation,
the pre-ECVIM Purina PPVD Symposium
has been re-timetabled.

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Myxomatous mitral valve disease in dogs

Classification, Incidence, Pathology and Pathogenesis

Professor Joanna Dukes-McEwan
BVMS, MVM, PhD, DVC, Dip ECVIM-CA (Cardiology), FRCVS

Jo is Professor of Veterinary Cardiology at the University of Liverpool Small Animal Teaching Hospital. Most of her time is within the clinics, providing a referral cardiology service, leading a team of 3 other lecturers and three residents following the ECVIM-CA Cardiology residency training programme.

Biography

Jo has worked at the University of Liverpool since 2004. She has also worked at the University of Glasgow, her alma mater, where she also did her internship and residency training, and the University of Edinburgh, where she also did her PhD, researching familial dilated cardiomyopathy in Newfoundland dogs. This led to a post-doc position, attempting tofind a gene implicated in DCM, which was not successful, but she learnt some molecular genetics skills. Jo has also worked in general practices in Hereford, Canterbury and Glasgow over her career.

Jo holds the UK Royal College of Veterinary Surgeons (RCVS) Diploma in Veterinary Cardiology and is a Diplomate of the European College of Veterinary Internal Medicine- Companion Animals (ECVIM-CA) (Cardiology). She enjoys teaching, inspiring the next generation of veterinarians and veterinary cardiologists. She is active in clinical research and she is author or co-author on over 80 publications in peer reviewed literature. She was awarded Fellowship of the Royal College of Veterinary Surgeons in 2017 for meritorious contributions to clinical practice.

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Myxomatous mitral valve disease in dogs

Classification, Incidence, Pathology and Pathogenesis

Professor Joanna Dukes-McEwan
BVMS, MVM, PhD, DVC, Dip ECVIM-CA (Cardiology), FRCVS

Myxomatous degenerative valvular disease can be regarded as almost ubiquitous in dogs, associated with ageing. It is much less common in humans (estimated to be 1-3% of the adult population[1]), but there are similarities between Barlow's disease and MMVD in canine patients [1]. Valvular myxomatous degeneration is also reported in other species, such as horses and pigs. In dogs, the mitral valve is affected to a much greater extent that other heart valves, but others (tricuspid > aortic > pulmonic) can also be affected.

Incidence / Prevalence

It has been estimated that heart disease affects 10% dogs in first opinion general practices in North America, and of these, 75% have chronic valvular disease [2]. From electronic patient records in the UK, between 0.36% (confirmed MMVD) and 3.54% (compatible heart murmur) of all dogs attending first opinion practices confirm high incidence and prevalence [3]. Even going back over 50 years, prevalence of valvular heart disease is common (6% of screened dogs, increasing with age) [4].
In some breeds, prevalence may be 100% in older dogs (e.g. Cavalier King Charles spaniels >10 years old [5]).

Pathological Classification

A pathological classification scheme was originally proposed by Whitney[6] and this is still widely used in staging disease severity. It is graded with increasing severity from I – IV, and it includes gross pathological assessment of the mitral valves. However, it should be appreciated that progression of disease is a continuum and a simple four-stage classification may not be easy to follow, nor be easily applicable to clinical cases.

- Type I lesions represent valve leaflets that contain a few, small, discrete nodules in regions where leaflets contact each other, with small areas of opacity in the proximal valve.
- Type 2 lesions are on leaflets with larger nodules which being to coalesce at the leaflet edges at points of contact. Areas of diffuse opacity may be present.
- Type 3 lesions have larger nodules which may have coalesce into irregular, plaque-like deformities, and extend to involve proximal portions of the chordae.
- Type 4 lesions denote gross distortion and ballooning of the valve cusps. Chordae tendineae are thickened proximally.

Pathology

Early valvular changes are most evident along leaflet edges at the juncture of leaflet apposition, particularly where first-order chordae attach. The normal, thin, translucent valve leaflets develop nodular thickening, focal and then diffuse opacity and the distal third of the leaflet becomes thickened. As the disease progresses, the valve leaflet edges may roll, the valves become deformed and the valves may bulge into the left atrium. Changes can also affect the chordae tendinae in more advanced disease [7, 8]. There is redundancy of valve tissue and progressive lengthening of the chordae tendinae, which can contribute to the tendency to balloon in the left atrium; mitral valve prolapse, which can result in a parachute appearance to the closed valve (Figures 1-3).

Histopathological changes have been well described [7-9]. Affected valves show loss or disruption of the normal laminated valve structure (atrialis, spongiosa, fibrosa and ventricularis layers). The lesions are most marked in the distal third of the valve leaflets. There is progressive expansion of the spongiosa layer with increased extracellular matrix (glycosaminoglycans and proteoglycans) and accumulation of amorphous, mucoid substance, which gives the term myxomatous degeneration. The fibrosa layer is disrupted. Instead of dense, circumferentially oriented layer of collagen fibres extending to the chordae, this collagen layering becomes fragmented. In very advanced cases,

it may be difficult to identify distinct spongiosa and fibrosa layers. There is decreased cellularity in distal tissue of affected valves [10].

Beautiful scanning and transmission electron-microscopy images further show some of these changes. The endothelial cells can become denuded, exposing the underlying stroma [11]. The disruption of the organised collagen bundles and replacement with fibrillar, immature collagen can be seen [12]. Endothelial cells and valve interstitial cells can become activated [12, 13].

Humans also may develop myxomatous mitral valve disease (often just called mitral valve prolapse; Barlow's syndrome). Differences between the canine and human pathology exist, despite the remarkably similar pathology. In humans, the posterior leaflet is predominantly affected, and there is extensive fibrous tissue deposition superimposed on both the atrialis and ventricularis layers of the valve [1, 14]. Despite old synonyms of chronic valvular disease in dogs, such as "chronic mitral valvular fibrosis" (in Ettinger & Suter's famous Canine Cardiology book of 1970), fibrosis is not a feature of the canine valve histopathology [1].

Clinical (Echocardiographic / Radiographic Classification of MMVD

The myxomatous degenerative process leads to mitral regurgitation. This leads to a volume overload of the left atrium and left ventricle. These chambers then progressively dilate, which is identifiable from echocardiography or thoracic radiographs. The ACVIM consensus statement (updated in 2019) [2] gives four distinct stages of the disease:

- Stage A: at risk (e.g. all CKCS)
- Stage B: Preclinical MMVD. The dog has the characteristic murmur but no clinical signs of congestive heart failure. This is subdivided based on evidence of significant left atrial and left ventricular remodelling (i.e. dilatation):

  – Stage B1: no or minimal left atrial and left ventricular dilatation

  – Stage B2: Left atrial size increased (LA/Ao 2D short axis ratio in early diastole ≥ 1.6; left ventricle size increased (normalised for body weight by allometric scaling) (LVIDdN >1.7). These criteria are important as they meet the inclusion criteria of the EPIC study, so identifying this stage is important for the individual patient, to prolong the asymptomatic phase of the disease.
- Stage C: Congestive heart failure
- Stage D: Refractory congestive heart failure; treatment to be tailored for each individual patient.

Early identification of mitral valve prolapse forms the basis of heart testing schemes in some breeds (CKCS) to avoid breeding from prematurely affected individuals [15]. There are breed differences in echocardiographic progression of MMVD. Large breed dogs tend to develop systolic dysfunction [16, 17] and less florid valvular pathology.

Pathogenesis

Role of valve interstitial cell (VIC)

VICs are normally present within the mitral valve, which are fibroblast-like and non-contractile. They contribute to homeostatic remodelling of the matrix constituents, which have low turnover. When activated in MMVD, VICs transition to a myofibroblast-like phenotype, and express smooth muscle associated contractile proteins, matrix metalloproteinases and inflammatory cytokines. These result in remodelling of the extracellular environment and the myxomatous degenerative pathological process [1, 13, 18]. It has also been suggested that the activated VIC contractile properties may support valve function in diseased cells (i.e. consequence rather than the cause) [9].

Signalling

There are differences based on immunohistochemistry, protein expression, gene expression and the transcriptome analyses between canine and human MMVD. In a canine study, with valves graded in severity by the Whitney classification, there are many differentially expressed genes, in particular those of the extracellular matrix (ECM) and inflammation. Transforming growth factor (TGF) β1 appears to be the dominant signalling pathway controlling pathogenesis at all severities [19] and it is expressed on diseased valve tissue [9]. TGFβ1 is released from activated VICs and addition of TGFβ1 to cultured VICs results in their activation [19]. In humans, TGFβ1 canonical SMAD pathway signalling drives fibrosis [1]. In dogs, the ERK1/2 cascade is a down-stream component of non-canonical TGFβ signalling and 5HT signalling. The reason why high TGFβ1 does not result in significant fibrosis in the canine valve is unclear. Aberrant TGFβ1 signalling appears to initiate and perpetuate the valve pathology [19]. Serotonin (5HT) can lead to up-regulation of TGFβ1.

Serotonin or 5HT signalling has also been implicated in MMVD [20]. Conditions associated with high levels of serotonin are associated with valvulopathy with myxomatous degeneration (e.g. drugs, serotonin-secreting tumours, etc). Free serotonin in the circulation is taken up by platelets or the Serotonin (5HT) membrane (or re-uptake) transporter (SERT). Immunohistochemistry studies show that Tryptophan hydroxylase 1 (TPH1) (the rate limiting step to produce serotonin from tryptophan) is increased in myxomatous valves, and present in VICs. The 5HT-R2B receptor is also increased but SERT is reduced in myxomatous lesions [20]. Metabolised serotonin is excreted as 5-HIAA in the urine. Serotonin's biological effects are through a large range of 5HT-receptors. The 5HT2 receptor family have been implicated in heart disease. 5HT2B mediates ERK 1 / 2 signalling, which can activate VICs (and is inter-related to the TGFβ signalling) [21]. Dogs with MMVD have higher serotonin concentrations than healthy controls. Cavalier King Charles spaniels in health have higher plasma serotonin concentration than other breeds [22] but this does not appear to be associated with stage of the disease [23]. However, dogs with severe MMVD have lower serotonin concentrations than those with mild disease [24]. It has been reported that expression of SERT is down-regulated in dogs with advanced MMVD [25]. CKCS show some transcriptome profile differences (as well as similarities) compared to non-CKCS with advanced MMVD [26].

Aetiology

The primary cause of MMVD is not known, but it is associated with ageing. Premature onset of disease appears to be hereditable in CKCS [27] and successful heart testing schemes aim at selecting breeding dogs with good parental status (i.e. older age of onset) [15]. In CKCS, a genome wide association study (GWAS) compared premature onset with late onset MMVD, which identified two loci on chromosomes 13 and 14, but the associated genes are not currently known [28]. In Maltese dogs with MMVD compared to controls, polymorphisms were identified in the SERT encoding gene [29], which may be implicated in altered expression or function which could be implicated in aetio-pathogenesis of MMVD. These authors have also carried out a GWAS in the Maltese with MMVD and found a locus on Chromosome 17 [30] (not SERT gene location). There also is a heritable basis to age of onset of MMVD (shown in CKCS) [27, 31]. This influence of parental status was adopted in the UK scheme, where CKCS of >2.5 years old could be bred provided their parents were over 5 years of age with no heart murmur. However, this did not affect the prevalence or age of onset in CKCS in the UK [32]. In contrast, the Danish scheme was successful, probably because it included echocardiography and identification of mitral valve prolapse [15], rather than merely the presence of a heart murmur. The UK has now adopted a modification of this scheme Click here for more information In the UK scheme, the maximal prolapse is measured and graded. Both the presence and grade of the heart murmur and grade of the prolapse are taken with the age of the dog to score on a traffic light system: green, go ahead with breeding, amber, caution and red, do not breed.

Sequelae of MMVD

Congestive heart failure is the most common consequence of progressive MMVD once the left sided filling pressures increase – typically and initially left sided (L-CHF; pulmonary oedema). This stage C will be associated with neuroendocrine activation with increased sympathetic drive (loss of vagal tone and sinus arrhythmia) and renin-angiotensin-aldosterone system (RAAS) activation. Some dogs with severe atrial stretch (especially larger breeds) may develop atrial fibrillation, which will further decompensate the CHF. High left atrial pressure may lead to pulmonary venous, pulmonary capillary and eventually pulmonary arterial hypertension (i.e. post-capillary pulmonary hypertension). This may lead to clinical signs such as exercise intolerance, syncope and shortness of breath in absence of pulmonary oedema. It may also result in right sided congestive heart failure (R-CHF) signs. The myxomatous degenerative process affects chordae tendinae as well, so one potential reason for acute decompensation into L-CHF is rupture of one or more chordae. Another rare consequence of mitral regurgitation includes left atrial tear. The mitral regurgitant jet can result in jet lesions, endocardial injury which can lead to endocardial or full left atrial perforation, so pericardial haemorrhage, possibly with cardiac tamponade.

Conclusions

Myxomatous degenerative valvular disease is an "old" disease and we may think there is nothing new to know. However, recent publications have provided a range of insights into aetiopathogenesis, mechanisms and signalling which may give future opportunities to intervene with the disease progress, which may benefit both dogs and humans.

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Figures

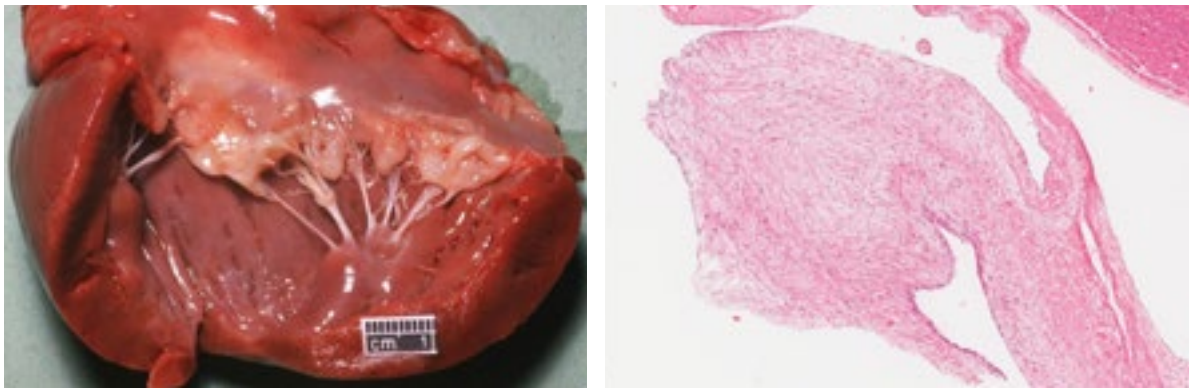

Figure 1.
Gross pathology (left) and histopathology (right) showing myxomatous nodular degeneration. The histopathology images shows the valve cusp spongiosa exhibiting an increased and proliferative fibroblastic population within an excess of deposited mucinous extra-cellular matrix. At the periphery of the cusp the mucoid material deforms the anatomical architecture and expands the cusp into a discrete myxomatous nodule. (Images courtesy of Dr Richard Blundell, University of Liverpool).

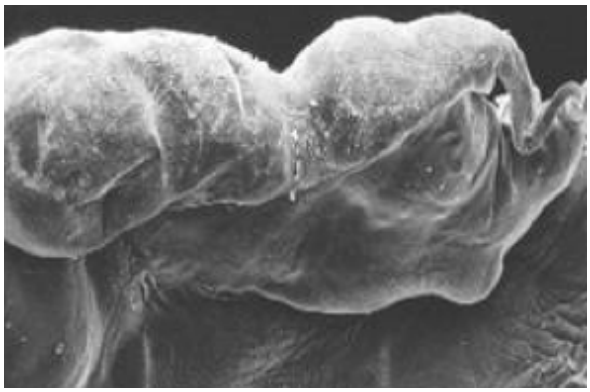

Figure 2.
Scanning electron-microscopy of the thickened edge of a myxomatous mitral valve leaflet. On the right, a ruptured chorda tendina can be seen. (Image courtesy of Professor Brendan Corcoran, University of Edinburgh).

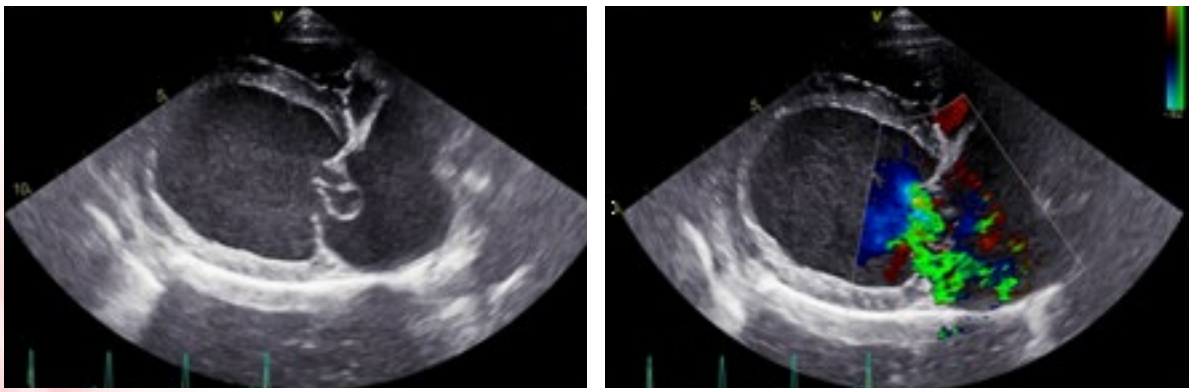

Figure 3.
Echocardiogram. Right parasternal four-chamber view showing severe prolapse of the mitral valve leaflets (left) associated with mitral regurgitation shown on colour flow Doppler (right). The left atrium and left ventricle are both dilated.

Key Highlights

1. Myxomatous degenerative valvular disease is "old" in the veterinary literature, but there is so much more to learn about it.
2. Gross pathology and histopathology is typical of the condition, but scanning and transmission electron-microscopy offers tantalising glimpses of cellular interactions and activation.
3. Valvular interstitial cells (VICs) become activated, and are no longer quiescent fibroblast like. Activated VICs express smooth muscle, and becoming contractile may be a consequence of the condition, to attempt to stabilise the valve.
4. Serotonin signalling pathways were initially considered to be most important in progression of MMVD, but the transforming growth factor beta $TGF_{\beta 1}$ pathway is the dominant signalling pathway, but there are interactions with this and the serotonin pathway.
5. Aetiology of MMVD is not known, and it appears to be polygenic in CKCS as far as determining premature age of onset (rather than merely presence of the disease). Polymorphisms in the serotonin transmembrane transporter SERT are implicated in Maltese dogs.
6. Identification of premature onset evidence of disease such as mitral valve prolapse on echocardiography may reduce prevalence in CKCS (the Danish KC heart testing programme).
7. The ACVIM consensus statement can be used to stage MMVD in Stages A – D, with recommendations for each stage.
8. Sequelae of MMVD is usually development of congestive heart failure. In addition, pulmonary hypertension (post-capillary, due to high left atrial pressure), arrhythmias such as atrial fibrillation, ruptured chordae tendinae or left atrial rupture can all occurand result in decompensation.

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Heart disease - therapeutic considerations for the dog

Steve Ettinger DVM, DACVIM (SAIM and Cardio)

After graduating from the College of Veterinary Medicine at Cornell University in 1964 he completed intern and resident training at the Animal Medical Center in New York City. His specialty training was a National Institutes of Health Postdoctoral Fellow in Cardiology, which was completed at the Bronx Veteran's Administration Hospital and the Animal Medical Center (AMC), both in New York City. He practiced veterinary medicine at the AMC in New York City until moving west to California.

Dr. Ettinger and three other specialists founded the Berkeley Veterinary Medical Group in California in 1971, the first group veterinary specialty practice in the United States. During this period, he was also a Clinical Professor of Veterinary Medicine at UC Davis (1972-1980). He relocated to the California Animal Hospital in Los Angeles in 1980. That group developed into a 25+ DVM specialty-general medicine (hybrid) practice as well as a veterinary post graduate teaching hospital. Over 100 interns and 20 residents trained there before the hospital was sold. In July-August of 2011, Dr. Ettinger was a Visiting Professor at the Veterinary School at the University of Sydney in Australia.

Dr. Ettinger served as Chief Medical Officer (CMO)) of PetDRx, a national veterinary practice group from 2007 until July 2010 and prior to that was the medical director of the California Animal Hospital Veterinary Specialty Group in Los Angeles from 1980 until 2009.

He completed a four-year term as an elected member of the Board of Trustees of Cornell University in Ithaca, New York and New York City in 2011.

In 1970, Dr. Ettinger co-authored with Dr. P.F. Suter, the first veterinary small animal specialty textbook, Canine Cardiology (1971) and he has been author and editor of the Textbook of Veterinary Internal Medicine, a two-volume treatise on veterinary medicine, available in five languages. The 8th edition, (2016) incorporated over 320 author contributions to both a printed textbook and a digital version. The 9th edition of the textbook is now in preparation.

Dr. Ettinger has presented talks throughout the world and has published over 180 professional articles in the veterinary literature. His areas of specialization are small animal veterinary internal medicine, small animal cardiology, hospital management and professional veterinary development. He is a Diplomate of the American College of Veterinary Internal Medicine (Cardiology and Small Animal Internal Medicine) and is an Emeritus Fellow of the American College of Cardiology (FACC) and the American Heart Association (FAHA).

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Heart disease - therapeutic considerations for the dog

Steve Ettinger DVM, DACVIM (SAIM and Cardio)

The discussion on Therapy of Dogs Afflicted with Mitral Valve Disease encompasses all of the major approaches to treating patients we follow that present with questions regarding the need for therapy. Prior to a specific discussion of unique drugs, it is relevant to first understand the nature of the animal's problems and the history that comes along with the animal at the time of the initial examination. Clients are presenting their pet either on a first visit evaluation or have been referred for services based upon a prior consideration of cardiac disease. It is incumbent upon the DVM to ask the client to relate information regarding signs that the pet presents with. First it is also necessary to ascertain information about the pet including breed, age, weight, intact or neuter status. Past pertinent history may be relevant but should not significantly deter the examination.

Upon conclusion of redefining the basics the examiner will need to listen to the client present historical signs which the DVM should carefully listen to and then ask further questions such as changes in water consumption, frequency of urinating, type and nature of respiratory problems all of which may or may not have been reported by the owner. It is important that the veterinarian identifies to a new client what they summarize as this provides the owner with the sense that you have heard the nature of the problem.

Examination of the patient follows after which the DVM can determine the need for further evaluation of the patient. Once this has been completed a tentative or definitive diagnosis may be developed and along with that, a plan for care of the patient. The dog at this time should likely be evaluated in a manner that allows a classification system of the disease. Stage or Grade the nature of the problem. All reputable grading systems are similar and help identify the most likely appropriate therapeutic approach that may be needed.

<table>
<tr><th>CAH</th><th>Simplified CAH Canine</th><th>ISACHC</th></tr>
<tr><td>0</td><td>0
CARDIAC NORMAL</td><td>Normal</td></tr>
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CARDIAC PATHOLOGY
NO CARDIAC REMODELING
NO ATRIAL ENLARGEMENT
(LA:AO<1.7)</td><td>Class Ia</td></tr>
<tr><td>2a</td><td rowspan="2">Class Ib</td></tr>
<tr><td>2b</td><td rowspan="2">2
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<tr><td>3b</td><td rowspan="4">3
HEART FAILURE EITHER PARTIALLY CONTROLLED WITH DRUGS OR OVERT HEART FAILURE.</td><td>Class II</td></tr>
<tr><td>4a</td><td rowspan="3">Class III</td></tr>
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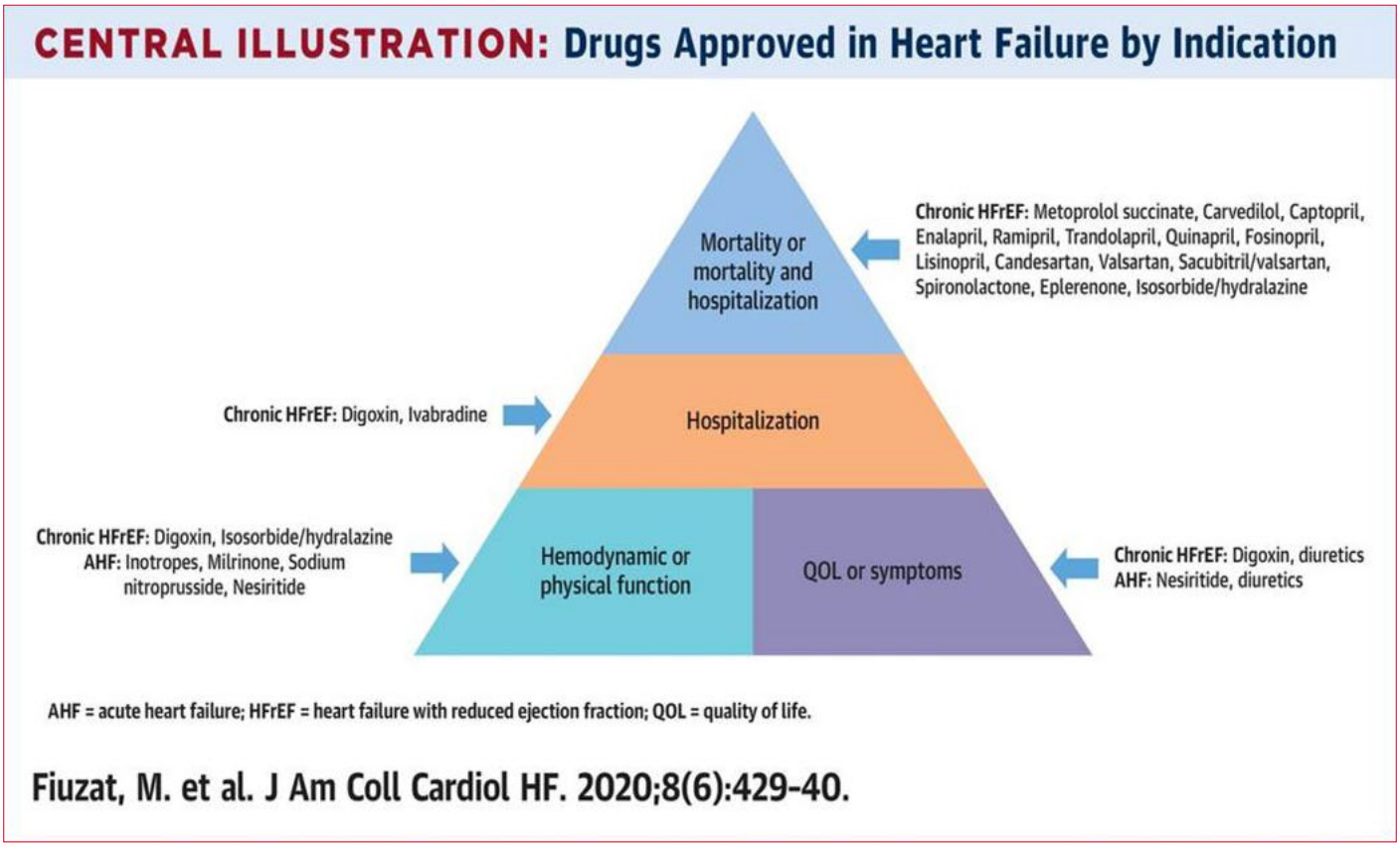
We will discuss the various mechanisms appropriate for each stage of cardiac disease and then one can discuss with the owner options for therapy, restrictions, dietary alterations, need for supplements and more. In the notes and slides there are several heart disease classification systems presented.

The nature of this talk is to suggest my approach to each stage of disease and to identify my favored modes of therapy at each level. As you will see in the slides I do not believe therapy for Stage (Grade) 0 disease is needed. Likewise in Stage 1 disease where there is no significant pathology no medications have been shown to alter the disease process. Stage 2 disease is usually without signs

and often requires minimal care such as antitussive medicine or weight control initially. Late stage 2 or more likely Stage 3 disease does require attention.

We discuss in a somewhat numerical manner the choices of drugs to be used when signs do occur, the dosages recommended and the caveats required for discussion of ACE agents; diuretics including furosemide and torsemide and then the advantages of pimobendan when there is significant evidence of heart failure. In addition, we discuss the general virtues of antialdosterone agents, possible salt level restrictions, dietary modifications and the use or benefit of supplements.



A final reminder completes our voyage and reminds us that non-cardiac or extra cardiac problems may be involved as well as changes in the general health finding in the animal that need to be identified. Heart disease often is not a single entity but part of a multisystem process resulting in co-morbid disease that requires thoughtful evaluation.

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Dietary Intervention in Dogs with Myxomatous Mitral Valve Disease

Johnny Li PhD

Dr. Johnny Li is a Senior Research Scientist at Nestlé Purina PetCare Company in St. Louis. He earned his Bachelor's degree in Biochemistry from Xiamen University in China, a Master's degree in Computer Science from Columbia University, and a Ph.D. in Molecular Biology and Genetics from the University of Texas at Austin where he studied molecular signaling and genetics in his dissertation work. Dr. Li joined Nestlé Purina after completing a postdoctoral fellowship in Bioinformatics at Johnson & Johnson Pharmaceutical R&D. In his current research, he applies nutrigenomics and bioinformatics to study common chronic diseases in dogs and cats.

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Dietary Intervention in Dogs with Myxomatous Mitral Valve Disease

Johnny Li PhD

Abbreviations

MMVD: myxomatous mitral valve disease

CPB: cardiac protection blend

CON: control diet

LAD: left atrial diameter

LA/Ao: left atrial to aortic root diameter

MCT: medium chain triglycerides

Myxomatous mitral valve disease (MMVD), the most common naturally-occurring heart disease in dogs, is associated with deranged energy metabolism, and increased oxidative stress and inflammation [(1).] The failing heart is compared to "engine out of fuel" [(2).] A cardiac protection blend (CPB) of nutrients containing medium-chain triglycerides as an alternative energy source, fish oil and other key nutrients important to cardiac health was formulated to slow or prevent the progression of MMVD. Nineteen dogs with early stage MMVD and breed-, age-, and sex-matched 17 non-MMVD dogs were enrolled for a 6-month blinded, randomized, placebo-controlled study [(3).] The primary endpoint of this study was to assess echocardiographic changes in response to CPB. Metabolomics analysis on the serum samples from these dogs was performed to evaluate changes in circulating metabolites with the diet intervention [(4).]

CPB reduces left atrial enlargement in MMVD dogs. Linear mixed effect models with repeated measures showed significant diet by time interactions in left atrial diameter (LAD) and LA/Ao ($P = 0.005$ and $P = 0.037$, respectively) [(Fig. 1A,B).] Dogs on the control diet (CON) showed a significant increase in LA/Ao over baseline at 3- and 6-months ($P = 0.012$ and $P = 0.010$, respectively) while the CPB-fed dogs showed decreases. Similar effects were found in LAD. Remarkably, while the average increases at 3 months and 6 months were 6.6% and 10.8% in LAD in CON-fed dogs, the CPB-fed dogs showed 3% decreases. No change was found in non-MMVD dogs.

CPB attenuates MR and slows MMVD progression. While the majority of CON-fed dogs showed no change in grade (none/trace, mild, moderate, or severe) in the severity of MR, 2 (25%) worsened by the end of the study and no dog improved in this group. In contrast, just 1 (10%) CPB-fed dog progressed from moderate to severe, while 3 (30%) improved in this group ($Pdiet \times 6mo = 0.041$). Consistent with this, CON dogs showed progression of MMVD from stage B1 to B2 by 6 months, but none of the CPB dogs had progressed ([Fig. 2,] $Pdiet \times 6mo = 0.0014$).

Correlation between LAD and BP in MMVD dogs but not healthy dogs. Although blood pressure increased slightly over baseline in both diet groups at 6 months, these changes did not reach statistical significances. The within-subject changes in LAD were positively correlated with those in SAP and DAP in CPB-fed dogs ($r > 0.6$ and $P < 0.05$ in both cases), but not in the CON dogs. Notably, the same 6 dogs that had reductions in LA size also showed decreases in blood pressure.

Effects of diet intervention on serum metabolome. Untargeted metabolomic analysis on the serum samples from these dogs was performed. Principal component analysis showed no significant clustering at baseline ($P = 0.08$), but the separation between diet groups was evidenced at 6 months ($P = 1.6 \times 10\text{-}4$) (Fig 3). Linear mixed models identified 102 significant metabolites with significant diet by time interactions (adjusted $P < 0.05$). The concentrations of caprate (C10:0) and caprylate (C8:0) were significantly increased from baseline in CPB-fed dogs, compared to little change in CON-fed dogs ($P < 0.001$ and $P = 0.025$ respectively). The ratios of omega-6 to omega-3 fatty acid changed from 2.41 and 1.46 in CON and CPB groups at baseline to 4.30 and 0.46 at 6 months, respectively. Arginine and citrulline, precursors of nitric oxide biosynthesis, were both increased 2-fold, although the arginine contents were the same in both diets. There was no change in any measured parameters in the healthy dogs.

Conclusions

Prior metabolomic and transcriptomic data suggested that dogs with MMVD have altered energy metabolism, increased inflammation and oxidative stress [1]. Our study demonstrated that dietary intervention with a blend of nutrients designed to address metabolic changes associated with preclinical MMVD in dogs was able to reduce left atrial enlargement and to slow or prevent cardiac changes in dogs with early preclinical MMVD. Serum metabolomic analysis supports the hypothesis that CPB improves cardiac bioenergetics and reduces ROS and inflammatory mediators in MMVD dogs.

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Figures

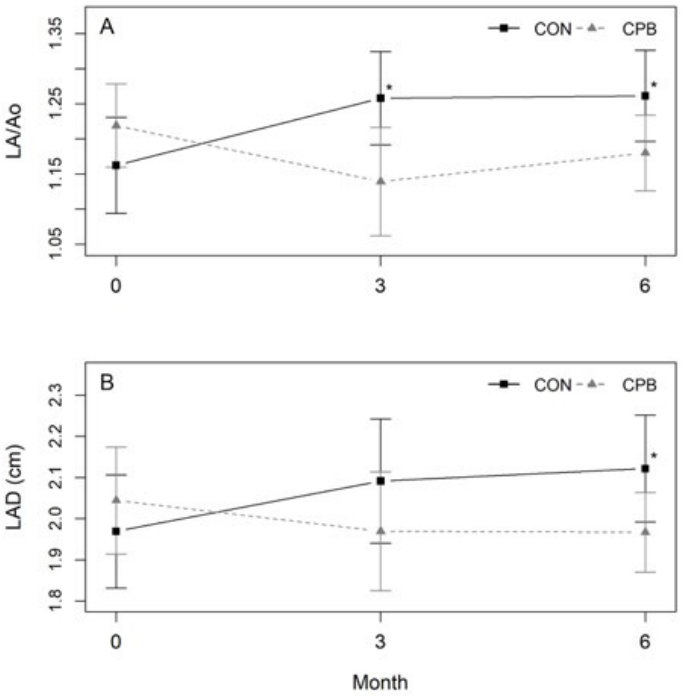

Fig. 1.
Effect of diet and time on left atrial size in MMVD dogs. Plots show estimated means with standard error bars for (A) LA/Ao and (B) LAD in dogs with MMVD fed the control (CON) or test (CPB) diet. There was a significant diet x time interaction ($P < 0.05$) for both parameters, with CON dog increasing and CPB dogs decreasing over time. Both groups differed significantly from baseline as indicated: *$P < 0.05$.

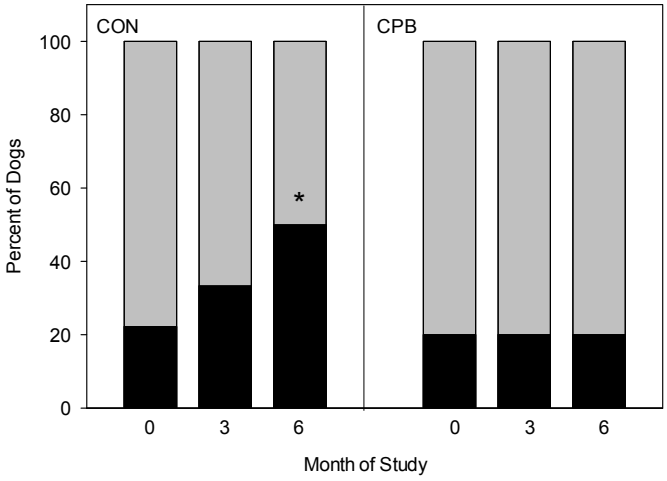

Fig. 2.
Progression of disease in MMVD dogs based on ACVIM stage. Figure shows percent of dogs in ACVIM Stage B1 and B2 at 0-, 3- and 6-months of the study. *CPB differed from CON at 6 months, $P < 0.001$.

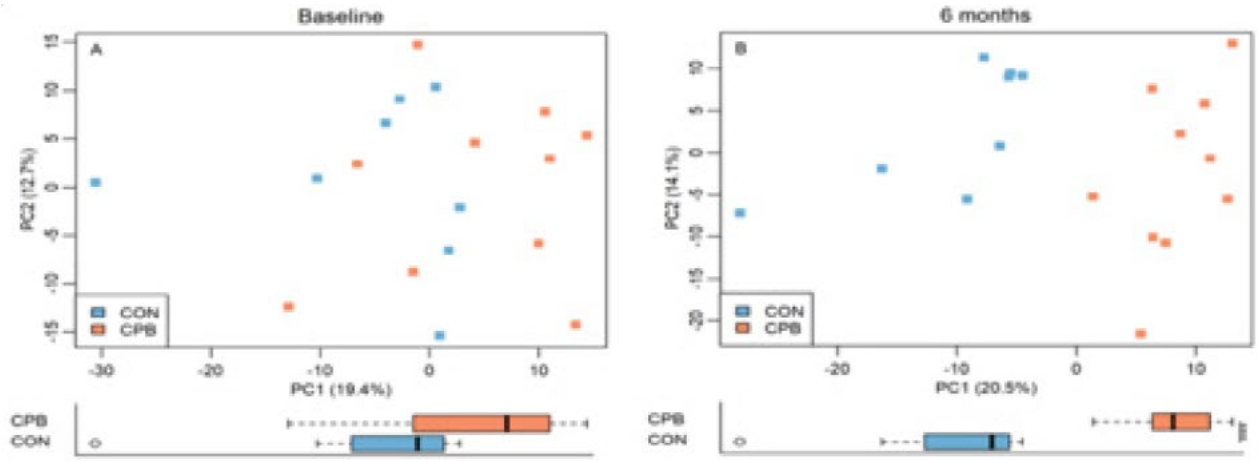

Fig. 3.
Principal component analysis (PCA) at baseline (A) and 6 months (B). The percentages of data variation explained by the first two principal components (PCs), PC1 and PC2, are indicated on the x and y axes respectively. Distributions of samples along PC1 by diets were plotted below each PCA plot. Blue squares represent CON diet while orange ones represent CPB diet.
***P < 0.001.

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Nutritional Management in Canine Heart Disease

Dottie Laflamme DVM, PhD, Dipl ACVN

Dr. Dottie Laflamme received her DVM, Best Masters of Science (MS) in ruminant nutrition, and PhD in nutrition and physiology, from the University of Georgia. She completed her clinical nutrition residency as an ALPO Postdoctoral Fellow in Clinical Nutrition. Dr. Laflamme is a Diplomate and past-President of the American College of Veterinary Nutrition. She is an author on over 200 scientific and technical publications; and has been a speaker at a number of veterinary, research, and continuing education programs worldwide. She worked for Purina (first Ralston Purina, now Nestle Purina) in the Research and Development Department from 1990 until her retirement in 2015. Her research focused on therapeutic nutrition, especially obesity management, and geriatric nutrition. She currently works as an independent consultant. Dottie lives in the Blue Ridge Mountains of western Virginia.

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Nutritional Management in Canine Heart Disease

Dottie Laflamme DVM, PhD, Dipl ACVN

Most veterinarians don't think about changing the diet of dogs for their heart health until those dogs have advanced heart failure. The American College of Veterinary Internal Medicine (ACVIM) guidelines for diagnosing and managing heart disease in dogs mention dietary change, based on stage of disease.[1] According to this system, the nutrients of concern for dogs with heart failure include sodium, long chain omega-3 polyunsaturated fatty acids (n-3 PUFA), and adequate protein and calories. Mild sodium restriction is recommended beginning in dogs with ACVIM stage B2. By stage C, with the onset of congestive heart failure (CHF), dietary recommendations are focused on reducing cachexia by providing palatable diets and assuring adequate intake of calories and protein; providing modest sodium restriction; and addressing any electrolyte abnormalities, such as potassium and magnesium, that may occur secondary to disease or medical treatments. Supplementation with n-3 PUFAs are mentioned although not specifically recommended at this stage. Dietary recommendations for dogs in Stage D continue those of Stage C and to further restrict sodium "if it can be done without compromising appetite or renal function". [1]

This version of dietary management for dogs with heart disease is over simplified. Although it does consider the different stages of heart disease and heart failure, it fails to consider all the nutrients that may be important to cardiac health. This paper and presentation discusses a broader view of nutrition for heart health, including nutrients that may slow the progression of heart disease.

Key nutrients in heart health and disease

Sodium and potassium

Sodium is a key extracellular electrolyte and is the most important osmotic agent in blood and extracellular fluid. As such, sodium attracts water molecules which can increase blood volume. A decrease in body water or sodium results in upregulating the RAAS (Renin –Angiotensin-Aldosterone System). This causes sodium to be retained by the kidneys, and water along with it.

A failing heart is not able to pump enough blood to the body, resulting in a drop in circulating blood volume or pressure, and the release of RAAS. This increases sodium and blood volume but if the volume is in excess of what the heart can handle, it leads to congestion and congestive heart failure. When congestion occurs, treatment is targeted at reducing the blood fluid volume. Since water is attracted to sodium, low sodium diets may reduce the amount of water retained by the body. ACE-inhibitors, which block the RAAS, encourage sodium and water excretion by the kidneys.

But low sodium intake causes the body to activate the RAAS. In addition to the impact on sodium and water balance, aldosterone promotes inflammation and oxidative stress. Excessive restriction of sodium is actually detrimental in heart failure, causing an increase in mortality in human patients and upregulating RAAS in dogs and cats.[2] Further, pharmaceutical care in CHF combined with low sodium intake can result in other electrolyte abnormalities, such as hyperkalemia.[3] Avoiding excessively high or low sodium intake seems a reasonable approach, although further research is needed to define "excess".

Potassium is a key intracellular electrolyte. Potassium and sodium exchange across cell membranes as part of active transport systems. In addition, potassium is necessary for normal muscle function, including cardiac muscle.

In the face of congestive heart failure, the most common diuretic used (furosemide) promotes excretion of sodium and potassium, and can lead to potassium deficiency. For this reason, supplementation with potassium was considered important. However, newer diuretics (e.g. spironolactone) as well as ACE-inhibitors spare potassium, so it is not excreted. Supplementation in this case can contribute to excess potassium. Currently, restriction or supplementation is recommended only if an individual patient shows evidence of excess or deficiency.[4]

Magnesium (Mg)

Although Mg is an essential mineral in the body, less than 1% is in plasma and the concentrations are tightly regulated to maintain a constant Mg concentration. Because of this, it is difficult to diagnose a deficiency of Mg, especially a subclinical deficiency, based on serum testing.[5] In veterinary medicine, although hypomagnesemia is not uncommon in critical care and diseased patients, the role of magnesium for dogs has not been thoroughly studied.[6-8]

Magnesium serves as a co-factor in hundreds of enzymes in the body, and has a role in glucose and energy metabolism, protein production, ATP synthesis and utilization, and in cardiovascular function.[5,9,10] Magnesium modulates vascular smooth muscle tone and endothelial functions to enhance vasodilation, which helps reduce blood pressure.9 Within the heart, Mg is critical for electrolyte transmembrane flux, so is required for normal cardiac electrophysiology and function.[11] Under ischemic conditions, Mg protects the heart through several mechanisms including serving as a Ca ion antagonist; protecting ATP and energy-dependent processes; reducing myocardial oxygen demand and consumption; and, protecting the myocardium from oxidative damage.[9] Magnesium stabilizes cardiac membranes and modulates myocardial excitability to treat or prevent cardiac arrhythmias.[9]
In humans, there is a significant association between low Mg intake or low serum Mg and cardiovascular diseases or heart failure.[10,11] Each 0.2mmol increase in serum Mg was associated with a 30% lower risk for cardiovascular disease in a meta-analysis of human clinical trials.[11] Short-term Mg restriction induced cardiac arrhythmias which were corrected by Mg supplementation.[11]

In human diabetic patients, low Mg is a significant contributor to mitral valve calcification and cardiovascular mortality.[12] Mitral valve prolapse is strongly associated with Mg deficiency in humans, as well as in Cavalier King Charles Spaniel dogs,[13,14] although a causal role has not been confirmed.

In addition to direct effects on cardiovascular functions, magnesium helps reduce inflammation and oxidative stress.[5,15] Inflammation plays an important role in the pathogenesis of heart failure, and inflammatory cytokines are elevated in the blood of dogs with MMVD.[16] In humans and animals, hypomagnesemia is associated with increased levels of inflammatory mediators such as interleukin (IL)-1β, tumor necrosis factor (TNF)-α and C-reactive protein, and with increased production of reactive oxygen species (ROS).[5] There is also evidence that Mg reduces oxidative stress by scavenging free radicals, through increased production of glutathione and superoxide dismutase, and decreased nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activity. [5] In a rat model of coronary heart disease, Mg supplementation not only reduced oxidative stress but reduced hyperlipidemia and enhanced mitral valve and cardiac function.[15]

Given the sum of the evidence, it is clear that provision of adequate dietary Mg is important for cardiac health in humans, and also likely in dogs.

Taurine and Carnitine

Taurine is a sulfur-containing beta-amino acid that can be produced within the body from the sulfur amino acids methionine and/or cysteine. In dogs, endogenous production is normally adequate to maintain health, so long as the precursor amino acids are available in sufficient supply. In recent years, however, some exceptions to this have been reported.[17,18]

Taurine serves many roles in the body. Perhaps best known is the binding of bile acids. Both dogs and cats bind bile acids exclusively with taurine, which results in significant quantities of taurine being excreted from the body. Taurine also is involved with numerous metabolic processes, including antioxidation, retinal photoreceptor activity, stabilization of neural membranes, reduction in platelet aggregation, and others, as well as normal myocardial function.[17]

A deficiency of taurine can cause dilated cardiomyopathy (DCM) in both cats and dogs.[17-19] One potential mechanism for this is the role taurine plays in cardiac energy metabolism and oxidative phosphorylation. Taurine deficiency reduces the functionality of the mitochondrial respiratory chain, leading to decreased ATP production.[20]

Carnitine is an amino acid derivative that is found abundantly in meat-based diets or produced endogenously from the amino acids lysine and methionine. Carnitine serves a key role in fat metabolism by transporting long-chain fatty acids across the inner mitochondrial membrane. Here, the fatty acids undergo beta-oxidation and further metabolism to generate ATP. Fatty acids can yield up to 90% of the ATP produced in healthy cardiac mitochondria, so having adequate, active carnitine

is critical to normal cardiac function.

Carnitine supplementation has been recommended for dogs with heart disease for many years. However, the evidence to support this practice is very weak. Several Boxer dogs with DCM and low myocardial carnitine showed improvement with supplementation.[21] No controlled trials have been done to document a benefit from carnitine supplementation alone in dogs but a study in American Cocker Spaniels showed benefits from a combination of carnitine and taurine.[22] It is suggested that between 17% and 60% of dogs with DCM have a myocardial carnitine deficiency.[17] This suggests that dogs with DCM may benefit from carnitine but it also implies that there is not a problem with making carnitine, rather, the problem lies in getting carnitine into the heart muscle.

Use of carnitine precursors appears to be a good option for increasing serum carnitine, and may have an advantage over supplementing preformed carnitine. There is growing evidence that TMAO (tri methyl amine N-oxide), a by-product from carnitine, can be associated with increased cardiac morbidity and mortality in people.[23] This compound is formed from carnitine: the gut microflora break down carnitine to form trimethylamine which is subsequently converted in the liver to form TMAO. Supplementation with carnitine led to increased plasma TMAO in mice and humans.[24,25] Dogs with congestive heart failure secondary to MMVD had significantly greater plasma concentrations of both carnitine and TMAO, compared to healthy dogs, or dogs with asymptomatic MMVD.[23] However, at this time there is no data on causality versus simple association with disease, nor on the impact of supplementation with carnitine-precursors on TMAO production.

Omega-3 polyunsaturated fatty acids (n3 PUFA)

The long chain n3 PUFA, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), help to reduce inflammatory mediators known to be associated with heart failure, such as TNFα, IL-1β and -6, and others, as well as reducing oxidative stress.[26,27] The n3 PUFAs also lead to increased production of the anti-inflammatory mediators resolvins and protectins. Other benefits associated with n3 PUFAs are reduced cardiac arrhythmias, reduced cardiac remodeling and dysfunction, and reduced blood pressure.[26,28]

In addition to direct cardiovascular benefits, there is some evidence that the anti-inflammatory effects of fish oil rich in EPA and DHA might help reduce the risk for cachexia, which is a common complication of advanced heart disease in dogs,[26] as discussed below.

Antioxidants

ROS are unstable molecules with a singlet electron that can initiate a cascade of oxidative damage to cellular lipids and proteins, destroying them and even destroying DNA. Although ROS are formed naturally during normal metabolism, the healthy body has abundant anti-oxidant metabolites that neutralize the ROS.

Oxidative stress occurs when ROS exceed the available antioxidants. This can happen in disease, such as heart disease. The mitochondria in disease hearts become less efficient and produce more ROS.[29] Coupled with a shortage of antioxidants, this can contribute to oxidative stress.

There are numerous antioxidants, including vitamin E, vitamin C, and many proteins produced in the body to fight ROS. Dietary supplementation can include the antioxidant vitamins, but also precursors to support endogenous production of antioxidant compounds such as gluthathione, superoxide dismutase, nitric oxide and others. In addition, providing alternative energy sources and mitochondrial support can reduce ROS production and decrease oxidative stress.[30]

Energy and alternate energy sources

Based on transcriptomic and metabolomics analyses, many changes occur in dogs with MMVD, including antioxidant functions, nitric oxide signaling, extracellular matrix homeostasis and energy metabolism.[31] The heart itself uses a considerable amount of energy. Under normal conditions, up to 90% of ATP generated in the adult mammalian heart comes from fatty acid oxidation.[32] However, in the face of heart disease, the cardiac mitochondria become less efficient and begin to rely on alternate energy sources. Ketone bodies and fatty acids (MCFAs) from medium chain triglycerides (MCTs) can provide that energy source.

Compared to LCFAs, MCFAs increase the oxidative capacity of muscle mitochondria while also decreasing production of ROS.[33] The increased oxidative capacity was demonstrated through upregulated expression of complex I – V subunits of the electron transport chain in MCFA fed mice, whereas superoxide dismutase 2 was downregulated. Concurrently, markers of

oxidative stress were decreased in the MCFA-fed mice compared to those fed LCFAs.[33] In addition to protection from oxidative stress, MCFAs are relatively anti-inflammatory compared to LCFAs. In one in vitro study using intestinal cells, octanoic acid (C8:0) reduced IL-8 secretion by over 3-fold compared to oleic acid (C18:1).[34] Given that IL-8 expression is progressively increased in dogs with advancing MMVD,16 this effect from MCTs may be beneficial in dogs with MMVD.

Obesity and Cachexia in heart disease

Obesity is not typically considered a risk factor for developing heart failure. However, obesity can compromise cardiopulmonary function in dogs.[35,36] Therefore, it may be considered a confounding factor that can make clinical signs of heart disease worse. For dogs with mild heart disease, or those at risk for developing heart failure, maintaining a healthy body weight and body condition score of 5 to 6/9 is important. In the face of existing heart disease (not failure), gradual weight loss should be encouraged.

Although many dogs may be overweight when diagnosed with heart disease, weight loss also is common.[37,38] In one study, cardiac cachexia – defined as a loss of muscle condition - occurred in about 50% of dogs with advanced heart failure and was associated with shorter survival times.[38] Although the exact cause of this phenomenon is not known, it is thought that the inflammatory mediators present in increased amounts in heart disease are a contributing factor. Poor appetite, alterations in nutrient absorption, and altered metabolism all may also contribute.[39]

Although diet alone cannot prevent cachexia, consuming supplemental protein and calories may help offset or slow the tissue loss associated with cachexia.[40] Inadequate intake of either can make cachexia worse. In one study of dogs with heart failure, the group that gained weight during the study had longer survival compared to other dogs.[37] As heart failure progresses, many dogs have reduced appetites, due in part to the effect of medications and in part to the effect of disease. To compensate, feeding a nutrient dense, highly digestible and highly palatable diet is often recommended. In addition, nutrients that can reduce the inflammation, such as n-3 PUFA might be helpful.[26,39] These may also provide a direct benefit for reducing the loss of muscle mass. In in vitro and human studies, n-3 PUFA, especially EPA, increase endogenous protein synthesis and reduce protein breakdown.[41,42] Decreased muscle loss was observed in dogs with CHF receiving n-3 PUFA supplements.[37]

Diet for pre-clinical heart disease

The most common canine heart disease is Myomatous Mitral Valve Disease (MMVD). Although many dogs with MMVD live out their lives without developing heart failure, about 30% of dogs will progress to more advanced stages or die from heart failure.[43]

MMVD is associated with numerous metabolic changes that may be a cause or consequence of this disease. Perhaps most critical is altered mitochondrial energy metabolism, with compromised fatty acid oxidation, and an increased reliance on anaerobic glucose metabolism.[31] Concurrent with this are increases in oxidative stress and markers of inflammation.

Recent research in asymptomatic dogs with MMVD showed that addressing these changes through dietary modification resulted in a slowing of MMVD progression.[30,32] The study was performed in 19 small breed dogs with MMVD stages B1 and B2.[32] A diet containing a "cardiac protection blend" (CPB) of MCTs, fish oil, antioxidants, Mg, taurine, and carnitine precursors was fed to half the dogs, while a control diet was fed to the remaining dogs. Dogs were followed for 6 months. Despite the fact that MMVD is generally a slowly progressive condition, dogs in the control group had an average increase of 10% over baseline in left atrial diameter (LAD) and left atrial to aortic root ratio (LA/Ao), based on echocardiography at 6 months. The CPB-fed dogs averaged a 3% decrease over the same period. Twenty percent of dogs were in Stage B2 at the beginning of the study, but this increased to 50% in the control dogs by the end of the study, whereas there was no progression in the CPB-fed dogs. Consistent with this, there was an overall decrease in mitral regurgitation in the CPB-fed dogs and a slight worsening, overall, in the control dogs. The study showed it is possible to slow progression of MMVD through dietary management, at least in pre-clinical dogs.

Summary

Dogs with heart disease or heart failure, like all dogs, need complete and balanced nutrition. Therapeutic diets must meet the nutritional needs of the patient, while also addressing the key nutrients appropriate to health management. For dogs with heart disease, the key nutrients extend far beyond sodium. Nutrients that aid mitochondrial function, that support energy metabolism, address oxidative stress and inflammation, and promote normal sinus rhythm and maintain myocardial function all are important for heart health. For dogs at risk of developing cardiac cachexia, assuring adequate intake of calories and protein are key, while also addressing inflammation through nutrients such as EPA and DHA. Even dogs with sub-clinical MMVD have disturbed metabolic functions. Addressing these through a diet enriched with alternative energy sources (MCTs), carnitine precursors, taurine, magnesium and antioxidants helps to address these changes and might slow the progression of MMVD.

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Review on Feline cardiomyopathy

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Luca graduated with honours in 1992 from the University of Bologna. After 3 years research in endocrinology at the BBSRC Institute in Cambridge, he was awarded his PhD in 1996.

Following 3 years as Assistant Professor at Padua University, Luca moved to Bristol University, where he taught cardio-respiratory medicine of the dog and cat for 7 years. In 2005-2007, he was Associate Professor in Cardiology at the University of Minnesota. He returned to the UK in 2008 working in various referral institutions, as well as offering telemedicine service and post-graduate teaching. He obtained the RCVS certificate in cardiology in 2001, the certificate in Teaching & Learning in Higher Education in 2002, the ECVIM diploma (cardiology) in 2004 and a Certificate in Business & Professional Studies in 2011. In 2019, Luca was awarded a Fellowship of the Royal College of Veterinary Surgeons for his Meritorious Contributions to Clinical Practice. Luca has also vastly contributed to the veterinary literature with articles, abstracts, and book chapters, including the chapter on coughing in the latest edition of Ettinger's textbook of Internal Medicine.

He also acted as chairman of the ECVIM examination committee and was member of the RCVS examination board and BSAVA congress committee. Luca is a regular speaker worldwide. His main professional interests include feline cardiology, exercise physiology, as well as investigation and management of syncope and coughing.

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Review on Feline cardiomyopathy

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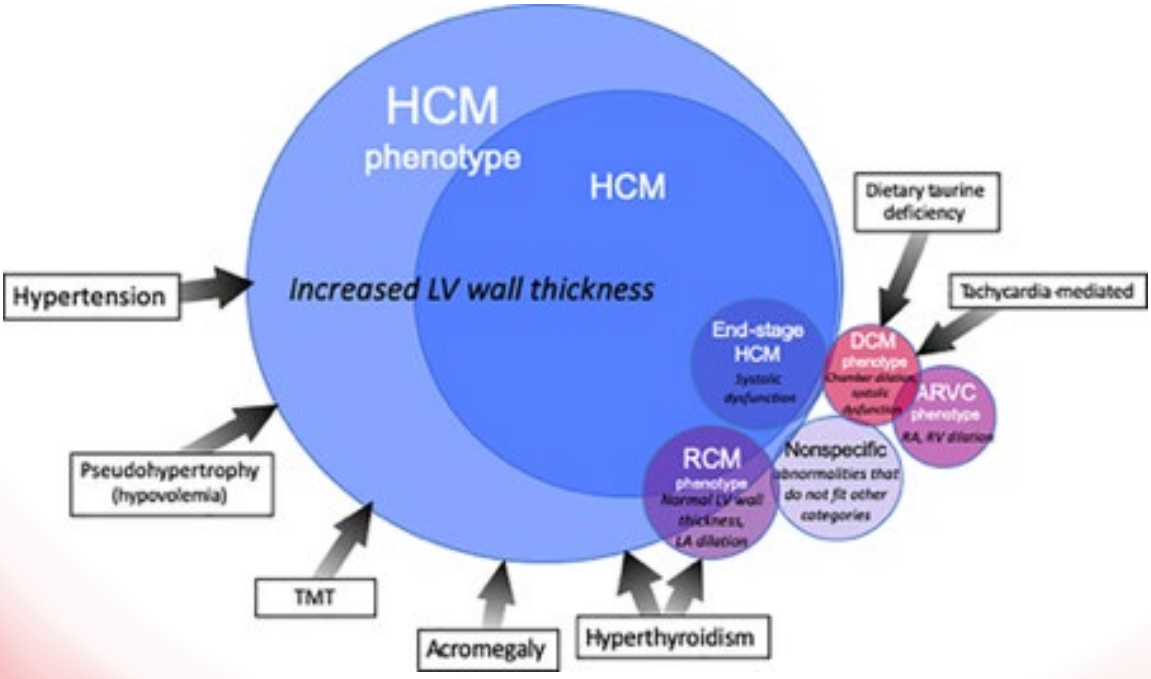
Introduction

Cardiomyopathies are common in cats and they represent a common cause of death in this species. A new consensus statement of the American College of Veterinary Internal Medicine (ACVIM) on feline cardiomyopathy proposed an updated classification based on echocardiographic phenotype and provides recommendations for the diagnostic approach and management of cats with myocardial disease. The ACVIM consensus proposes an adaptation of the European Society of Cardiology (ESC) classification for use in cats, as this scheme is based on phenotypic features without assumptions on underlying causes, and it focuses on a clinical, rather than a genetic approach. The traditional classification includes the following forms of CM: hypertrophic cardiomyopathy (HCM), restrictive cardiomyopathy (RCM), dilated cardiomyopathy (DCM), unclassified cardiomyopathy (UCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC). The ACVIM consensus retained all the above categories, with the exception of UCM.

The concept of "phenotype"

The proposed ACVIM cardiomyopathy classification does not define specific disease entities but describes cardiac morpho-functional categories or "phenotypes". For example, a cat with left ventricular hypertrophy and hyperthyroidism would be classified as an "HCM phenotype" in conjunction with hyperthyroidism. Some cats have myocardial disease that does not fit well into any category. However, rather than describing these cases as having "unclassified cardiomyopathy (UCM)", according to the proposed new ACVIM classification, these cats should be described as having cardiomyopathy with a "non-specific phenotype". This term should always be accompanied by a description of the morphologic and functional features to characterise the phenotype in more detail.



The concept of "staging"

For describing the clinical impact of cardiomyopathy on affected cats, the staging system below has been adapted from the AHA and ACVIM heart disease staging systems with the aim of providing an objective framework for prognostication and therapeutic decisions.

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, with an estimated prevalence of approximately 15% in the general cat population. The prevalence might be as high as 30% in older cats, even when those with hypertension and hyperthyroidism are excluded. 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).

Primary HCM is an inheritable condition in people with eleven mutated sarcomeric genes presently associated with the disease. Familial HCM has also been described in Maine coon and Ragdolls cats with an autosomal dominant mode of inheritance. A similar inheritance may also be present in other pedigrees, such British shorthair breeds. A causative mutation for HCM has been identified in the sarcomeric gene for the cardiac myosin binding protein C (MYBPC3) both in Maine coons and 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), hypersomatotropism and myocarditis. LV concentric hypertrophy commonly observed in hyperthyroid people presents less commonly in feline hyperthyroidism.

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. 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

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).

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. Cats with ARVC may also present with arrhythmias.

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.

Prognosis

Prognosis varies depending on different published studies. Markers of increased risk of CHF or ATE include presence of a gallop sound or arrhythmia on physical examination, moderate to severe LA dilation, reduced LA fractional shortening (LA FS%), extreme LV hypertrophy, reduced LV systolic function, spontaneous echo-contrast or intracardiac thrombus, regional wall thinning with hypokinesis, and a restrictive diastolic filling pattern.

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