Understanding, Diagnosing & Managing
Feline Cardiomyopathies

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Topics:

Overview of Cardiomyopathies:
• Pathology & Echo correlates
• Other types of feline heart disease

Feline Hypertrophic Cardiomyopathy:
• Epidemiology (etiology)
• Pathology/Phenotypes/Functional Changes
  HCM – HOCM – (ES)HCM
• Clinical findings & Clinical outcomes
• Diagnostic Testing in HCM
• Case example: Approach to murmurs

Risk Stratification
• Prognostic factors in cardiomyopathies

Treatment approaches:
• HCM: Asymptomatic cat
• Acute & Chronic CHF
• Arterial thromboembolism & Anti-thrombotic therapy

OVERVIEW

Review of Feline Cardiomyopathy Phenotypes
• Hypertrophic: thick LV + normal to ↑ LV ejection fraction
• Dilated: dilated, hypokinetic left ventricle (↓ EF)
• Restrictive: non-hypertrophied, fibrotic, (low-)normal LVEF + severely-dilated left atrium ± right atrium ± fibrous bands
• Right ventricular (ARVC): dilated RV + RA + arrhythmias
• Nonspecific: some combination of above
• RCM or end-stage HCM? Myocardial infarctions?
• High-output states: Anemia, ↑ T4

Hypertrophic Cardiomyopathy
• Disorder primarily affecting the LV and characterized by LV hypertrophy unexplained by other known causes of LVH.
• Many breeds affected including mixed; genetic tests for MCC, Sphynx, Ragdoll currently (NCSU genetic lab)
• DDx of the HCM phenotype includes:
  o Congenital HD (AS, mitral obstruction of LVOT) - uncommon
  o Systemic Hypertension – common in older cats with CKD
    Mild-moderate LVH is typical – Can also have ↑ T4
  o Endocrinopathies & LV wall thickening:
    Hyperthyroidism, Diabetes, Acromegaly (↑ GH) - graph
  o Transient Myocardial Thickening

1 – John Bonagura, DVM, DACVIM – Feline Cardiomyopathies (Presentation Outline – Vermont VMA)
Transient Myocardial Thickening
- Reversible form LV “Hypertrophy” or thickening
- Often present with (treatable) CHF – pulmonary edema
- Causes? Myocarditis, Repositol corticosteroid (DepoMedrol®)? Myocardial edema from other causes?

Feline (Endo)myocarditis
- Etiology? Post-viral? Bartonella?
- Focal vs Diffuse → necrosis (CHF)
- Subacute or chronic → PVCs | potential for → SCD
- Myocardial fibrosis → Restrictive CM

Restrictive Cardiomyopathy
- RCM – Myocardial Fibrosis
- Example: Restrictive (or Nonspecific) Cardiomyopathy
- Myocardial Ischemia/Fibrosis/Infarctions
  Commonly Seen with end-stage HCM, RCM & NCM
  Can β-blockers or RAAS inhibition prevent (?)
- Dilated Cardiomyopathy in Cats
  Rare today & usually idiopathic (not taurine deficiency)

Others –
- Dilated Cardiomyopathy in Cats - Rare today & usually idiopathic (not taurine deficiency)
- Right Ventricular Cardiomyopathy (ARVC)
- Nonspecific Cardiomyopathy
- Tachyarrhythmia & CHF

Luis Fuentes, et al.
ACVIM Consensus Statement, JVIM 2020
(free download)
Congenital vs. Acquired Diseases: Common forms Feline HD

- Myocardial Diseases
- Valvular & Endocardial (CHD)
- Vascular diseases
  - Coronary (Cardiomyopathy)
  - Systemic (ATE & HTN; Ao Ectasia)
  - Pulmonary HTN (Lung Dz, HWD)
- Arrhythmia (CM, Metabolic & AVB)
- Pericardial (PPDH, CHF, Infections)

Syncope / Sudden Death in Cats
- DDx: Cardiomyopathies & Primary Rhythm Disturbances

Pericardial Diseases in Cats
- Peritoneopericardial Diaphragmatic Hernia (2 cats)
- Pericardial Effusion
  - Usually due to CHF; uncommonly from primary pericarditis

HCM - CLINICAL FEATURES

Definition/Etiology
Thickening of the LV due to myocyte hypertrophy.
- In typical cases LV systolic function (ejection fraction) is hyperdynamic and diastolic dysfunction is considered the major abnormality.
- However, systolic dysfunction can develop and is often observed in cats presented in chronic CHF often with myocardial segment thinning or hypokinesis (likely ischemic injury/infarction/replacement fibrosis)
- Dynamic LV outflow tract obstruction (LVOTO) is commonly observed (HOCM).
- LA dilation occurs with progressive ventricular dysfunction, predisposing to arterial thromboembolism.
- The RV can be mildly thickened.

Considered a sarcomeric Disease with an assumed mono- or polygenetic basis, although presently most cases are “idiopathic” or “primary” due to an absence of available genetic testing.

Epidemiology
Prevalence of HCM is debated related to the diagnostic criterion used for feline wall thickening. The disease is common and among the most frequent reasons for a heart murmur in cats.

“Genetic testing for the MyBPC3-A31P mutation and the MyBPC3/R820W mutation is recommended in Maine Coon and Ragdoll cats intended for breeding... Cats homozygous for either mutation not be used for breeding, but heterozygous cats can be bred to genotype-negative cats if they have..."
other outstanding characteristics (LOE low).” From the Consensus statement of Feline Cardiomyopathies, JVIM 2020

**Hypertrophic Cardiomyopathies – Different Phenotypes**
- Severity & Distribution Vary: Mild – challenging to diagnose (Wall thickness cut-off: 5.0? 5.2? 5.5? 6.0? mm)
- Generalized vs. Asymmetric – freewall vs. LV wall
- Focal – Segmental - Papillary muscles, Midventricular Subaortic focal in older cats (DUST or DISH)
- Mitral valve abnormalities
- LA size usually tracks functional severity

**HOCM: Left Ventricular Systolic Obstruction**
- Systolic Anterior Motion of the MV (and chords)
- Mitral valve is often abnormal
- Other obstructions: Septal bulges, Midventricular

**Myocardial Tissue Abnormalities**
- Hypertrophy
- Fiber Disarray (variable)
- Infarction
- Fibrosis

**Arterial Thromboembolism in Feline CM**
Cardiomyopathy with LA Dilation: High Risk of Thromboembolism with LA enlargement or impaired auricular function

_Risks_: ♦ Endothelial injury ♦ Abnormal coagulation ♦ RBC Stasis

_DDx of ATE_: ♦ Cardiomyopathies ♦ Endocarditis ♦ Lung CA

**Presenting Signs in Cardiomyopathies**
- Virtually any age, either sex, breed risks (HCM)
- Healthy cat with Murmur, Gallop, Arrhythmia, Cardiomegaly, ↑NT-proBNP test
- Resp Distress (CHF) – usually due to CHF
- Prior History: veterinary visit, surgery, anesthesia, stress, Depomedrol
- Arterial Thromboembolic event
- Syncope (or Sudden Cardiac Death)

**Clinical Evaluation**
- **Cardiac Auscultation**: (Systolic) Murmurs, Gallop sounds & Clicks, Heart Arrhythmias, Distant or soft sounds
- Evaluate for thyroid disease, pallor, abnormal pulses
- CHF – biventricular – look for elevated JVP
- Cardiogenic shock: ↓Temp ↓HR ↓↓BP
- CHF: anorexia, ↓activity, tachypnea & respiratory distress
**Signs of Arterial Thromboembolism**
- Sudden onset of Pain (vocalization)
- Neurologic deficits: paresis & eventual loss of sensation
typical saddle thrombus (rear limbs + tail)
- Forelimb (either one)
- Vascular insufficiency: cold, pulseless, pale limbs
down to absent Doppler flow signals
- Skeletal muscles: painful, contracture, ↑↑↑CK ↑↑AST ↑ALT

**Differential Diagnosis During Exam:**
- Exclude systemic HTN (measure systolic BP)
  - Cuff: 30 – 40% limb circumference (#1 to #2)
  - Site(s) for cuff | crystal (forelimb, tail, hindlimbs)
  - Limit “white-coat” hypertension
  - Obtain optimal signals first | Repeat 3-5x
  - High: >150 to 160 mm Hg
- Evaluate for Hypertensive heart disease
  - Ocular – detachments, edema, hemorrhages
  - CNS signs
  - LV hypertrophy (usually mild)
  - Renal injury (also the cause of HTN)

**Diagnostic Cardiac-focused Testing**
- **Thoracic Radiography:** Only detects *advanced* heart disease
  Critical in the DDx of Respiratory Signs
  - Effusions are Common in Cardiomyopathies
    Pleural Effusions (including chylothorax) & Pericardial effusion
- **Echocardiography:** “Gold standard” for diagnosis
  - More advanced imaging skills; technically challenging
  - Do not over-interpret wall thickness
  - Follow-ups: Focus on left atrium/auricle, effusions, B-lines
  - Doppler Studies– Regurgitation – Diastology – Obstruction
- **Electrocardiogram** – Voltages & Frontal Axis Shift
  - ECG: Most useful for Dx of Arrhythmias
  - Voltages > .7 mV (to 1.0 mV)
  - Left axis deviation: qR complex Leads I & aVL ; rS in lead II
  - S-wave progression leads II → aVF → III
• **NT-proBNP** (released by stretch, ischemia & hypertrophy)
  - Cardiopet® IDEXX Point of Care SNAP® Test
    = to + control (usually >150 pmol/L)
    > positive control (usually >270 pmol/L)
  - POC NT-proBNP Reference Lab:
    o ≥ 100 pmol/L suspicious
    o ≥ 150 pmol/L abnormal
    o ≥ 270 pmol/L higher risk CHF

• Predictive value of biomarker tests very much depends on the population that is sampled
  o Asymptomatic murmurs
  o Respiratory distress
  o Every healthy cats sampled – don’t do this

• Asymptomatic cats with murmur – recommend reference lab test

• “Urgent need” for an answer (pre-anesthetic or dyspneic cat) – POC SNAP test makes sense (good negative predictive value for moderate to severe disease)

• **Cardiac Troponin (cTnI)** – injury or necrosis – there are “standard” and (less available) high-sensitivity assays for cTnI
  o 0.163 ng/ml was the “cut-off” for asymptomatic HCM in one study with a 100% PPV for the study sample
  o cTnI – more often used to screen for myocarditis or infarctions or to identify myocardial disease in cats with arrhythmias (VPCs)

**Evaluation of Asymptomatic Cardiac Murmur**

**General Causes of Murmurs in Cats:**
• Congenital Heart Disease
• Functional (physiological) murmurs
• Cardiomyopathies
  • Primary / genetic / idiopathic; Especially HOCM
  • Secondary myocardial diseases: Especially Hyperthyroidism & hypertension
• Functional Murmurs in Cats – Influence of Sympathetic Tone on Blood Flow in RVOT (CW Doppler)
Outcomes of Feline Cardiomyopathies

- Asymptomatic for life - Follow up & treatment costs
  - Client and cat inconvenience
- Reversible cardiomyopathy
  - Taurine deficiency (now rare)
  - TMT
  - Pseudohypertrophy (dehydration)
- Life-altering outcomes
  - Sudden death
  - CHF
  - Arterial thromboembolism

- **Prognosis**: Data from REVEAL (retrospective)
  HCM carried higher mortality risk than controls REVEAL Study (Fox, et al., 2018)
- 1730 cats – world-wide study >50 centers
  (HCM=430, HOCM=578, healthy=722)
- CHF/ATE risk: 7.0/3.5% at 1 year, 19.9/9.7% at 5 years and 23.9/11.3% at 10 years (28.3% cardiac death) ~25% CHF/ATE in 5 years
HCM – Negative Prognostic Factors
- LA Dilation & Impaired LA function
- Intra-atrial contrast (smoke) or thrombus
- Extreme LVH | Asymmetric LVH (LV wall)
- Impaired LV systolic function
  - Global – Regional – Apical-basilar (MAPSE)
- Prior history of CHF or ATE
- History of Syncope (?) with VT (?)

Feline Cardiomyopathies: Proposed Staging System

**HYPERTROPHIC CARDIOMYOPATHY – THERAPY**

Current Guidelines for Therapy
- Therapy: in the consensus statement the level of evidence for most treatments was indicated as “low” aside from furosemide + oxygen & clopidogrel (Plavix®)
- There are various opinions/experiences...
  - but a lack of quality clinical trial evidence
- A single-center prospective study failed to demonstrate any 5-year survival benefit of atenolol (the study samples were small with low event rate).
- In a colony of MC cats with HCM, neither the ACE-inhibitor ramipril nor spironolactone significantly altered hypertrophy, diastolic function, or MRI-estimated fibrosis in a small study in a Maine coon cat colony. These were healthy HCM cats and the effect of these drugs in advanced disease or in cats with CHF might be different.
- Mavacamten, an inhibitor myosin ATPase and contractility decreases LV contractility and outflow tract obstruction in humans. Preliminary data in cats suggest a statistically-significant, but clinically small reduction in LV hypertrophy.
Asymptomatic HCM / HOCM

- Staged as B1 or B2 (if mod-severe LA dilation)
- Is Atenolol Useful in Asymptomatic HOCM – No definitive data to support use; theoretic; ↓LVOT obstruction & HR
- If there are negative prognostic factors
  - **Start clopidogrel** (Plavix®) as anti-platelet therapy (future: Xa inhibitors apixaban or rivaroxaban? $$$)
  - ¼ of a 75-mg tablet daily (bitter!)
- If moderate to severe LA enlargement on Echo (or no Echo) ⇒ obtain chest radiographs to r/o CHF
- If “incipient CHF” on radiography ⇒ dispense “rescue doses” of furosemide
- If severe LVOT obstruction (HOCM >65 mm Hg) consider 6-month course of atenolol (especially in young cats)

CHF in Cats with Cardiomyopathies

- **Acute therapy of CHF**
  - Oxygen & Butorphanol Sedation Help!
  - Determine is respiratory difficulty due to Acute pulmonary edema vs. large pleural effusions
  - POCUS is very helpful for initial assessment

- Furosemide for pulmonary edema (±topical NTG)
- Thoracocentesis for Pleural Effusion - right sided tap for cats with CHF if possible
- Pimobendan? With DCM, RCM, RVCM or HCM with moderate Pleural Effusion: consider starting Pimobendan in hospital (no definitive clinical trial data); most cardiologists do not use this for HOCM, at least initially. Note that cats without a murmur unlikely to have HOCM and it is well tolerated even in cats with HOCM although theoretically contraindicated.
• **Chronic Therapy of CHF**
  - CHF in Cats – *Chronic* Medical Therapy

  | Clopidogrel (Plavix®): Anti-thrombotic | ?ACEI: Enalapril or Benazepril | Furosemide: Titrate dose to fluid retention & renal function (mild azotemia acceptable) |

  “Cats Are For Special People”

• **Cat with CHF: Follow-up**
  - Medication compliance?
  - Sleeping Respiratory Rate: Trends & Rate (25–30/min is usually a good sign)
  - Quality-of-life indicators – diet, activity, “interest”
  - Recheck: Gabapentin 3h prior to travel
  - Major examination assessment: for effusions or pulmonary edema or arrhythmias
  - History ⇒ Exam ⇒ Rapid Ultrasound/Echo ⇒ ± thoracic radiography or ECG
  - Follow renal function & electrolytes: Accept mild azotemia
  - Focused US of left atrium/auricle
    Thrombus or spontaneous contrast (“smoke”) – consider more aggressive combination therapy for anti-thrombotic effects (clopidogrel + ASA or clopidogrel + one of the factor Xa inhibitors such as apixaban or rivaroxaban or low-molecular weight heparins.
    The Xa inhibitors and LMWH carry significant drug costs.
• **Arterial Thromboembolism**

  • Phases (arbitrary):
    - **Acute phase:** Pain + Vascular + Skel Muscle + Lower motor neuron signs
    - **Subacute:** ↓Pain, ↑Vascular supply (tail movement) ± Muscle & Neurologic improvement
    - **Chronic:** Functional + variable residual deficits or adverse outcomes (from severe rhabdomyolysis)

• What are the Outcomes in Cats with ATE?
  - Most cats are not released from hospital
  - Median survival in *retrospective* Mn study: 223 days; but only 77 days if in CHF
  - Revascularization is likely – median hospital stay of 2-3 days in Mn study (Smith, et al. JVIM 2003)
  - Personal experience: ~40% walk given time (72h) & support
  - **Client resources & motivation**
    - Veterinary perspective are critical factors
  - Therapy of acute ATE – see figure & reference notes. tPA has not been shown to be better than “conventional” therapy.

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<tr>
<th>Aggressive Analgesia</th>
<th>Decision re: Treatment Underlying Heart Disease</th>
<th>Clopidogrel Enoxaparin or Dalteparin (LMWH)</th>
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<tr>
<td>Fentanyl</td>
<td>Underlying Heart Disease</td>
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<td>Methadone / Morphine</td>
<td>Eval for: CHF &amp; Temp</td>
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<td>Home: buprenorphine (LA) tramadol or gabapentin</td>
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<td>? Tissue plasminogen activator (tPA): BLASTT: Negative results for the 48h endpoints</td>
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<td>Supportive care</td>
<td>Monitor temperature ECG &amp; Serum K⁺</td>
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<td>Plavix ± micro-dose ASA or LMW or alternatively Apixaban or rivaroxaban</td>
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<td>Home nursing care</td>
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• FATCAT secondary prevention trial (Hogan, et al., 2015)
  - MST longer for Clopidogrel ~14.8 months post ATE
  - MST ~6.4 months in the aspirin group (difference p = 0.019)

• **Thromboprophylaxis:** All cats receive clopidogrel; the author adds in aspirin (as a minimum; ≈5-10 mg/cat/day in the gel cap with clopidogrel) for cats with prior spontaneous echo contrast (smoke); auricular thrombus; low auricular emptying velocities (<20 cm/s). Instead of aspirin LMWH or rivaroxaban (or apixaban) can be used, accepting the lack of definitive clinical trial evidence for all combination therapies at the time of this writing. See reference notes for more details and antithrombotic therapy dosages.