Emergent Heart Failure in Dogs and Cats: Pathophysiology, Diagnosis, & Treatment

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Curriculum Vitae

Education

- Texas A&M University - B.S. Biomedical Sciences, 2013
- UC Davis - Doctor of Veterinary Medicine, 2018

Prior Publications

- Biomechanical evaluation of two plating configurations for fixation of a simple transverse caudal mandibular fracture model in cats. Greiner, et al. AJVR 2017

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Curriculum Vitae

Specialty Training & Employment

- VCA Loomis Basin, Loomis, Ca - Rotating Internship, 2018-19
- BluePearl Stone Oak, San Antonio, Tx - Surgery Internship, 2019-20
- Mississippi State University, Starkville, Ms - Surgery Internship, 2020-21
- BluePearl Stone Oak, San Antonio, Tx - ER Associate, 2021-23
- Cape Cod Veterinary Specialists, Emergency & Critical Care Residency, 2023-present

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Outline

1. **Relevant Anatomy**
2. Pathophysiology Review
3. Diagnosis
4. Canine Heart Disease
5. Feline Heart Disease
6. Disease Staging
7. Treatment
8. Prognosis

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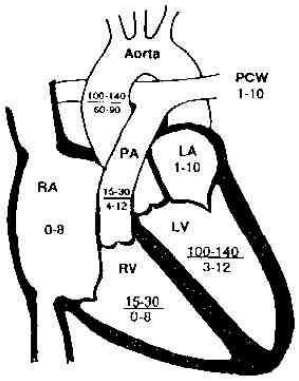
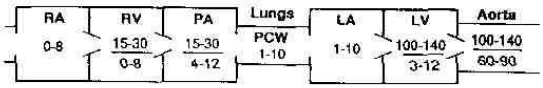
Relevant Anatomy



- Venous filling pressure (preload)
  - Left atria: pulmonary venous pressure, pulmonary capillary wedge pressure
  - Right atria: central venous pressure



Brown University, Normal Circulation and Congestive Heart Failure[1]

*Note: Diagram is of a human heart

1. Normal blood flow vena cava -> right atrium -> right ventricle -> pulmonary artery -> pulmonary parenchyma (alveoli) -> pulmonary veins -> left atrium -> left ventricle -> aorta
   - Although a single organ with 4 chambers, the heart can be very accurately described as two pumps in series: the right heart pumping blood into the pulmonary circulation and the left heart pumping blood into the peripheral circulation
2. Due to contiguous vessels without valves: Right atrial pressure = central venous pressure; left atrial pressure = pulmonary venous pressure = pulmonary capillary wedge pressure

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Pathophysiology

Definitions of Heart Failure

1. Heart's inability to maintain adequate perfusion to meet the metabolic demands of peripheral tissues
   a. Aka: Forward heart failure, low-output heart failure
2. Heart's inability to maintain adequate perfusion without the presence of increased venous filling pressures
   a. Aka: backward heart failure, ***congestive heart failure***

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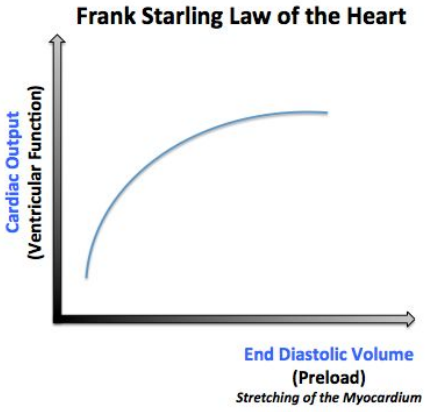
1. Heart failure is a clinical syndrome caused by a variety of underlying cardiac abnormalities
   a. Useful clinical syndrome as treatment of the syndrome is the same regardless of cause
2. Low-output heart failure: clinical signs and manifestations
   a. Syncope
   b. Weakness
   c. Activity intolerance
   d. Hypotension
   e. Hypothermia
   f. Obtundation
   g. Lactic acidosis
   h. Pre-renal azotemia with oligiuria
2. Congestive heart failure: clinical signs and manifestations
   a. Cough
   b. Dyspnea
   c. Pulmonary edema
   d. Ascites
   e. Pleural effusion
   f. Pericardial effusion
   g. Peripheral edema (rare in veterinary medicine)

1. Depending on the disease process, either/both manifestations of failure can occur in either/both sides of the heart, i.e. right ventricular vs left ventricular vs biventricular failure

Pathophysiology

Frank-Starling Law of the Heart

"The energy of contraction [...] is a function of the length of the muscles fibers" - Ernest Starling, 1915



https://www.wikidoc.org/index.php/Pressure_volume_diagram

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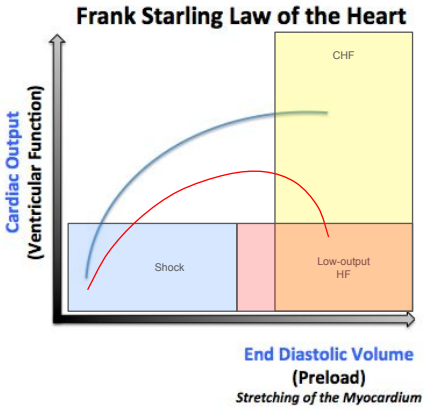
1. A clinically succinct summary: Cardiac output increases, to a certain degree, with increases in preload (aka: ventricle filling pressure, venous filling pressures, venous return)
    - This is an intrinsic quality of myocardiocytes, allowing for beat to beat alterations in systolic function based on venous return, resulting in stable cardiac output.

Pathophysiology

Frank-Starling Law of the Heart

- Extreme elevations in preload/venous filling pressure:
  1. Decrease cardiac output
  2. Promotes fluid extravasation at the preceding capillary bed



https://www.wikidoc.org/index.php/Pressure_volume_diagram + additions by Dr. Greiner

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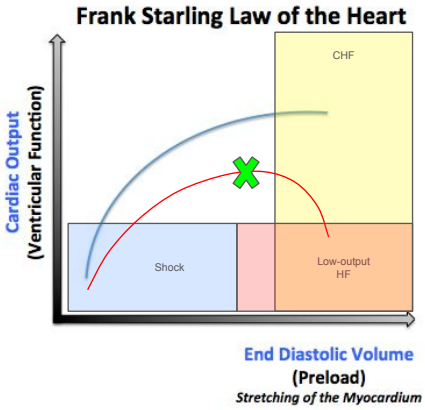
1. Note: stereotypical decreased contractility/high afterload curve in red compared to healthy heart in blue
2. With sufficiently elevated preload, two effects can be noted
   - A decrease in cardiac output due to sarcomere length exceeding the optimal length for contraction.
   - The elevation in venous filling pressure (>20mmHg central venous pressure, >25mmHg pulmonary venous pressure) results in hydrostatic forces supporting fluid extravasation at the preceding capillary bed and subsequent tissue edema/effusion:
     - Pulmonary edema if left atrial/pulmonary capillary wedge/pulmonary venous pressure excessive.
     - Ascites if right atrial/central venous pressure is excessive.
3. Low-output heart failure is a type of shock where preload is adequate but contractility is insufficient to provide an adequately perfusing cardiac output.

Pathophysiology

Frank-Starling Law of the Heart

- How do we address heart failure?
  - Diuresis
  - Positive inotropy
  - Arterial vasodilation
  - Venous vasodilation



https://www.wikidoc.org/index.php/Pressure_volume_diagram + additions by Dr. Greiner

1. Diuresis
   - Reduce preload, moving cardiac output to the left along the curve
2. Positive inotropes
   - Shift entire curve upwards
3. Arterial vasodilators/afterload reduction
   - Shifts entire curve upwards same as positive inotropes
4. Venous vasodilators
   - Shifts curve leftward

Pathophysiology

Neurohormonal Response to Heart Failure

- Renin-Angiotensin-Aldosterone System (RAAS)
  - Deficits in renal perfusion stimulate renin release and culminates in excess AngII and aldosterone activity
- Sympathetic nervous system
  - The typical increase in sympathetic tone in response to decreased cardiac output becomes chronic

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1. Renin-Angiotensin-Aldosterone system
   - Deficits in renal perfusion stimulate renin release and culminates in the excessive activity of AngII and aldosterone
     - AngII
       - Vasoconstriction/afterload elevation increases myocardial oxygen demand
       - Directly promotes myocardial hypertrophy, necrosis/apoptosis, and fibrosis
       - Arrhythmogenic
       - Increased ROS
       - Increased thirst
     - Aldosterone
       - Water and Na^+ retention, K^+ wasting
       - Directly promotes myocardial hypertrophy, necrosis/apoptosis, and fibrosis
       - Systemic hypertension
       - Arrhythmogenic
       - Increased ROS
     - These deleterious effects on the cardiovascular system promotes the negative progression of heart disease, especially after the development of heart failure

1. Sympathetic nervous system
    - The typical increase in sympathetic tone in response to decreased cardiac output becomes excessively prolonged in cases of heart failure.
        - Chronic SNS activity secondary to heart failure results in increased myocardial oxygen demand, hypertrophy, fibrosis, and down-regulation of adrenergic receptors

Pathophysiology

Neurohormonal Response to Heart Failure

- Vasopressin
  - Decreased cardiac output and increased AngII activity stimulate non-osmotic vasopressin release
- Endothelin
  - Typically mediates local vasoconstrictive activity
  - Myocardiocytes in heart failure can synthesize and release Endothelin-1 resulting in systemic activity

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1. Vasopressin system
   - Decreasing cardiac output stimulates non-osmotic AVP release via reduced baroreceptor stimuli
   - Increased AngII activity is also a direct stimulus for non-osmotic AVP release
   - This AVP release supersedes the typical negative feedback of hypo-osmolality, this mechanism in health is used to restore blood volume following acute loss
   - AVP is significantly increased in patients with CHF compared to healthy patients
   - Hyponatremia, secondary to the non-osmotic AVP release, is a negative prognostic indicator for survival in CHF dogs
   - AVP stimulates V1 and V2 receptors: excessive V1 increases SVR (both arterial and venous constriction), direct cardiac remodeling/LV hypertrophy; excessive V2 activity results in water retention, blood volume expansion, increased preload, and dilutional hyponatremia/hypoosmolality
   - V1a/V2 receptor antagonism is currently under investigation in human medicine for its aquaresis effects as an alternative for loop-diuretic therapy + cardioprotective effects
2. Endothelin system

- Endothelin 1, among other isoforms, are typically present for local vasoconstrictive activity in a paracrine manner from endothelial cells within their vascular beds of action
- Under pathophysiologic conditions such as heart failure, endothelin 1 can be synthesized and released by myocardiocytes, resulting in systemic circulation and activity
- In human medicine, SGLT-2 inhibitors (re: the “gliflozin”s, i.e. Bexacat) are thought to inhibit ET 1 activity as part of their mechanism for reducing progression of chronic renal disease and heart failure.

Pathophysiology

Neurohormonal Response to Heart Failure

- Natriuretic peptide system
  - Atrial natriuretic peptide (ANP) and B-type natriuretic peptide (BNP) are released from the myocardium in response to cardiac wall stretch
  - Counter-regulatory to RAAS, sympathetic activity, vasopressin

1. Natriuretic peptide system
   - Atrial natriuretic peptide (ANP) and B-type natriuretic peptide (BNP) are released from the myocardium (atrium/ventricle respectively) in response to cardiac wall stretch.
     - Stored as a prohormone, proteolytically cleaved into the active hormone (ANP/BNP) and an inactive peptide (NT-proANP/NT-proBNP)
       - The inactive peptide is typically more stable in vitro and used for diagnostic purposes
   - Counter-regulatory properties to RAAS, SNS, and vasopressin
     - Antagonized renin release, induces natriuresis with diuresis
     - Vasodilation in direct opposite to AngII and vasopressin
     - Decreases aldosterone synthesis in the adrenal cortex
     - Decreases sympathetic tone
     - Direct inhibition of cardiac remodeling via reduction of myocardial fibrosis and hypertrophy
   - In heart failure, despite a substantial increase in ANP/BNP release, the underlying cardiac disease and progressive maladaptive cardiac remodeling effects of the RAAS, SNS, endothelin, and vasopressin systems exceed this counter-regulatory effect.

- BNP receptor agonism is currently under investigation for its use in acute heart failure in humans

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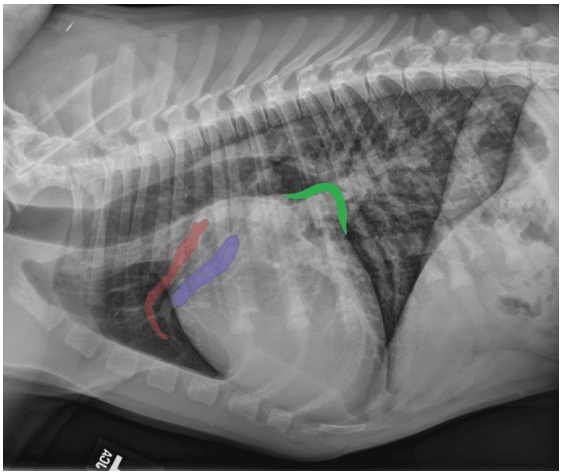
Diagnosis

Imaging - Thoracic Radiographs



- Left-sided heart failure
  - Left-side cardiomegaly
  - Pulmonary venous distension
  - Pulmonary interstitial edema
  - Alveolar edema
  - Pleural effusion (cats >>> dogs)

Today's Veterinary Practice, Thoracic Radiology in the Diagnosis of Congenital Heart Disease in Dogs. E. Huguet, R. Cole, C Berry. October 2022.

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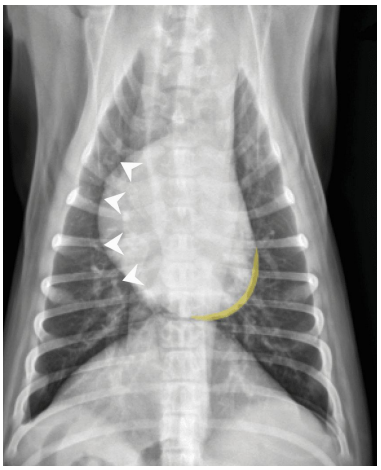
1. Thoracic Radiographs
   - Left-sided heart failure
     - Left-sided cardiomegaly* (may be subtle or minimal change with acute cardiac disease/arrhythmia origin)
     - Pulmonary venous distension
       - Especially perihilar, near insertion into left atrium
       - Pulmonary vein diameter > corresponding pulmonary artery diameter
     - Interstitial edema
       - Diffuse increased radiopacity of the lungs
       - Pulmonary vascular margins are indistinct due to perivascular edema
       - Prominent peribronchial markings due to peribronchial edema
     - Alveolar edema
       - Air bronchogram
       - In cats: can be well marginated, "cloud like"
       - In dogs: can be asymmetric, right > left
       - Completely obscures pulmonary vasculature
       - Greatest opacity in the perihilar regions, fading to periphery

- Pleural effusion
  - Particularly cats but severe left-sided or biventricular failure in dogs
  - In cats, pleural effusion is due to CHF in 53.4% cases. Radiographic cardiomegaly + pleural effusion has a 90% positive predictive value for CHF.[12]

Diagnosis

Imaging - Thoracic Radiographs



- Right-sided heart failure
  - Right-side cardiomegaly
  - Hepatomegaly
  - Ascites
  - Pleural effusion

Today's Veterinary Practice, Thoracic Radiology in the Diagnosis of Congenital Heart Disease in Dogs. E. Huguet, R. Cole, C Berry. October 2022.

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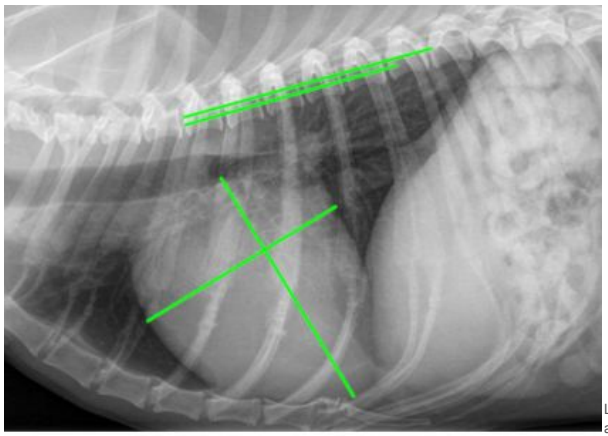
1. Thoracic Radiographs
   - Right-sided heart failure
     - Right-sided cardiomegaly* (may be subtle or minimal change with acute cardiac disease/arrhythmia origin) - correlate to clinical signs
     - Hepatomegaly
     - Ascites
     - Pleural effusion: interlobar pleural fissures, loss of cardiac silhouette, separation of visceral pleura margin from thoracic wall

Diagnosis

Imaging - Thoracic Radiographs, VHS



- Vertebral heart scoring
  - Right lateral view
  - Long axis: Ventral border of left mainstem bronchus to ventral cardiac apex
  - Short axis: Perpendicular to long axis, originating from the caudal cardiac silhouette and ventral caudal vena cava intersection
  - Cranial T4 edge

Levicar, C., et al. Comparison of different radiographic scores with associated echocardiographic measurements and prediction of heart enlargement in dogs with and without myxomatous mitral valve disease. *J Vet Cardiol* 2022; 44, 1-12

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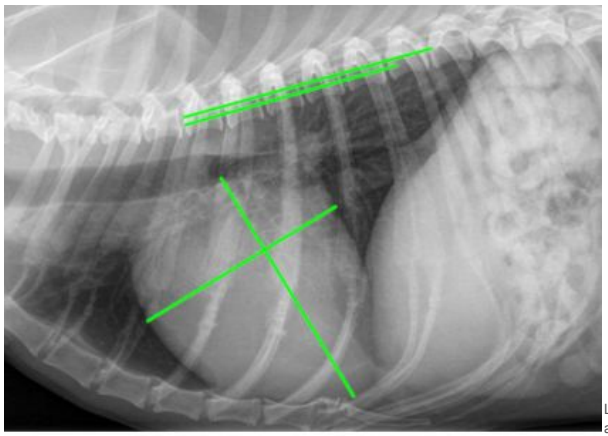
1. Vertebral heart scoring (VHS)
   - Objective measurement of generalized heart size standardized to the thoracic vertebral length
     - Right lateral thoracic view
     - Long axis: Ventral border of the left main stem bronchus to most distant ventral contour of the cardiac apex
     - Short axis: Maximal axis perpendicular to the long axis within the central 1/3rd of the cardiac silhouette
       - More recent studies have standardized the short axis measure to be a perpendicular line to the long axis originating from the intersection of the caudal cardiac silhouette and the ventral border of the caudal vena cava
     - Measured from the cranial edge of T4, vertebral length estimated to nearest 0.1 vertebrae for each axis, summation of length = VHS

Diagnosis

Imaging - Thoracic Radiographs, VHS



- Dogs
  - ACVIM MMVD Stage B2
  - VHS ≥ 11.5 in the absence of echocardiography
  - VHS ≥ 10.5 with concurrent echocardiography measurements supportive of Stage B2

Levicar, C., et al. Comparison of different radiographic scores with associated echocardiographic measurements and prediction of heart enlargement in dogs with and without myxomatous mitral valve disease. *J Vet Cardiol* 2022; 44, 1-12

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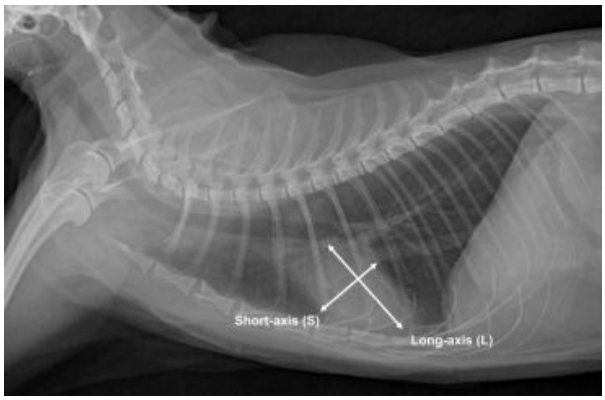
1. Vertebral heart scoring (VHS)
   - Dogs:
   - ACVIM MMVD Stage B2
     - VHS ≥ 11.5 in the absence of echocardiography
     - VHS ≥ 10.5 with concurrent echocardiography measurements supportive of Stage B2
     - Significant breed variability is present
     - VHS will significantly increase in size in the months before first onset of CHF, with a ΔVHS/month ≥ 0.08 in CKCS representing 15-fold increased likelihood of CHF within 1 year
   - In dogs with respiratory signs, VHS has a poor specificity for CHF until it is severe, VHS >12.2 required to achieve 91.5% specific (34% specific at VHS >10.6)

Diagnosis

Imaging - Thoracic Radiographs, VHS



Kim, S., et al. Radiographic findings of cardiopulmonary structures can predict hypertrophic cardiomyopathy and congestive heart failure in cats. *AJVR* 2023; 84:9.

- Cats
  - VHS > 8.0 has high sensitivity for underlying cardiac disease
  - VHS > 9.3 has high specificity for underlying cardiac disease

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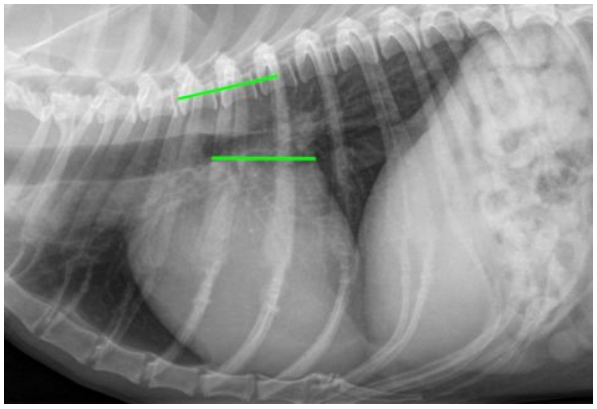
1. Vertebral heart scoring (VHS)
   - Cats
   - VHS >8.0 has a high sensitivity for underlying cardiac disease, >9.3 for high specificity for cardiac disease[18]
   - In cats, VHS has been documented to be significantly increased in HCM cats compared to normal cats but there is no appreciable difference in VHS between HCM cats with and without CHF[19]

Diagnosis

Imaging - Thoracic Radiographs, VLAS



- Vertebral Left Atrial Score
  - Ventral carina to the caudal cardiac silhouette and dorsal caudal vena cava intersection
  - Cranial T4 Edge
  - Dogs: Positive correlation between VLAS and LA:Ao
    - VLAS ≥ 3.0 correlates with ACVIM MMVD Stage B2
  - Cats: Does not correlate with LA:Ao

Levicar, C., et al. Comparison of different radiographic scores with associated echocardiographic measurements and prediction of heart enlargement in dogs with and without myxomatous mitral valve disease. *J Vet Cardiol* 2022; 44, 1-12

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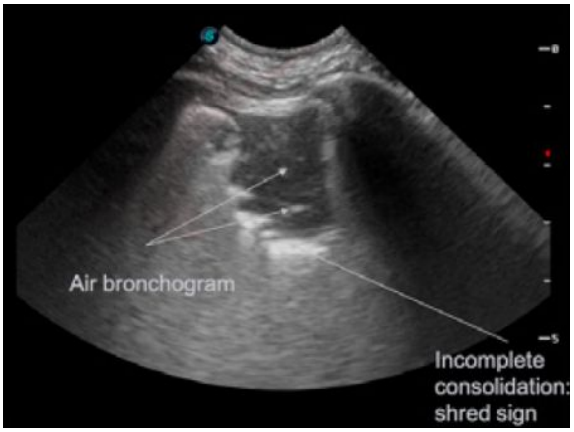
1. Vertebral Left Atrial Score
   - Objective measurement of left atrial size standardized to thoracic vertebrae length
     - Right or left lateral thoracic view
     - Ventral carina to the intersection of the caudal cardiac silhouette with the dorsal caudal vena cava
     - Cranial edge of T4 vertebral body, to the nearest 0.1 vertebra
   - Positive correlation between VLAS and LA:Ao, with a VLAS ≥ 3.0 correlating with MMVD Stage B2
   - As with VHS, no difference between VLAS and patients with or without CHF have been identified, cannot be used for the diagnosis of CHF
   - In cats, VLAS has been shown to NOT correlate with LA:Ao

Diagnosis

Imaging - POCUS



- Pulmonary Edema
  - B-lines
  - Shred sign

Boysen, S., State-of-the-Art Lecture: Advanced Lung Ultrasound: Subpleural Consolidations and Bronchograms. WSAVA Congress Proceedings, 2019.

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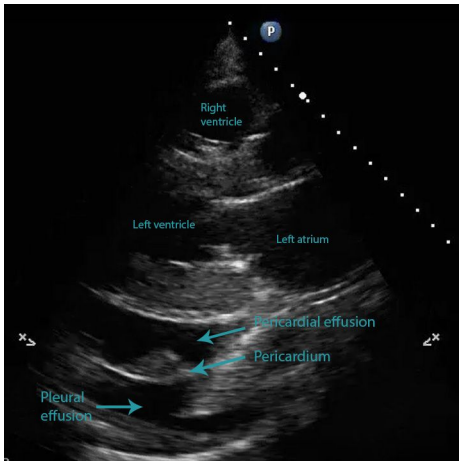
1. Pulmonary edema
   - B-lines, a low number can be present in the absence of lung disease
     - Vertical lines originating from the lung pleural-parietal pleura interface (PP-line), oscillates with the respiratory cycle, extends all the way to the far field (shorter lines are more likely artifact)
     - Shred sign: severe alveolar flooding with lung aeration
       - Deviation of the typical horizontal PP-line with poorly echogenic tissue, focal b-lines within tissue, hyperechoic foci (consistent with air within bronchioles surrounded by fluid filled alveoli)
     - Rule outs: cardiogenic pulmonary edema (CHF), NCPE, acute pneumonia, contusions, hemorrhage (non-trauma/coagulopathic)
     - Lung ultrasound can be falsely negative if the pathology is not located on the periphery

Diagnosis

Imaging - POCUS



- Pleural Effusion
  - Typically anechoic but echogenicity is poorly specific
- Pericardial Effusion
  - Cardiac tamponade

Jutkowitz, L. Managing pericardial effusion in the dog. Animal Ultrasound Association, 2008.

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1. Pleural effusion
   - Best assessed in the most gravity-dependent portion of the thorax, i.e. sternally if in sternal recumbency
   - Loss of the typical hyperechoic PP-line with unorganized fluid, anechoic fluid is more consistent with modified transudate (i.e. CHF) but echogenicity is poorly specific
2. Pericardial effusion
   - Anechoic fluid delineated by the pericardium (hyperechoic curved line in the mid-cranial/ventral thorax with the cardiac champers within)
   - Ensure your depth of field is sufficient to visualize all 4 chambers of the heart or there is possibility of misinterpreting a heart chamber (particularly a dilated right ventricle) as pericardial effusion
   - Cardiac tamponade can be visualized by collapse of the right atrium/ventricle during diastole due to pericardial effusion
     - Cardiac tamponade = right heart failure (inadequate venous filling pressure)
     - Emergent pericardiocentesis is indicated to stabilize patient
   - Prior evaluation of focused cardiac ultrasound in cats has found that pericardial effusion was 100% specific for CHF in cats emergently presenting for dyspnea

Diagnosis

Imaging - Echocardiogram

- Is an echo necessary?
  - "An echocardiogram is not a prerequisite for the diagnosis and management of heart failure." - Dr. Quinn, DACVIM (Cardiology)
  - Signalment, physical exam, and clinical signs are highly predictive of underlying cause of heart failure

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1. Echocardiogram
   - Per Dr. Quinn: "An echocardiogram is not a pre-requisite for the diagnosis and management of heart failure."
     - The diagnosis of left-sided congestive heart failure is made upon interpretation of thoracic radiographs, with echocardiogram input only needed in edge cases.
     - Emergency treatment of heart failure is needed immediately
     - Echocardiograms are performed on stable patients to tell you WHY a patient is in heart failure
     - Patient signalment, physical exam, and clinical signs are highly predictive of underlying cause
       - 55/56 dogs perceived to have MMVD by primary care veterinarian POCUS had a true diagnosis of MMVD on echocardiogram when limited to a study population of >/= 6yo, <20kg, >/= 3/6 left apical systolic murmur, and no hemodynamically significant arrhythmia on exam (HR 60-160bpm)[22]
         - No difference in LA:Ao measurements between pDVMs and cardiologists however all pDVMs had didactic and practical training from those same cardiologists on obtaining LA:Ao ratio

Diagnosis

Imaging - Echocardiogram

- An echocardiogram is required:
    1. Atypically young patients, i.e. suspect congenital heart disease
    2. Refractory to heart failure treatment, i.e. ACVIM Stage D
    3. Owners desiring boarded cardiologist disease management +/- cardiac interventions
    4. Suspected comorbidities, i.e. pulmonary hypertension

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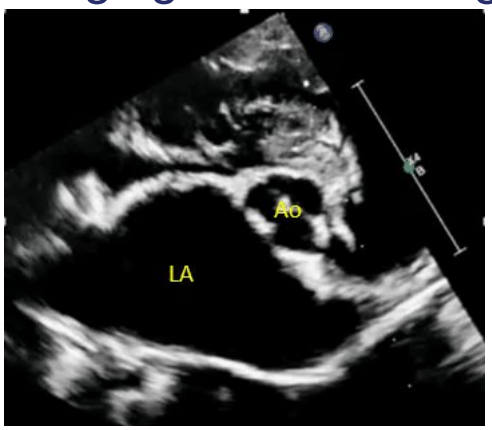
1. Echocardiogram
    - Echocardiography is needed for heart failure management in the following cases:
        - Atypically young patients: possible congenital heart disease
        - Patients refractory to heart failure treatment, i.e. quantify staging to ACVIM Stage D
        - Owners desiring cardiologist oversight of disease management +/- cardiac interventions to halt/reverse disease process
        - Patients with suspected comorbidities such as pulmonary hypertension

Diagnosis

Imaging - Echocardiogram, LA:Ao



Huh, T. Use of Focused Cardiac Ultrasound in the Small Animal Practice. MSPCA-Angell. March 2024

- Left atrial : aortic root ratio
  - Right parasternal short axis view
  - Early diastole
  - Dogs: LA:Ao ≥ 1.6 = ACVIM MMVD Stage B2
  - Cats: LA:Ao ≥ 1.5
    - Even subjective evaluation is correlated with correct diagnosis of cardiac disease

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1. Left atrial:aortic root ratio, LA:Ao
   - Right parasternal short axis view, focus on heart base, early diastole (aortic valve closure)
   - LA:Ao >/= 1.6 = ACVIM MMVD Stage B2 Dogs
   - Shown to be predictive of increased risk of cardiac mortality once LA:Ao > 1.7
   - In dogs, the emergent evaluation of a dyspneic patient found that focused cardiac ultrasound did not significantly improve the correct disease categorization of cardiac vs non-cardiac/respiratory compared to categorization based on history/exam alone however, LA:Ao measurement by ECC clinicians was median 2.1 with echocardiography LA:Ao median of 2.3 +/- 0.5
     - This study did not analyze the agreement between ECC LA:Ao and cardiologist LA:Ao
   - In cats, focused cardiac ultrasound significantly improved correct diagnosis of cardiac vs non-cardiac/respiratory cause of dyspnea
     - Both subjective left atrial evaluation and LA:Ao by ECC clinician were significantly correlated with correct diagnosis
     - LA:Ao >/= 1.5 had a 95% positive predictive agreement with an 86.7% negative predictive agreement
     - LA:Ao >1.5 is 93.9% sensitive and 94.4% specific

- LA:Ao ECC was significantly correlated with LA:Ao Echo

Diagnosis

Biomarkers - NT-proBNP

- Amino-terminal pro-brain natriuretic peptide
- Cats: High sensitivity and specificity for the presence of moderate/severe occult cardiomyopathy
  - SNAP proBNP: High sensitivity, specificity, PPV, NPV in dyspneic cats
  - False positives: hyperthyroidism, systemic hypertension, renal azotemia

CCVS CAPE COD VETERINARY SPECIALISTS

1. NT-proBNP - amino-terminal pro-brain natriuretic peptide
   - The non-active peptide remnant from the release of BNP (c-terminal brain natriuretic peptide)
     - Longest half-life of all the natriuretic peptides
     - Reference lab assay and feline SNAP proBNP available
   - In cats: highly sensitive and specific for the presence of moderate/severe occult cardiomyopathy (all causes), less accurate for evaluation of mild occult cardiomyopathy
     - False positives with hyperthyroidism, systemic hypertension, and renal azotemia
     - For dyspneic cats presenting emergently, SNAP proBNP had a 100% positive predictive agreement with cardiac cause and a 86.7% negative percent agreement
     - Positive SNAP proBNP reported to have a 93.9% specificity and 72.2% sensitivity for dyspneic cats presenting emergently

Diagnosis

Biomarkers - NT-proBNP

- Amino-terminal pro-brain natriuretic peptide
- Dogs: Quantitative assays, benchtop and send-out options
  - Quantitative NT-proBNP is higher in dyspneic dogs with CHF compared to noncardiac cause of dyspnea but sensitivity/specificity is not high for either right or left sided heart disease.

CCVS CAPE COD VETERINARY SPECIALISTS

1. NT-proBNP - amino-terminal pro-brain natriuretic peptide
   - In dogs: There is a benchtop testing unit available for quantitative NT-proBNP
     - Quantitative NT-proBNP is significantly higher in dyspneic dogs with CHF compared to noncardiac respiratory distress cases however sensitivity (81.1%) and specificity (73.1%) is moderate
       - Quantitative NT-proBNP is significantly higher in patients with cardiogenic non-hemorrhagic ascites compared to patients with noncardiogenic non-hemorrhagic ascites however, a sensitivity of 53.8% and a specificity of 85.7% is reported

Diagnosis

Biomarkers - cTnI & cTnT

- Cardiac troponin I & Cardiac troponin T
  - cTnI - Unique to cardiomyocytes and strictly intracellular in health
  - cTnT - false positives due to high homology with non-cardiac/fetal TnT
  - Elevation is non-specific for both primary and secondary cardiac diseases
    - Persistent elevation represents ongoing myocardial injury
    - False positives with renal insufficiency/azotemia

CCVS CAPE COD VETERINARY SPECIALISTS

1. cTnI - Cardiac troponin I & cTnT - Cardiac troponin T
   - Parts of the troponin unit (troponin C + troponin T + troponin I) mediating actin/myosin interaction
     - cTnI is a unique isoform to cardiomyocytes, strictly intracellular therefore, increased cTnI = cardiomyocyte injury (immediate release from cytosol + release from contractile apparatus during breakdown)
       - Not believed to be released during cardiomyocyte apoptosis or normal cell turnover
     - cTnT has high homology with non-cardiac TnT and diseased skeletal muscle can release fetal isoforms with very high homology to cTnT, resulting in false positives
     - There is some interassay variability reported but typically degree of elevation correlate well
     - cTnI is more assayed in veterinary medicine due to the low incidence of acute myocardial infarction (AMI) in our patient population (cTnT is typically assessed in humans due to its diagnostic/prognostic qualities related to AMI)
   - Non-specific elevation occurs in response to both primary cardiac disease (myocarditis, cardiac hemangiosarcoma, ARVC, etc) as well as secondary myocardial injury from critical illness (parvoviral enteritis,

- SIRS/sepsis, pancreatitis, Leptospirosis, GDV, envenomation, etc)
  - Persistent elevation or progressive elevation is representative of ongoing myocardial injury
    - Does not differentiate between reversible/irreversible injury
  - Progressive elevation over time is documented as a negative prognostic indicator in dogs and cats with underlying cardiac disease
  - Elevated troponins has been documented in dogs and cats with renal insufficiency/azotemia as it has been documented in humans however, studies suggest this may be caused by secondary/concurrent cardiac disease in patients with renal disease rather than lack of clearance

Diagnosis

Biomarkers - cTnI, Dogs

- Cardiac troponin I
  - Plasma cTnI > 0.25ng/mL has 100% specificity for cardiac hemangiosarcoma for dogs with pericardial effusion
    - Sample acquisition before pericardiocentesis as iatrogenic elevation can occur

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1. cTnI - Cardiac troponin I & cTnT - Cardiac troponin T
   - cTnI > 0.25ng/mL has 100% specificity and 81% sensitivity of identifying cardiac hemangiosarcoma as cause of pericardial effusion in dogs
     - Sampling for cTnI should be obtained prior to pericardiocentesis as that may result in iatrogenic elevation
   - cTnI > 0.24ng/mL had a 100% sensitivity for cardiac disease, cTnI > 0.66ng/mL had a 100% specificity for cardiac disease in dyspneic cats presenting emergently

Diagnosis

Biomarkers - cTnI, Cats

- Cardiac troponin I
  - In cats presenting emergently for dyspnea:
  - Plasma cTnI > 0.24ng/mL had 100% sensitivity for cardiac disease
  - Plasma cTnI > 0.66ng/mL had 100% specificity for cardiac disease

CCVS CAPE COD VETERINARY SPECIALISTS

1. cTnI - Cardiac troponin I & cTnT - Cardiac troponin T
   - cTnI > 0.25ng/mL has 100% specificity and 81% sensitivity of identifying cardiac hemangiosarcoma as cause of pericardial effusion in dogs
     - Sampling for cTnI should be obtained prior to pericardiocentesis as that may result in iatrogenic elevation
   - cTnI > 0.24ng/mL had a 100% sensitivity for cardiac disease, cTnI > 0.66ng/mL had a 100% specificity for cardiac disease in dyspneic cats presenting emergently

Outline

1. Relevant Anatomy
2. Pathophysiology Review
3. Diagnosis
4. **Canine Heart Disease**
5. Feline Heart Disease
6. Disease Staging
7. Treatment
8. Prognosis

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CAPE COD VETERINARY SPECIALISTS

Canine Heart Disease

Myxomatous mitral valve disease

- 75% of canine heart disease in North America
  - Up to 30% of cases have concurrent tricuspid valve disease
- Prevalence
  - Small breed dogs (<20kg)
  - ~1.5x more often in males than females
  - Increases with age
- Disease onset is typically years before development of significant cardiac dysfunction
  - Large portion of cases never develop consequences in their lifespan

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1. Myxomatous mitral valve disease (MMVD) - 75% of heart disease seen in dogs in North America
    - Progressive valve thickening and incompetence, typically of the mitral valve, up to 30% of tricuspid valves are also affected
    - Prevalence
        - Typically small breed dogs (<20kg adult weight)
            - Can affect larger breed dogs who typically carry a faster disease progression and development of arrhythmias
        - Approximately 1.5x more often in males than females
        - Typically prevalence increases with age, with up to 85% of small breed dogs having valve lesions by 13 years of age
    - Typically disease onset is years before development of significant cardiac dysfunction/remodeling, large proportion of patients never develop attributable clinical signs/findings in their lifespan

Canine Heart Disease

Myxomatous mitral valve disease

- Chordae tendineae rupture
  - Uncommon, typically only reported in patients with severe mitral valve regurgitation
  - Can be the cause of acute decompensation into CHF

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1. Myxomatous mitral valve disease (MMVD) - 75% of heart disease seen in dogs in North America
    - Chordae tendineae rupture
        - An uncommon sequelae of severe valve disease, most often reported in patients with severe mitral valve regurgitation
        - Can cause the acute decompensation of a patient into clinical heart failure

Canine Heart Disease

Dilated Cardiomyopathy

1. Primary
2. Diet-associated DCM phenotype
3. Tachyarrhythmia/atrial fibrillation DCM phenotype
4. Arrhythmogenic right ventricular cardiomyopathy (ARVC) DCM phenotype

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Canine Heart Disease

Dilated Cardiomyopathy - Primary

- Strong breed predistribution
  - Most common: Doberman Pinschers, Irish Wolfhounds, Great Danes
- Males more than females
- Age of onset: typically 6-8yo but 3-12yo is not uncommon
- Prolonged occult phase with peracute/acute development of signs: syncope, tachyarrhythmias, congestive heart failure
  - 40% of Doberman Pinschers with occult DCM manifest sudden death as their first clinical sign
- Cardiac remodeling/eccentric hypertrophy resulting in systolic dysfunction

CCVS CAPE COD VETERINARY SPECIALISTS

1. Primary
   - Strong breed predistribution: Doberman Pinschers, Irish Wolfhounds, Great Danes
   - Males predisposed more than females
   - Typical onset of 6-8years old but 3-12years old is not uncommon
   - Prolonged occult phase with an peracute/acute development of clinical signs: syncope, symptomatic tachyarrhythmias, congestive heart failure
     - 40% of Doberman Pinschers with occult DCM manifest sudden death as their first clinical sign

Canine Heart Disease

Dilated Cardiomyopathy - Diet-associated

- Taurine deficiency - Golden Retrievers and American Cocker Spaniels
- Nontraditional diets (grain-free/high pulses content) - all dog breeds
    - Not clearly connected to taurine deficiency
- Cardiac remodeling and dysfunction is partially reversible
    - Dogs with symptomatic DCM that successful transition to a traditional diet results in significantly prolonged survival times compared to those who fail to transition

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1. Diet associated DCM phenotype
    - Seen with taurine deficiency, particularly in Golden Retrievers and American Cocker Spaniels
    - Additionally seen with feeding of nontraditional diets (i.e. high pulse content) without clear connection to taurine deficiency in other dogs breeds
        - Pulses, type of legume: peas, chickpeas, lentils
    - Cardiac remodeling and dysfunction can improve with diet change in dogs clinical with DCM, resulting in significantly prolonged survival times compared to those who fail to change diet

Canine Heart Disease

Dilated Cardiomyopathy - Tachyarrhythmia/A-fib

- Uncontrolled SVT can manifest a DCM phenotype
  - Reversible
  - Rate control may result in return to normal cardiac function and reversal of cardiac remodeling
- Atrial fibrillation
  - Common sequella of atrial enlargement
    - Secondary to DCM or MMVD
  - Primary disease reported in Irish Wolfhounds, Great Danes, other giant breeds
  - Rate control can improve survival in primary DCM

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1. Tachyarrhythmia associated/Atrial fibrillation DCM phenotype
   - Uncontrolled supraventricular tachyarrhythmia can manifest a DCM phenotype that can be reversed with rate control/cather ablation of ectopic foci, potentially resulting in return to normal cardiac function and reversal of cardiac remodeling
   - Atrial fibrillation is a common sequela of atrial enlargement related to both DCM and MMVD but can also occur in a primary fashion, often in giant breeds predisposed to DCM (Irish Wolfhounds, Great Danes)
     - Can complicate the case, is it primary DCM with secondary A-fib or primary A-fib with secondary DCM?
     - A-fib rate control can improve cardiac function and improves survival time in primary DCM[53]

Canine Heart Disease

Dilated Cardiomyopathy - ARVC

- Breeds:
  - Most often Boxers (aka: Boxer cardiomyopathy)
  - English bulldogs
  - Case reports in many other breeds as well as several cats
- Heritable with a ventricular arrhythmia component
- Fibrofatty tissue replacement of myocardium with variable myocarditis
  - Typically affects right ventricle but, if there is biventricular involvement, a DCM phenotype can result
    - Can manifest as L-CHF

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1. Arrhythmogenic Right Ventricular Cardiomyopathy: ARVC most known in boxers but is also found frequently in English Bulldogs and individual reports in multiple other breeds as well as in cats
    - Heritable cardiomyopathy with ventricular arrhythmia component
    - Characterized by fibrofatty tissue replacement of the myocardium with variable myocarditis
    - Typically affects the right ventricle but, a DCM phenotype can result if there is pathology to the left ventricle as well, resulting in disease manifestation of L-CHF

Canine Heart Disease

Septic cardiomyopathy

- Manifestation of SIRS/MODS/sepsis
  - Some degree of cardiac dysfunction appreciated in 75% of septic dogs
  - Ventricular diastolic and/or systolic dysfunction
- Negative prognostic indicator
  - BUT reversible if the inflammatory foci is addressed

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1. Septic cardiomyopathy
   - A manifestation of SIRS/sepsis/MODS consisting of ventricular diastolic and systolic dysfunction
     - Some degree of myocardial dysfunction has been appreciated in 75% of septic dogs
   - Notably, this cardiomyopathy can be a negative prognostic indicator BUT it is reversible if the underlying inflammatory foci is addressed and the patient is supported through this illness

Canine Heart Disease

Clinical Signs

- Left-CHF:
  - Cough, dyspnea, lethargy, exercise intolerance, tachycardia
    - Note: Relatively normal HR or a notable sinus arrhythmia in a dyspneic patient is supportive of noncardiac disease
- Right-CHF:
  - Dyspnea with dull lung sounds, abdominal distension with fluid wave, weakness, collapse/syncope
- Low-output HF:
  - Weakness, collapse/syncope, obtundation, brady/tachyarrhythmia, hypothermia, poor pulses, delayed CRT, pallor

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1. Clinical signs
   - L-CHF: Cough, dyspnea, lethargy, exercise intolerance, tachycardia (relative normal heart rate or a pronounced sinus arrhythmia are findings more supportive of a noncardiac cause of dyspnea)
   - R-CHF: Dyspnea with dull lung sounds (pleural effusion), abdominal distension with fluid wave, weakness, collapse/syncope (pericardial effusion)
   - Low-output heart failure: Weakness/collapse/syncope, obtunded, brady/tachyarrhythmia, hypothermia, pallor/delayed CRT, poor pulse quality

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Feline Heart Disease

Feline cardiomyopathies

1. Hypertrophic cardiomyopathy (HCM)
2. Dilated cardiomyopathy (DCM)
3. Restrictive cardiomyopathy (RCM)
4. Nonspecific cardiomyopathy
5. Transient myocardial thickening

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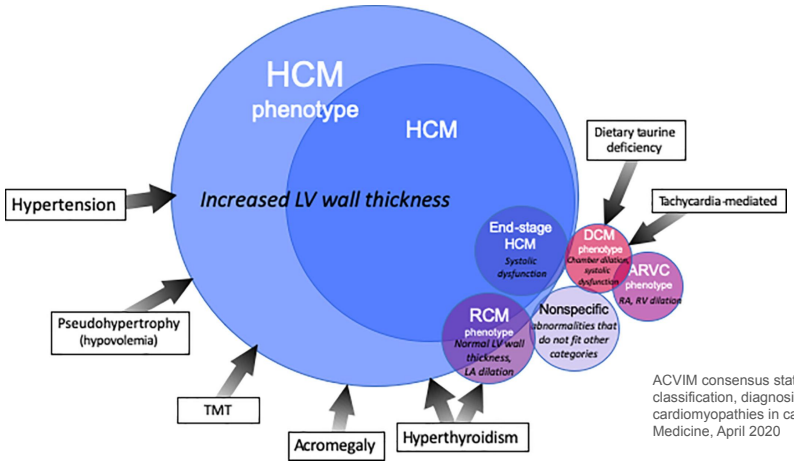
Most relevant feline cardiac diseases

Feline Heart Disease

Feline cardiomyopathies



ACVIM consensus statement guidelines for the classification, diagnosis, and management of cardiomyopathies in cats. Veterinary Internal Medicine, April 2020

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Most relevant feline cardiac diseases

Feline Heart Disease

Feline cardiomyopathies - HCM

- Most often seen in older, male cats
- Majority of HCM cats have subclinical disease
  - Manifestations: CHF, fATE, sudden death
- Cardiac remodeling and concentric hypertrophy resulting in diastolic dysfunction
- Breeds predisposed to primary disease:
  - Ragdolls, Maine Coons, Sphynx, Bengal, Persians, British Shorthair, Norwegian Forest Cat, Birman
- Affects approximately 15% of all cats
  - Up to 29% in older cats

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1. HCM
   - Most often seen in older, male cats.
   - Majority of cats with HCM have subclinical disease
     - Congestive heart failure is most common manifestation, fATE second-most, and sudden death
   - Cardiac remodeling/concentric hypertrophy resulting in diastolic dysfunction
   - Primary
     - Ragdolls, Maine Coons, Sphynx, Bengal, Persians, British Shorthair, Norwegian Forest Cat, Birman
     - Diagnosis of exclusion

Feline Heart Disease

Feline cardiomyopathies - HCM

- Hypertensive associated
  - May only cause mild/moderate ventricular thickening in isolation
  - Significant concern in patients with concurrent primary HCM -> may precipitate disease manifestation
  - Anti-hypertensive therapy is indicated in all patients with HCM, especially with prior disease manifestation
- Hyperthyroid associated
  - May cause sufficiently severe cardiac remodeling to trigger disease manifestation on own
  - Anti-thyroxine therapy is indicated: euthyroidism reduces cardiac remodeling and improves cardiac function

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1. HCM
   - Hypertensive associated
     - In isolation, hypertension may only cause mild/moderate ventricular thickening, can be of concern in cats with occult cardiomyopathy
     - Anti-hypertensive therapy, especially if CHF is present, is indicated
   - Hyperthyroid associated
     - May cause sufficiently severe LV hypertrophy and atrial dilation to trigger CHF/fATE but suspect underlying occult HCM is contributing
     - Anti-thyroxine therapy is indicated as appropriate euthyroidism will reduce cardiac remodeling and improve cardiac function

Feline Heart Disease

Feline cardiomyopathies - DCM

- Primary DCM
  - Rare
- Taurine deficiency
  - Rare outside of homemade diets without appropriate veterinary supervision
  - Reversible within weeks with supplementation
  - All DCM cats should have plasma/whole blood taurine checked
- Tachyarrhythmia associated
  - Rare

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1. DCM[58]
   - Primary
     - Rare
   - Taurine deficiency
     - Since discovery in 1987, rare outside feeding homemade diets without appropriate supervision
     - All DCM cats should have plasma/whole blood taurine checked
     - Reversible with supplementation within weeks
   - Tachyarrhythmia associated
     - Rarely reported in cats

Feline Heart Disease

Feline cardiomyopathies - RCM & Nonspecific

- RCM
  - Fibrous banding of the myocardium or endocardium resulting in diastolic dysfunction
- Nonspecific cardiomyopathy phenotype
  - Myocardial dysfunction not adequately described by the other categories

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1. RCM
   - Restrictive cardiomyopathy
   - Fibrosis banding of the myocardium/endocardium resulting in diastolic dysfunction
2. Nonspecific cardiomyopathy phenotype
   - Not adequately described by the other categories

Feline Heart Disease

Feline cardiomyopathies - Transient Myocardial Thickening

- Typically younger cats
- No sex predisposition
- Antecedent events:
  - Surgery/anesthesia, trauma, vaccination, corticosteroids, illness, IV fluids
- Disease manifestation as severe as CHF may be present
- Phenotypically HCM but cardiac remodeling and function improves overtime
  - Corresponds with a drop in cTnI from initial diagnosis

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1. Transient myocardial thickening
   - Typically younger cats without a sex predisposition and often with an antecedent event such as surgery/anesthesia, trauma, vaccination, illness, IV fluids, corticosteroids.
   - Can present in congestive heart failure.
   - Phenotype mimics HCM but cardiac remodeling measurements and function improves overtime, corresponding drop in cTnI at initial diagnosis

Feline Heart Disease

Clinical Signs

- Left-CHF: **Dyspnea*****, hiding, inappetence, gallop/audible arrhythmia more often than audible murmur, tachycardia, hypothermia
  - Cough is an uncommon clinical signs of Left-CHF in cats, more often seen in lower airway disease
- fATE: Paresis/paralysis of any limb(s), pain, vocalization
  - Left-CHF is commonly concomitant
- Low-output HF: Bradycardia, hypothermia, hypotension

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1. Clinical Signs
   - L-CHF: Labored breathing *may be only clinical sign*, less often cough, hiding, inappetence, gallop/audible arrhythmia more supportive of CHF than an audible murmur, tachycardia (HR>200), hypothermia
   - fATE: Paresis/paralysis - any limb(s), pain, vocalization
     - CHF is commonly concomitant
   - Low-output HF: Brachycardia, hypothermia (severe), hypotension

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Disease Staging

ACVIM Staging

- Originally developed for canine valvular disease
- Adapted to apply more generally to cardiac disease of dogs and cats
- Stages A, B1, B2, C, D

1. Originally discussed for canine valvular disease, has since been adapted to more generally describe cardiac disease in dogs and cats
2. ACVIM A, B1, B2, C, D

Disease Staging

ACVIM Staging - A

- Stage A
  - Patients at risk of the development of cardiac disease
  - Ex: Dachshunds, Cavalier King Charles Spaniels
  - Cats?
    - Not strictly stated but first-degree relatives with HCM, Maine Coons and Ragdolls homozygous for their known mutations are at higher risk

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1. A - Patients at risk of the development of heart disease
   - Ex: CKCS, Dachshunds, Maine Coons, Ragdolls
   - Cats: First-degree relatives with HCM, Maine Coons homozygous for MyBPC3-A31P, Ragdolls homozygous for MyBPC3-R820W - not strictly named as Stage A in the ACVIM Feline cardiomyopathy consensus statement but have documented increased risk of HCM compared to the general population

Disease Staging

ACVIM Staging - B1

- Stage B1
  - Patients with the development of underlying cardiac disease with no/minimal cardiac remodeling
  - No drug/dietary recommendations
  - Now/low risk of cardiac events
  - Routine monitoring recommended

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1. B1 - Patients with the development of underlying cardiac disease with no/minimal evidence of cardiac remodeling
   - Patients at no/low risk of cardiac events
   - There are no drug or dietary recommendations at this stage
   - Routine monitoring q6-12m

Disease Staging

ACVIM Staging - B2, Dogs

- Stage B2
  - Patients with the development of underlying cardiac disease with hemodynamically significant cardiac remodeling without a history of disease manifestation
  - Patients at higher risk for cardiac events
  - Dogs: initiate pimobendan therapy
  - Address underlying arrhythmias

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1. B2 - Patients with the development of cardiac disease with hemodynamically significant cardiac remodeling without a history of disease manifestation
   - Patients at higher risk for cardiac events
   - In dogs, initiation of pimobendan is indicated (0.25-3mg/kg PO q12h)
     - EPIC study
   - In cats, if there is evidence of increased risk of ATE (degree of LA enlargement, decreased LA FS%, low LA appendage blood velocity), thromboprophylaxis indicated. Clopidogrel monotherapy superior to aspirin monotherapy, can consider polytherapy: clopidogrel + factor Xa inhibitor vs clopidogrel + aspirin vs clopidogrel + aspirin + factor Xa inhibitor
   - If there is underlying arrhythmia, medical intervention is indicated

Disease Staging

ACVIM Staging - B2, Cats

- Stage B2
  - Cats: if there is evidence for increased fATE risk, thromboprophylaxis therapy indicated
    - Monotherapy: Clopidogrel > aspirin
    - Consider polytherapy: Clopidogrel +...
  - Address underlying arrhythmias

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1. B2 - Patients with the development of cardiac disease with hemodynamically significant cardiac remodeling without a history of disease manifestation
   - Patients at higher risk for cardiac events
   - In dogs, initiation of pimobendan is indicated (0.25-3mg/kg PO q12h)
   - In cats, if there is evidence of increased risk of ATE (degree of LA enlargement, decreased LA FS%, low LA appendage blood velocity), thromboprophylaxis indicated. Clopidogrel monotherapy superior to aspirin monotherapy, can consider polytherapy: clopidogrel + factor Xa inhibitor vs clopidogrel + aspirin vs clopidogrel + aspirin + factor Xa inhibitor
   - If there is underlying arrhythmia, medical intervention is indicated

Disease Staging

ACVIM Staging - C

- Stage C
  - Patients with the development of underlying cardiac disease with hemodynamically significant cardiac remodeling sufficient to cause disease manifestation
    - CHF, low-output HF, fATE
  - Treatment: *Coming in two more slides*

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1. C - Patients with cardiac disease + cardiac remodeling sufficient to cause congestive heart failure or fATE
   - Currently, this is a permanent designation

Disease Staging

ACVIM Staging - D

- Stage D
  - Stage C patients with sufficient disease and cardiac remodeling progression to become refractory to treatment
  - Dogs, therapy escalated beyond:
    - Furosemide ≥ 8mg/kg/day (or torsemide equivalent)
    - Plus pimobendan 0.25-0.3mg/kg PO q12
    - Plus standard ACEi dose
    - Plus spironolactone 2mg/kg/day
    - Plus, if arrhythmia is present, sufficient medication to achieve sinus rhythm or ventricular response daily mean <125bpm
  - Cats: Furosemide > 6mg/kg/day

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1. D - Patients with sufficient cardiac disease/remodeling progression to become refractory to treatment
   - Most cardiologists comment that the transition from Stage C to D is ill defined
   - Dogs - Therapy escalation beyond: Furosemide >/= 8mg/kg/day (or torsemide equivalent) + pimobendan 0.25-0.3mg/kg PO q12h + standard ACEI dosage + spironolactone 2.0mg/kg/day
     - If there is an underlying arrhythmia (i.e. AF), sufficient anti-arrhythmic medication to achieve sinus rhythm or a ventricular response mean daily HR <125bpm is needed before refractory diagnosis
   - Cats - Therapy escalation beyond: Furosemide >6mg/kg/day

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Treatment

Acute Heart Failure Stabilization

"Someone Please Obtain Furosemide"

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1. Treatment
    - "Someone Please Obtain Furosemide"
        - Sedation, pimobendan, oxygen, furosemide
        - Mainstay of acute heart failure stabilization

Treatment

Acute Heart Failure Stabilization - Sedation

- Removing anxious activity reduces oxygen demand
- Reduce dyspnea-associated panic
  - Anxious breathing can mask therapeutic response
  - Physiologic stress in heart failure cats may precipitate decompensation
- Butorphanol: 0.2-0.25mg/kg IV/IM
- Acepromazine: 0.005-0.05mg/kg IV
- Other low cardiovascular risk sedatives:
  - Benzodiazepines
  - Opioids

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1. Sedation
   - Reduce oxygen demand through removal of anxious activity
   - Reduce panic associated with dyspnea
     - Anxiety respiratory rate may mask response to therapy
     - Physiologic stress in heart failure cats may precipitate further decompensation
   - Butorphanol 0.2-0.25mg/kg IV/IM dogs and cats
     - Anti-tussive
   - Acepromazine 0.005-0.05mg/kg IV dogs and cats
     - Alpha-1 blockade resulting in hypotension = reduced afterload and increased cardiac output
   - Other low cardiovascular risk sedatives: diazepam/midazolam, methadone/hydromorphone/buprenorphine
     - Careful titration: avoid respiratory depression

Treatment

Acute Heart Failure Stabilization - Pimobendan

- Phosphodiesterase III Inhibitor + Myocardial calcium sensitizer, aka: inodilator
- Dogs: starting 0.25-0.3mg/kg PO q12h
  - Off-label: 0.3-0.5mg/kg PO q8h for Stage D MMVD
- Cats? What about SAM and DLVOTO?
  - 0.625mg-1.25mg per cat or 0.2-0.3mg/kg (lean body mass) PO q12h
  - Consider for DCM phenotype alongside taurine supplementation
  - Consider for low-output HF

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1. Pimobendan
   - Phosphodiesterase III inhibitor + myocardial calcium sensitizer
     - Positive inotrope without increased cardiac oxygen demand + systemic arterial vasodilation reducing afterload = inodilator
   - Dogs: 0.25-0.3mg/kg PO q12h
     - Indicated to start in Stage B2 MMVD
       - Titrated upwards over time with development of pulmonary edema
     - Off-label for Stage D MMVD: 0.3-0.5mg/kg PO q8h
   - Cats: 0.625mg-1.25mg per cat or 0.2-0.3mg/kg (lean body mass) PO q12h
     - Not indicated in majority of feline CHF cases due to lack of documented efficacy
     - What about DLVOTO?
       - The 2020 ACVIM Consensus on cat cardiomyopathies only recommended pimobendan in cats without DLVOTO
       - Subsequent studies on pimobendan and cats with/without DLVOTO found that it had no significant impact on worsening or inducing DLVOTO while also failing to find benefit with its use

- Consider if DCM phenotype alongside taurine supplementation (until plasma/whole blood taurine is back)
- Consider with low-output heart failure

Treatment

Acute Heart Failure Stabilization - Oxygen

- Oxygen Cage: FiO2 40-60%
- High-flow nasal oxygen
  - Tolerated and improves oxygenation compared to conventional O2 therapy
  - Currently no studies evaluating effects on outcome
- Positive pressure ventilation
  - Fulminant left-CHF
  - Majority survival to discharge
  - PPV duration: 1-2 days
  - No effect on long-term prognosis

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- Oxygen
  - Oxygen cage at FiO2 40-60%
  - High-flow nasal oxygen therapy
    - Tolerated by patients in acute heart failure and recommended on expert opinion but no currently published studies of effect on outcome
  - Positive pressure ventilation
    - Indicated for cases of fulminant L-CHF: expectorating serosanguinous pulmonary edema, respiratory failure
    - Survival to discharge 54-77%
    - Duration of PPV 1-2 days
    - No effect on long-term prognosis: 54% >2month survival in discharged L-CHF patients

Treatment

Acute Heart Failure Stabilization - Furosemide

- Loop diuretic
  - Sodium, potassium, chloride wasting
- Dogs:
  - 2mg/kg IV or IM, repeat q1h if significant improvement not achieved, max 8mg/kg
  - Fulminant left-CHF: 2mg/kg IV then 0.66-1mg/kg/hr CRI for 4-6hr
- Cats:
  - 1-2mg/kg IV or IM, repeat q1h if significant improvement not achieved, max 6mg/kg
  - Consider 0.5-1mg/kg/hr CRI

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1. Furosemide, initial therapy
   - Loop diuretic - Na-K-2Cl cotransporter inhibitor in the loop of Henle, increased Na/K/Cl excretion results in inability to reabsorb water in the distal nephron/collecting duct
   - Dogs: 2mg/kg IV/IM first, repeat q1h to max of 8mg/kg if significant improvement in dyspnea has not been achieved
     - Fulminant L-CHF: furosemide 2mg/kg IV then 0.66-1mg/kg/hr CRI for 4-6hr
   - Cats: 1-2mg/kg IV/IM first, repeat q1h to max of 6mg/kg if significant improvement in dyspnea has not been achieved
     - Can consider a 0.5-1mg/kg/hr CRI as well

Treatment

Diuretic Therapy - Furosemide

- Initial dosing based on total daily dose required to put patient's clinical signs into remission
- Titrate to effect
  - Recheck electrolytes + BUN/Crea in 3-7 days following each escalation
- Add in secondary diuretics + ACE-inhibitors before escalating to high dose therapy
  - I.e. Dogs >8mg/kg/day, Cats >6mg/kg/day

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1. Furosemide, home therapy
   - Initial home dosing based on total daily dose required to put patient's clinical signs into remission
   - Titrate to effect, maximum dose is determined by patient tolerance, recheck electrolytes and BUN/Crea in 3-7 days following dose escalations
   - Recommend addition of secondary diuretics (spironolactone) + ACE-inhibitors before deciding to increase to high dose furosemide: >8mg/kg/day dogs, >6mg/kg/day cats

Treatment

Diuretic Therapy - Spironolactone

- Aldosterone-receptor antagonist
  - Additional natriuresis with blunting of loop-diuretic kaliuresis
  - Potentially attenuates deleterious RAAS activity
    - Reduce mortality in combination with an ACEi compared to ACEi monotherapy
- Dogs: 2mg/kg PO q12-24h
- Cats: 1-2mg/kg PO q12-24h
  - High doses associated with ulcerative dermatitis in Maine Coon

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1. Spironolactone
   - Aldosterone-receptor antagonist
     - Natriuretic and blunts potassium wasting of loop diuretics
     - Potential cardiovascular protective effects due to the deleterious effects of RAAS activation on the heart
   - Not recommended for acute CHF management but for Stage C heart failure
   - BEEST, 2021[61]: Spironolactone + benazepril treatment group had significantly reduced mortality compared to benazepril alone for patients in stage C MMVD
   - Dogs: 2mg/kg PO q12-24h
   - Cats: 1-2mg/kg PO q12-24h
     - Doses of 2mg/kg q12h have been associated with ulcerative dermatitis in Maine Coon cats

Treatment

Diuretic Therapy - Torsemide

- Loop diuretic
  - 10-20x potency of furosemide
  - 2-4x duration of activity
- Dogs:
  - 0.1-0.2mg/kg PO q12-24h
  - OR 5-10% of current furosemide dose
- Cats:
  - 0.1-0.2mg/kg PO q24h

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1. Torsemide
   - Loop diuretic with 10-20x potency + a ~12hr duration of diuretic activity in dogs/cats compared to furosemide (3-6hr duration of diuretic activity)
   - Dogs: 0.1-0.2mg/kg (or 5-10% of the current furosemide dose) PO q12-24h
   - Cats: 0.1-0.2mg/kg PO q24h

Treatment

Afterload Reduction - ACE-inhibitors

- Benazepril/Enalapril
  - Reduce arterial vasoconstriction via attenuation of AngII activity
- Not routinely recommended for acute management of canine or feline heart failure
  - Consider in hypertensive patients
- Dogs & cats*: Enalapril/benazepril 0.25-0.5mg/kg PO q12-24h
- Monitor electrolytes + BUN/Crea in 3-14 days after starting

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1. ACE-inhibitors: reduced vasoconstriction through reduction of AngII activity
   - Not commonly recommended in the acute management of canine CHF due to known appetite reducing/GI upsetting adverse effects, not recommended in acute management of feline CHF.
     - Consider in the hypertensive patient
   - Dogs and Cats: Enalapril/benazepril 0.25-0.5mg/kg PO q12-24h
     - Note: In cats, benazepril failed to delay onset of treatment failure in one blinded placebo controlled prospective multicenter study, some cardiologists do not use ACEi in cats anymore because of stress of medication administration and lack of proven efficacy
   - Monitoring of electrolytes + Crea/BUN in 3-14 days following initiation of therapy due to reported risk of inducing AKI/renal intolerance

Treatment

Afterload Reduction - Arterial Vasodilation

- Acute decompensation of Stage D patients or failing to improve despite acute stabilization attempts
  - Requires blood pressure monitoring
  - Avoid prolonged hypotension
  - Positive inotropes available/given concurrently
- Hydralazine 0.5-2.0mg/kg PO
  - Titrate to effect: 0.5mg/kg PO q1h
- Amlodipine 0.05-0.1mg/kg PO q3h titrated to effect

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1. For patients with acute decompensation in Stage D or failing to improve with acute heart failure stabilization attempts, consider arterial vasodilatory therapy
   - Requires careful blood pressure monitoring, avoid prolonged hypotension, positive inotropes should be available/given concurrently
   - Hydralazine 0.5-2.0mg/kg PO, can titrate to effect orally with 0.5mg/kg PO q1h
   - Amlodipine 0.05-0.1mg/kg PO q3h titrated to effect

Treatment

Afterload Reduction - Arterial Vasodilation

- Fulminant left-CHF?
- Sodium nitroprusside 1.0mcg/kg/min CRI IV
  - Titrate q15-30min to effect, max 15mcg/kg/min
  - Thiocyanate and cyanide toxicity
  - Cats: Oxidative injury
- Dogs only: nitroglycerin transdermal 0.5”/10kg on unhaired skin for first 24-36hr
  - Wear gloves

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1. If patient is too unstable to wait for oral onset of action:
   - Sodium nitroprusside CRI IV 1.0mcg/kg/min, titrate every 15-30min to effect, max 15mcg/kg/min
     - Prohibitively expensive
     - Possible thiocyanate and cyanide toxicity with prolonged use
       - Increased risk of profound hypotension with concurrent renal/hepatic insufficiency
       - Metabolic acidosis = early cyanogen toxicity
       - Delirium with thiocyanate toxicity
       - Hydroxocobalamin (Vitamin $B12_a$) and sodium thiosulfate are antidotes
     - Cats risk oxidative injury (Heinz body anemia, etc), use minimal dose
   - Nitroglycerin transdermal (dogs only): 0.5”/10kg on unhaired skin for first 24-36hr
     - Wear gloves, may cause hypotension/syncope with accidental exposure to self/staff
     - Tachyphylaxis

Treatment

Positive Inotropes

- Continued low-output HF signs despite pimobendan
- ECG required due to possible induction of ventricular ectopy/tachyarrhythmia
- Dobutamine CRI IV
  - Dogs: 2.5mcg/kg/min, titrate to effect, max 10mcg/kg/min
  - Cats: 1mcg/kg/min, titrate to effect, max 5mcg/kg/min

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1. Positive inotropes
   - If continuing to exhibit signs of low-output heart failure (hypotension, hypothermia) despite pimobendan:
     - IV positive inotropes require ECG monitoring due to possible induction of ventricular ectopy/tachyarrhythmia
   - Dobutamine CRI IV
     - Dogs: 2.5mcg/kg/min, titrate up to 10mcg/kg/min
     - Cats: 1mcg/kg/min, titrate up to 5mcg/kg/min
       - Doses >5mcg/kg/min associated with tremors/seizures in nonanesthetized cats

Outline

1. Relevant Anatomy
2. Pathophysiology Review
3. Diagnosis
4. Canine Heart Disease
5. Feline Heart Disease
6. Disease Staging
7. Treatment
8. **Prognosis**

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Prognosis

Canine - Myxomatous Mitral Valve Disease

- Pre-Stage C: MST upwards of 5 years
- Post-disease manifestation:
  - Stage C: MST 388d (264-469d 95% CI)
  - Stage D: MST 171d (93-249d 95% CI)

Vezzosi, T., et al. The Mitral INsufficiency Echocardiographic score: A severity classification of myxomatous mitral valve disease in dogs. JVIM 2021; 35:3. https://doi.org/10.1111/jvim.16131

- Mitral Valve Repair?
  - More programs available
  - Increasing success rates and decreasing complication rates
  - Case selection critical - see a cardiologist ASAP

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- MMVD - Survival time is highly variable and is dependent on degree of regurgitation and amount of cardiac remodeling
  - Pre-CHF MST reported upwards of 5 years[63]
  - Post-CHF MST 388d, 95% CI 264-469d (stage C) to 171d, 95% CI 93-249 (stage D)[63]
  - Of special note, interventional correction of mitral valve regurgitation is continuing to improve with lower complication rates and demonstrating superior outcomes to medical management alone. However, case selection is important, consultation with a veterinary cardiologist for owners interested in this option is indicated ASAP following diagnosis.

Prognosis

Canine - Dilated Cardiomyopathy

- Prognosis significantly dependent on if primary vs secondary DCM as well as ability to correct inciting cause
  - Diet-associated DCM without diet change: MST 215d[a]
  - Diet-associated DCM with diet change: MST 337d[a]
  - Doberman Pinschers in CHF from DCM with pimobendan: 130.5d[b]

a: Freid, K., et al. Retrospective study of dilated cardiomyopathy in dogs. JVIM 2020; 35:1. https://doi.org/10.1111/jvim.15972
b: O'Grady, M.R., et al. Effect of pimobendan on case fatality rate in Doberman Pinschers with congestive heart failure caused by dilated cardiomyopathy. JVIM 2008; 2008; 22:4. https://doi.org/10.1111/j.1939-1676.2008.0116.x

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Prognosis

Feline

- Prognosis dependent on primary vs secondary cardiomyopathy
  - Primary HCM in Stage C: survival time variable, majority suffer mortality within months with few surviving 1-2 years[a]
  - Transient myocardial thickening: ***Multi-year survival time***
    - May recover sufficiently to no longer require medical therapy[b]

a. Virginia, L., et al. ACVIM consensus statement guidelines for the classification, diagnosis, and management of cardiomyopathies in cats. JVIM 2020; 34:3. https://doi.org/10.1111/jvim.15745
b. Novo Matos, J. et al. Transient myocardial thickening in cats associated with heart failure. JVIM 2017; 32:1. https://doi.org/10.1111/jvim.14897

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QUESTIONS?

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