Update on managing feline heart disease

Meg Sleeper VMD, DACVIM (cardio)
Gainesville, Florida

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Outline

- **Classification of cardiomyopathy**
- **Staging of cardiomyopathy**
- **Treatment of cardiomyopathy stages**
- **Sequelae of cardiomyopathy and treatments**
  - **Congestive heart failure**
  - **Arterial thromboembolic disease**

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Historical classification

- **Primary cardiomyopathies**
  - **Hypertrophic**
  - **Restrictive**
  - **Dilated**
  - **Unclassified**
- **Secondary cardiomyopathies**
  - **Metabolic**
  - **Infiltrative**
  - **Toxic**
  - **Inflammatory**

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Definition of cardiomyopathy phenotypes

Phenotype	Definition
Hypertrophic cardiomyopathy (HCM)	Diffuse or regional increased LV wall thickness with a nondilated LV chamber.
Restrictive cardiomyopathy (RCM)	
Endomyocardial form	Characterized macroscopically by prominent endocardial scar that usually bridges the interventricular septum and LV free wall, and may cause fixed, mid-LV obstruction and often apical LV thinning or aneurysm; LA or biatrial enlargement is generally present.
Myocardial form	Normal LV dimensions (including wall thickness) with LA or biatrial enlargement
Dilated cardiomyopathy (DCM)	LV systolic dysfunction characterized by progressive increase in ventricular dimensions, normal or reduced LV wall thickness, and atrial dilatation.
Arrhythmogenic cardiomyopathy (AC), also known as arrhythmogenic right ventricular cardiomyopathy (ARVC) or dysplasia (ARVD)	Severe RA and RV dilatation and often, RV systolic dysfunction and RV wall thinning. The left heart may also be affected. Arrhythmias and right-sided congestive heart failure are common.
Nonspecific phenotype	A cardiomyopathic phenotype that is not adequately described by the other categories; the cardiac morphology and function should be described in detail

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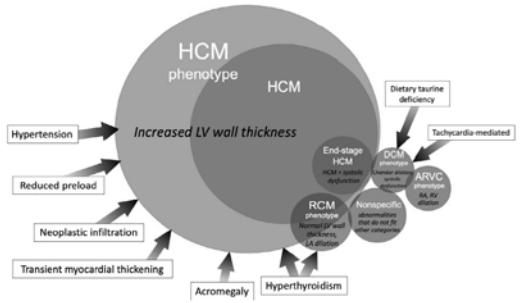
Classification of cardiomyopathy phenotypes



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Feline Murmurs

- **Prevalence of heart murmurs in overtly normal cats ranges from 16-44%.**
- Between 25% (Bonagura 2000) and 69% (Paige et al. 2009) of cats with murmurs on physical examination have no echocardiographic evidence of heart disease
- Many cats with cardiomyopathy have no auscultatory abnormality

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Hypertrophic cardiomyopathy (HCM)

- Prevalence of approximately 15% in general population and higher in older cats (up to 29% reported)
- Sex: Male > Female
- Breeds: Maine Coon, Ragdoll, Persian, American and British shorthair, Siberian, Norwegian forest cats, Scottish fold, Sphinx, Turkish Van, Himalayan, Birman
- Age: 6 months to 16 years (mean of 6 years)
- Approximately half of cats are asymptomatic and diagnosed incidentally
- Approximately half of cats diagnosed with heart failure secondary to HCM had a precipitating event
- Most cats have subclinical disease with a 5 year cumulative incidence of cardiac mortality of approximately 23%

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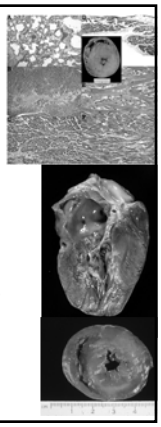
HCM- genetic screening



- Inherited as an autosomal dominant trait with incomplete penetrance in the Maine coon and Rag doll breeds
  - Disease apparent in most cats by 6 months to 2.5 years
- Inherited form of HCM has also been recognized in a family of American short hair cats, but pattern is less malignant than in the Maine coons
- > 1000 mutations have been recognized in 11 genes in humans

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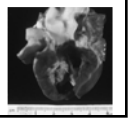
Restrictive cardiomyopathy (RCM)

- Endomyocardial form
  - Prominent endomyocardial scar, mid LV obstruction and often apical aneurysm
- Myocardial form
  - Normal LV dimensions (including wall thickness with LA or biatrial enlargement particularly late in the disease



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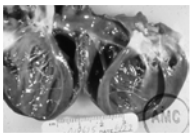
Dilated cardiomyopathy (DCM)

- Dilated heart with reduced systolic function
- Taurine deficient DCM is rarely diagnosed currently, although occasionally cats still respond to supplementation with taurine
- Abyssinian, Burmese and Siamese are over-represented



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Arrhythmogenic cardiomyopathy (AC)

- Rare form of cardiomyopathy in cats
- Fatty or fibrofatty infiltration of the RA and RV with subsequent dilation
- In case series of 12 cats, middle aged male DSH were most commonly affected
- Right ventricular wall may be thinned
- Ventricular tachyrhythmias are common

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Main indications for cardiology exam

History	Syncope Seizures (in the absence of other neurological abnormalities) Diagnosis of cardiomyopathy in a close relative Weakness Exercise intolerance/open-mouth breathing with exertion Intolerance to parenteral fluid administration Pedigree cat intended for breeding Maine coon or Ragdoll with a MyBPC3 mutation Any endocrinopathy Heartworm positive status Fever of unknown origin	Physical exam	Murmur Gallop sound or systolic click Muffled heart or lung sounds Arrhythmia Tachypnea Pulmonary crackles Jugular venous distention or pulsation Ascites Hypo- or hyperkinetic femoral arterial pulse pressure Acute paresis/paralysis Absent femoral arterial pulses
		Cats aged 9 years or older undergoing interventions that could precipitate CHF	General anesthesia Fluid treatment Extended-release glucocorticosteroids

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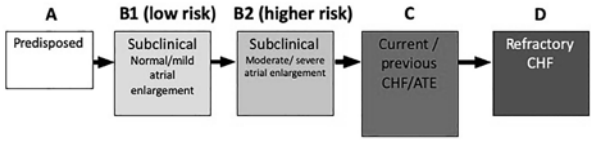
Staging system for feline cardiomyopathy



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Sequelae of cardiomyopathy

- Long subclinical progression (years)
- Congestive heart failure
- Feline arterial thromboembolic disease
- Sudden death

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Markers of poor outcome

- Gallop sound
- Arrhythmia
- Moderate to severe LA enlargement
- Decreased LA fractional shortening
- Extreme LV hypertrophy
- Decreased LV systolic function
- Spontaneous echo contrast or intracardiac thrombus
- Regional wall thinning with hypokinesis
- Restrictive diastolic filling pattern

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Markers of longer survival

- Reduction in nt-proBNP in response to therapy
- Resolution of CHF at recheck

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Cardiomyopathy- electrocardiography

- Cats experiencing episodic weakness and collapse (including seizure-like activity) should undergo a cardiovascular evaluation that includes echocardiography, ECG and telemetric or Holter ECG monitoring if necessary.
- Implantable loop recorders should be considered for cats with intermittent clinical signs that could be due to arrhythmias
- In some cases, use of a portable electrode plate (Kardia Alivecor) in conjuction with a smartphone is reasonable

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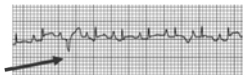
Cardiomyopathy-electrocardiography

- Body surface electrocardiogram



- Loop recorder

- K

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Cardiomyopathy- radiography

- Thoracic radiographs are insensitive for identification of mild or moderate heart changes in cats
- Radiographic pattern associated with cardiogenic pulmonary edema is highly variable in cats
- Restraint for radiographs can be dangerous in unstable patients
- Consider combination of physical exam, point of care ultrasound and point of care nt-proBNP in dyspneic patient (if radiographs not possible)

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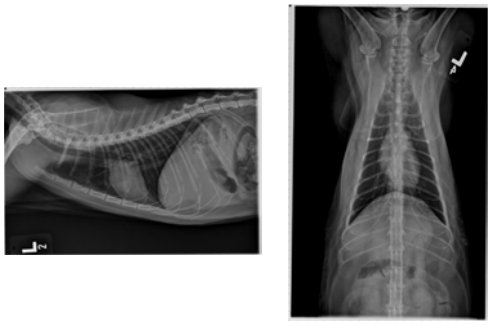
Cardiomyopathy- radiographs



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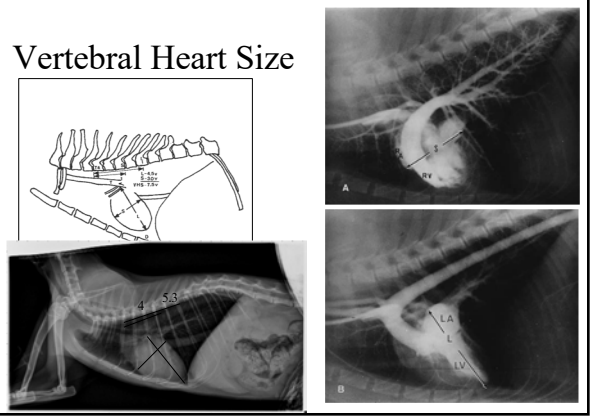
Vertebral Heart Size



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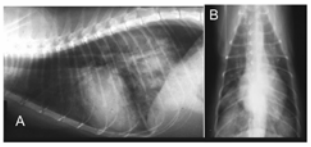
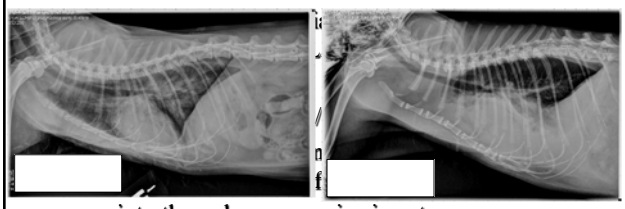
Congestive heart failure





into the pulmonary veins in cats

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Use of the vertebral heart scale for differentiation of cardiac and noncardiac causes of respiratory distress in cats: 67 cases (2002–2003)

Meg M. Sleeper, VMD, DACVIM; Risa Roland, DVM, DACVIM; Kenneth J. Drobatz, DVM, MSCE, DACVECC, DACVIM

Objective—To assess the effectiveness of the vertebral heart scale (VHS) system to differentiate congestive heart failure from other causes of dyspnea in cats.

Design—Retrospective case series.

Animals—67 cats with acute respiratory distress.

Procedures—Medical records of client-owned cats evaluated on an emergency basis because of acute respiratory distress during a 1-year period were reviewed. For study inclusion, cats must have undergone evaluation with echocardiography and thoracic radiography within 12 hours after hospital admission. The VHS was calculated for each cat by 2 investigators. Signalment, physical examination, and echocardiographic findings were reviewed for each patient.

Results—There was 83% agreement overall between the 2 investigators in assessment of cardiomegaly in cats with dyspnea (κ = 0.66). The VHS outperformed the same for both observers in terms of optimizing sensitivity and specificity. A VHS of > 8.0 vertebrae was the best cutpoint when screening for heart disease, whereas a VHS of > 9.3 vertebrae was very specific for the presence of heart disease. Measurements between 8.0 and 9.3 vertebrae suggested the cause of dyspnea was equivocal (ie, secondary to congestive heart failure or respiratory disease), in which case echocardiography would be most useful in providing additional diagnostic information.

Conclusions and Clinical Relevance—Results suggested that the VHS system may be a useful tool to help differentiate cardiac from noncardiac causes of respiratory distress in cats in an emergency situation when an echocardiogram is not available or is not plausible in an unstable patient. (*J Am Vet Med Assoc* 2013;242:366–371)

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Cardiomyopathy- Biomarkers

- Quantitative feline specific NT-proBNP using plasma or pleural fluid has good diagnostic accuracy but delay in results for external laboratory
- Point of care NT-proBNPis reasonably accurate and provides rapid results and should be considered when point of care ultrasound is not available
- When investigating cats with possible subclinical cardiomyopathy, the quantitative test can be considered when echo is not available
- Principle value of test is in differentiating cats with severe subclinical CM from normal cats or cats with only mild disease

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Cardiomyopathy- Biomarkers

- **CtnI is useful to discriminate between cardiac and noncardiac causes of respiratory distress, but only when results can be obtained rapidly**
- **May give prognostic value because an increased circulating cTnI is associated with increased risk of cardiovascular disease independent of LA size**

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Cardiomyopathy- Echocardiography

- **A focused point-of-care echocardiogram is feasible in first opinion practices with appropriate training and experience and can improve accuracy of diagnosis- especially in cats with more advanced disease**
- **When echo is unavailable, evaluation of NT-proBNP may be considered as a screening test for identifying advanced cardiomyopathy (normal NT-proBNP indicates low likelihood of cardiomyopathy that is imminently harmful**
- **Positive NT-proBNP should be followed by echo exam**

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Echo protocols for cardiomyopathy

Level of scan	Measurements	Qualitative assessment
Focused point-of-care		Note presence of: • Pleural, pericardial effusions • Left atrial size & motion • Pulmonary B-lines • LV systolic function
Standard of care	M-mode • IVSd, LVFWd • LVIDd, LVIDs, LV FS% • LA FS% 2D • IVSd, LVFWd • LVIDd, LVIDs • LA/Ao • LA diameter from RP long axis view	Note presence of: • Papillary muscle hypertrophy • End-systolic LV cavity obliteration • Papillary muscle/mitral leaflet abnormalities • SAM or mid LV obstruction • Dynamic RVOTO • Abnormal cardiac chamber geometry • Presence of spontaneous echo-contrast or thrombus • Regional wall motion abnormalities
Best practice	M-mode and 2D as for standard of care, with the following additional measurements: *Spectral Doppler* • Mitral inflow velocities • Isovolumic relaxation time • LVOT velocities • RVOT velocities • PVF velocities • LAA blood flow velocities *Tissue Doppler imaging* • Lateral and septal mitral annular velocities (pulsed wave Doppler mode).	Qualitative assessment as for standard of care

Screenshot

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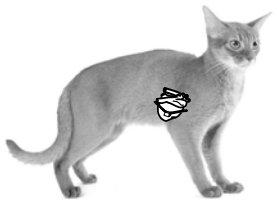
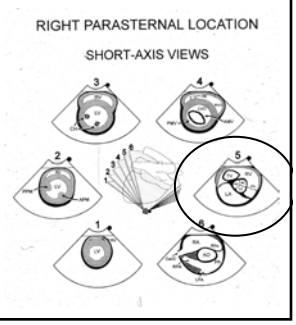
Echocardiogram- focused point of care



RV=right ventricle
LV=left ventricle
RA=right atrium

LA=left atrium
AO=aorta



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Echocardiogram- focused point of care

- **Note presence of:**
  - **Pleural, pericardial effusion**
  - **Left atrial size and motion**
  - **Pulmonary B lines**
  - **Left ventricular systolic function**

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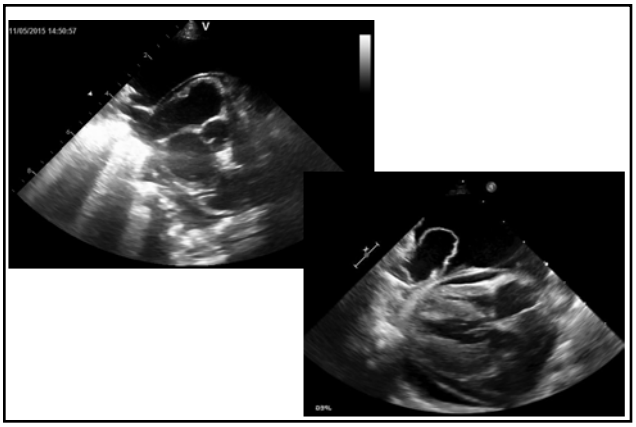

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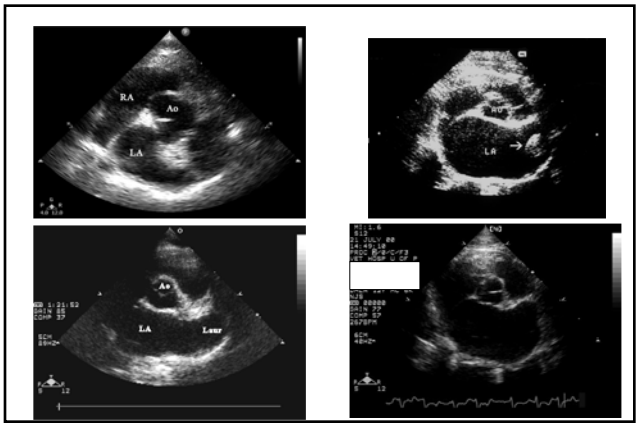

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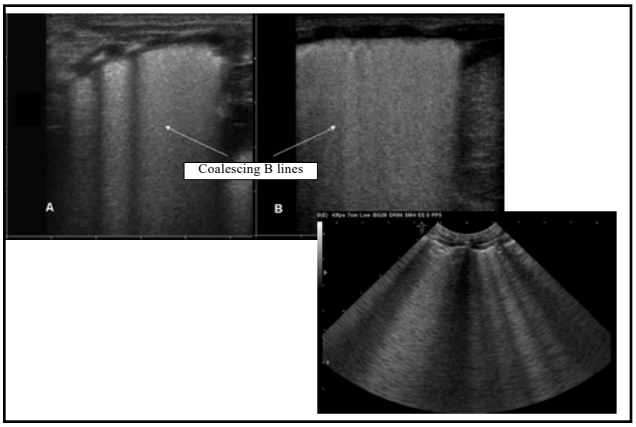

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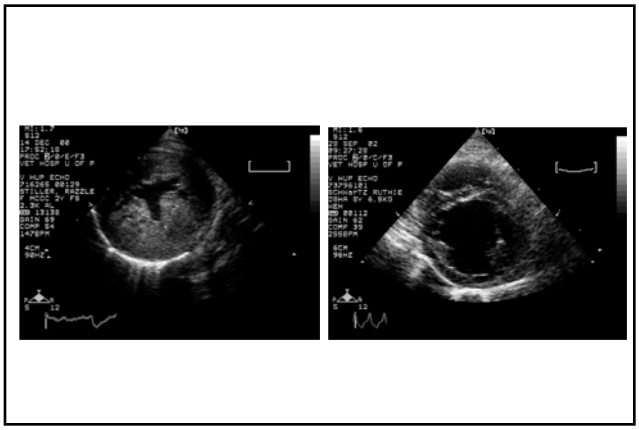

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Echocardiography

- Standard of Care
  - M-mode
  - 2D
  - Subjective assessment of:
    - Papillary muscles
    - Presence of SAM
    - Cardiac geometry
    - Regional wall abnormalities
    - Spontaneous contrast/thrombus
- Best practice
  - M-mode
  - 2D
  - Spectral Doppler
    - Valves
    - PVF and LAA velocities
  - Tissue Doppler
    - Lateral and septal mitral annular velocities

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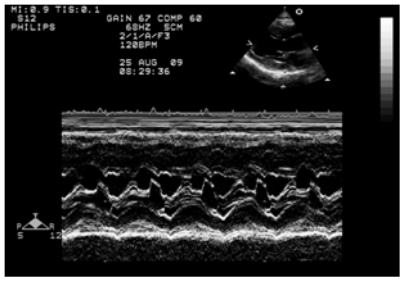
M-mode



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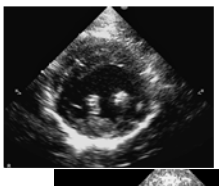
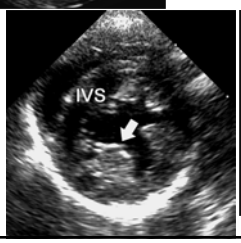
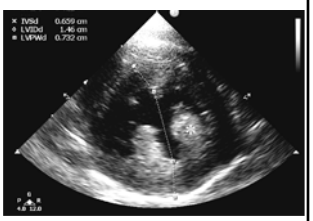


2-D echocardiography





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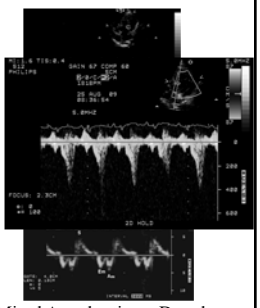
Doppler echocardiography

- Used to measure blood flow velocity and tissue velocity
  - Assess diastolic function
  - Diagnose restrictive cardiomyopathy (restrictive filling pattern
  - Diagnose LVOT obstruction



Mitral Annular tissue Doppler

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Possible cardiomyopathy outcomes

- Long, slowly progressive disease which never becomes symptomatic (or only very late in disease course)
- Sudden death
- Congestive heart failure
- Thromboembolic disease

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Feline cardiomyopathy treatment

- **Stage B1 (occult asymptomatic) cats**
  - No medications have been shown to alter progression of disease
  - Monitor annually for progression to stage B2
  - Risk for CHF or ATE is low
  - In specific cases, treatment may be considered
    - Systolic dysfunction or dilated cardiomyopathy
    - Symptomatic arrhythmias

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Feline cardiomyopathy treatment

- Stage B2
  - If left atrial enlargement is moderate to severe>> **clopidogrel**
  - Treat symptomatic arrhythmias
  - Resting respiratory rate monitoring by owner
  - Balance re-examination benefits vs. stress
  - Generally annual exams recommended, but therapy unlikely to change until clinical signs develop

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Cardiomyopathy- treatment (Stage C)

- **Symptomatic cats with congestive heart failure**
  - ***Acute stage***
    - Furosemide- 1-2 mg/kg every 1-2 hours until RR decreases significantly or CRI
    - Oxygen therapy
    - Sedation with an anxiolytic (eg butorphanol)
    - Minimize stress
    - Thoracocentesis if pleural effusion

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Cardiomyopathy- treatment (Stage C)

- **Symptomatic cats with congestive heart failure**
  - ***Acute stage (continued)***
    - IV fluid therapy is contraindicated in cats with clinically evident CHF
    - Ideally blood chemistry prior to treatment if possible, but diuretic therapy necessary for CHF regardless of azotemia
    - If low cardiac output signs that do not improve, consider pimobendan or CRI of dobutamine
    - Nitroglycerin has never been shown effective in cats, but unlikely to cause adverse effects
    - NEVER START BETA BLOCKERS IN ANIMALS WITH UNCONTROLLED CHF

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Cardiomyopathy- treatment (Stage C)

- **Symptomatic cats with congestive heart failure**
  - *Acute stage (following discharge)*
    - Discharge to owners care as soon as possible to minimize stress
    - Owners should be instructed to monitor resting RR
    - Re-examination in 3-7 days to ensure resolution of CHF and to evaluate renal function and electrolytes
      - If normal renal function, consider adding ACE inhibitor
      - Pimobendan in cats without clinically relevant LVOTO

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Cardiomyopathy- treatment (Stage C)

- **Symptomatic cats with congestive heart failure**
  - *Chronic stage*
    - Furosemide- 0.5-2 mg/kg twice daily
    - ACE inhibitor (enalapril or benazepril)- 0.5 mg/kg once to twice daily
    - Rhythm control if necessary (atenolol or diltiazem)
    - +/- Anticoagulant therapy
    - +/- Pimobendan (if systolic dysfunction)
    - Recheck frequency?

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Cardiomyopathy- treatment (Stage D)

- **Refractory cardiomyopathy**
  - Torsemide may be considered in place of furosemide starting at 0.1-0.2 mg/kg PO q 24 hours and titrating up to effect
  - Spironolactone at 1-2 mg/kg S-BID
  - Taurine supplementation at 250 mg BID in cats with systolic dysfunction unless taurine in normal range
  - Avoid high salt diets, but avoidance of cardiac cachexia is most important
  - Monitor serum potassium

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Prevalence of ATE

- 17 year retrospective study at the U of Penn evaluated 3400 feline necropsies
  - 131 (3.9%) had TE disease as a major factor contributing to death
    - 70 had saddle thrombi associated with heart disease
    - 38 had TE in other vessels associated with
      - Heart disease (n=2)
      - Neoplasia (n=9)
      - Multisystemic inflammation/sepsis (n=12)
      - Hyperthyroidism (n=3)
      - Other (n=12)

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Prevalence of ATE

- Reported prevalence in cats with heart disease ranges from 12-28%
- In the general feline population, the reported prevalence ranges from 1 in 142 to 1 in 175 cats.

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Clinical presentation

- Signalment
  - Males may be overrepresented
  - Age range of 1-20 years (mean of 7.7 and a median of 10.5 years)
- Clinical manifestation
  - Depends on site of embolization with distal aorta being most common and less commonly a foreleg or various abdominal organs, duration of occlusion, and collateral circulation

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Presentation

- Peracute paresis
- Evidence of pain (vocalization, tachypnea)
- Congestive heart failure (dyspnea, tachypnea)
- Auscultation findings may be normal or suggest underlying heart disease (gallop, murmur, arrhythmia)
- Dehydration and hypothermia
- Firm cranial tibial and gastrocnemius muscles
- Less commonly: azotemia, bloody diarrhea, neurologic signs, sudden death

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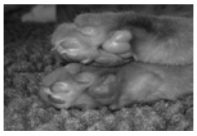
The 5 "P"s

- Paralysis
- Pain
- Pulselessness
- Pallor
- Poikilothermia



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Differential diagnosis

- Trauma
- Intervertebral disc extrusion
- Neoplasia
- Fibrocartilaginous infarction

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Diagnostic testing

- Minimum data base
  - Biochemical profile and urinalysis
  - Thoracic radiographs
    - If tachypnea/dyspnea
  - Electrocardiography
    - If arrhythmia present
  - Echocardiography

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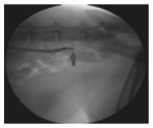
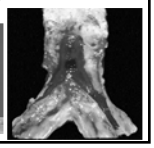
Thromboembolic Disease



- Feline patients with cardiomoypathy are predisposed:
  - Virchow's triad (prerequisites of thrombogenesis)
    - Abnormal endothelial surface
    - Abnormal blood flow (LA enlargement)
    - Increased coagulability



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Pathophysiology

- Lack of blood supply results in coagulative necrosis
  - tissue architecture is maintained because lysosomal enzymes are denatured
- Affected tissue appears paler than well vascularized tissue
- Following injury, muscle cells will undergo mitosis and replication

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Acute case management- FATE

- Manage pain
- Therapies to limit thrombus growth or future thrombus formation
- Control congestive heart failure and/or arrhythmias when present
- General supportive care

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ATE positive prognostic findings

- Normothermia
- Only one limb affected
- Absence of CHF

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Analgesia

- **Fentanyl**
  - 2-5 µg/kg/hr as a CRI until fentanyl patch takes effect
- Butorphanol
  - 0.1-0.2 mg/kg IV every 4 to 6 hours
- Buprenorphine
  - 0.005-0.015 mg/kg IV every 6 to 8 hours
- **Methadone**
  - 0.1-1.0 mg/kg IM or SQ q 4 to 6 hours
  - 0.05-0.2 mg/kg IV q 4 to 6 hours

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Acute anticoagulant therapy

- No effect on established thrombi
- Therapy is to prevent or reduce thrombus extension
  - Heparin
    - Unfractionated
    - Low molecular weight
  - Clopidogrel
  - Xa inhibitors
  - Aspirin
  - Combination therapy

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Heparin- unfractionated

- In normal cats a dose of 250-300 U/kg SQ every 8 hours (IV if in shock)
- aPTT and ACT are not particularly predictive of plasma heparin concentrations and anticoagulation
- Traditional goal has been to maintain aPTT or ACT at 1.5-2.5 times pretreatment
- Chromogenic factor Xa assay is more accurate, but less available

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Heparin- low molecular weight

- Unable to inactivate thrombin, but maintain ability to inhibit other clotting factors
- Do not alter aPTT and PT times; best way to assess activity is anti-Xa activity (proposed target of 0.3-0.6 U/mL)
- More predictable availability and less frequent dosing in humans
- No advantage over UF heparin in acute stage (when hospitalized and can give TID dosing)
- Unclear advantage in general: rapidly eliminated in normal cats and twice daily dosing appears inadequate.
- Monitoring of effect probably warranted

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Monitoring efficacy of LMWH

- Anti-Xa assay
  - Cornell University Department of Population Medicine and Diagnostic Sciences Comparative Coagulation Service
  - http://www.diaglab.vet.cornell.edu/coag/
- Thromboelastography
  - Bedside blood test assessing viscoelastic properties of blood
  - Not widely available

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LMWH doses

- Dalteparin 150 IU/kg SQ q 4 hours
- Enoxaparin 1.5 mg/kg SQ q 6-8 hours

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Clopidogrel

- Thienopyridine derivative which interferes with primary and secondary platelet aggregation
- Dose: 18.75 mg/cat once daily
- FATCAT trial demonstrated superiority compared to aspirin therapy
  - Clopidogrel significantly prolonged time to subsequent thrombotic event compared to aspirin

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Xa inhibitors

- Consensus statement JVIM 2018
  - Insufficient data to make recommendations regarding this class of drug compared to clopidogrel or aspirin, but appear subjectively to be safe and effective antiplatelet agents
  - Both rivaroxaban and apixaban appear to have reliable pharmacokinetic and pharmacodynamic properties and were well tolerated in cats
  - Ongoing study evaluating rivaroxaban in cats with spontaneous disease (Super-Cat Trial)

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Aspirin

- When aspirin was given 1 hour before thrombus occlusion of the aorta, cats had better collateral circulation than those without aspirin
- Optimal dose has not been established for cats, but no difference between low (5 mg/cat q 72 hours) and high (>40 mg/cat q 24 hours) in ATE occurrence
- The FATCAT trial demonstrated superiority of clopidogrel compared to aspirin in cats with a history of ATE
- Unclear efficacy, but unlikely to cause adverse effects

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Combined anticoagulation therapy

- Human studies suggest combined therapy may be superior
- Veterinary studies are lacking, but some veterinary cardiologists recommend combined therapy in particularly high risk patients

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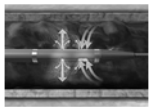
Thrombolytic therapy

- Streptokinase, urokinase and tissue plasminogen activator use have not altered outcome in case series so far published
- Similar results when using a rheolytic thrombectomy system (n=6)



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Thoracic radiographs

- May help screen for left atrial enlargement
- 40-60% of affected cats have congestive heart failure
- Tachypnea can be due to pain or CHF
- Screen for pulmonary neoplasia, particularly if LA size is normal

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Electrocardiography

- 85% of affected cats have abnormalities on ECG
  - Ventricular enlargement pattern (39%)
  - Ventricular premature beats (19%)
  - Supraventricular premature beats (19%)
  - Prolongation of the QRS interval (16%)
  - Left atrial enlargement pattern (16%)
  - Bradycardia or atrial standstill with a sinoventricular rhyhtm suggests hyperkalemia

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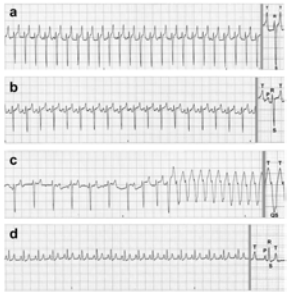
ECG- Hyperkalemia



Hyperkalemia can be addressed with:
*10% calcium gluconate (0.5-1.5 mL/kg IV slowly over 5 to 10 minutes and/or
*insulin and glucose to drive K+ intracellularly

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Echocardiography

- Echocardiography is not necessary to diagnose ATE and in an acute crisis management of ATE or CHF takes priority
- Extracardiac etiologies of thromboembolism should be considered in cats without left atrial enlargement
- Smoke or spontaneous echocardiographic contrast is associated with intracardiac blood stasis and may be a risk factor for ATE

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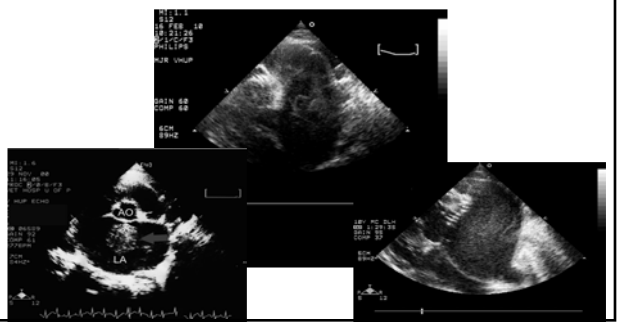
Echocardiography- FATE



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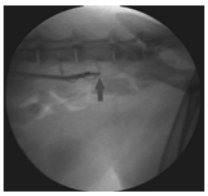
Invasive diagnostic techniques

- Rarely necessary, but occasionally additional techniques may be useful
  - Abdominal ultrasound
  - Angiocardiography
  - Nuclear scintigraphy



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Nursing care

- Address poor systemic perfusion (primary cause of hypothermia)
  - Cautious fluid therapy with vigilant monitoring of RR, effort and auscultation for development of a gallop sound
  - Cautious warming (avoid peripheral vasodilation and worsening of core perfusion)
- Excellent nursing care and clinical laboratory monitoring
- Physical therapy

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Post ATE

- RE-examination in 3-7 days and 1-2 weeks after ATE event
  - Electrolyte status
  - Appetite and treatment compliance
  - Improvement in neuromuscular function
  - Distal limbs for necrosis

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Complications and long term monitoring

- Underlying heart disease if present
- Chronic ambulation issues
- Irreversible loss of limb viability and necrosis
- Repeat TE events
  - Recurrence rates range from 20-75%

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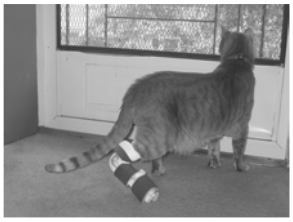
Permanent ambulation limitations

- Atrophy of cranial tibial muscle group can lead to permanent flexure of the metatarsus



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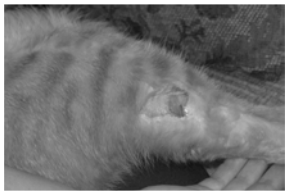
Soft tissue necrosis

- Aggressive wound management
- If severe, some cases benefit from amputation



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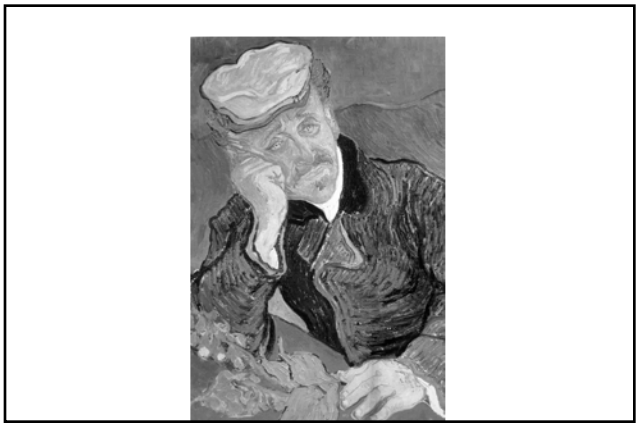

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