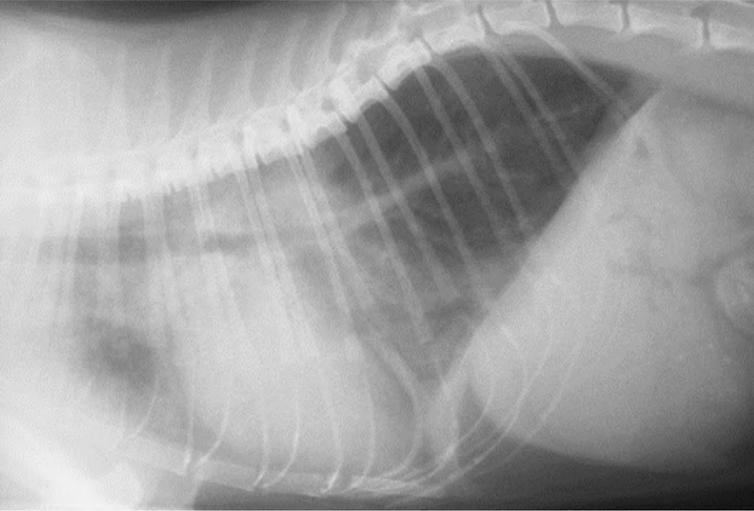
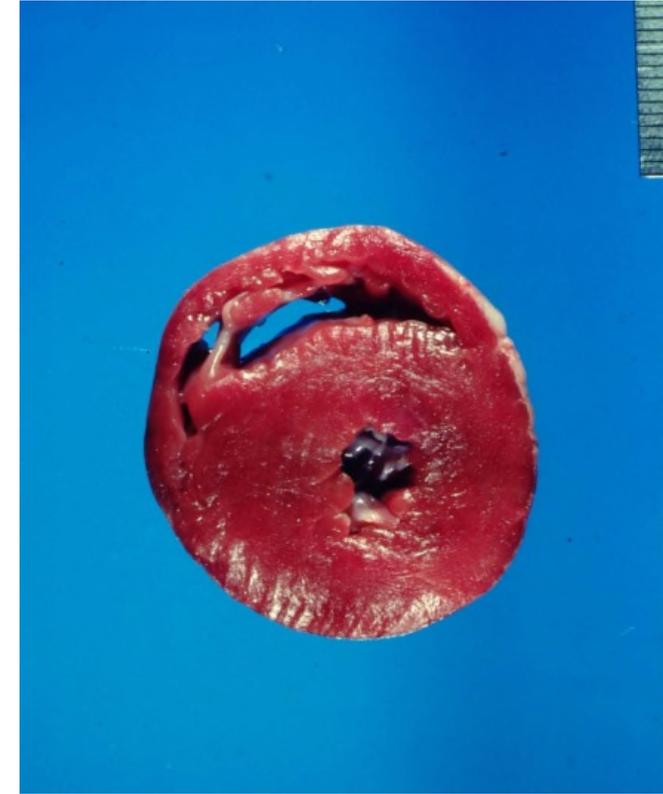


Feline Cardiomyopathy



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Disclosures

Recent Research Support, Sponsored Lecture, or Advisory Activity

Nestle Purina

Royal Canin Pet Foods

Idexx

Boehringer Ingelheim Vetmedica

Talk Overview

- Concentrate on Feline Hypertrophic Cardiomyopathy
 - Overall Feline HCM thoughts
 - Asymptomatic Feline HCM
 - LV hypertrophy, no outflow obstruction, no LA enlargement
 - LV hypertrophy and LV outflow tract obstruction
 - LV hypertrophy and moderate to marked LA enlargement
 - Feline HCM with Congestive Heart Failure
 - Diagnosis and initial management of CHF
 - Management of advanced CHF
 - Feline HCM and Arterial Thromboembolism
 - Prevention of ATE
 - Diagnosis and Management of ATE
- Other forms of Feline Heart Disease

Feline Hypertrophic Cardiomyopathy

- Most common cardiovascular disease in the cat
- Most common cause of:
 - ♥ CHF
 - ♥ Arterial thromboembolism
- Also causes:
 - ♥ Syncope
 - ♥ Sudden death
 - ♥ Unexpected anesthesia death
 - Risk 1:2000 >>>> 1:100?



Hypertrophic Cardiomyopathy

Main Pathologic Features

- Concentric or asymmetric LV hypertrophy
 - ♥ Thickening of the ventricular walls
 - ♥ Small LV internal cavity in systole (+/-)
 - ♥ Papillary muscle hypertrophy
 - ♥ Myocardial fiber disarray (+/-)
 - ♥ Fibrosis (+/-)
 - ♥ Coronary arteriosclerosis
- Left atrial enlargement
- Right heart enlargement and RVH



Hypertrophic Cardiomyopathy

Pathophysiology

- Typically, HCM is a disease of diastolic dysfunction
 - Hypertrophy leads to increased LV mass
 - Most coronary flow occurs during diastole
 - Tachycardia shortens the duration of diastole
 - Tachycardia >>> limits coronary flow to hypertrophied myocardium
- Systolic function is usually normal
 - Might not be true on the myocyte level
 - Latter stages of HCM can have reduced contractile function
- Reduced LV compliance leads to atrial enlargement
- Myocardial hypoxia/ischemia/fibrosis >>> arrhythmias

What Causes Feline HCM?

- Mutations of sarcomeric proteins
- Abnormalities identified in humans
 - B-Myosin heavy chain, Troponin T
 - Myosin binding protein C
 - > 700 specific mutations identified
- Abnormalities in cats
 - Sphynx cat – ALMS1 gene
 - Maine Coon cat and Ragdoll cat - Myosin binding protein C
 - MYH7 mutation
 - Should genetic testing be done?
 - Increased susceptibility to disease
- Role of the environment?
 - Head size, BCS and over-conditioning, nutrition role?

Feline Cardiomyopathy

Disease Manifestations

- Asymptomatic cat
- Congestive Heart Failure (CHF)
- Arterial Thromboembolism (ATE)
- Syncope
- Sudden Death
 - Anesthesia death or complication



The first clinical manifestation of cardiac disease is usually a “crisis” event

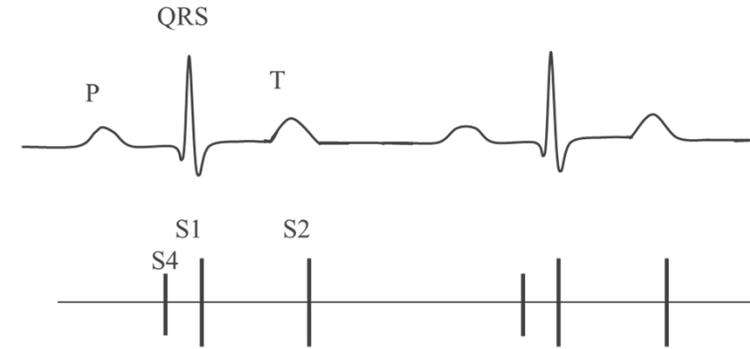
Feline Hypertrophic Cardiomyopathy

History

- Any breed
 - ♥ DSH, DLH, Maine coon, Ragdoll, American shorthair, Persian, Himalayan, Norwegian forest cat, Birman
- Any age
- Male (65%) > female (35%)
- Cardiac murmur or gallop
- Cough is less common (Ddx - asthma, HW, others)
- Dyspnea, open mouth breathing
- Lethargy, weakness, hiding, anorexia, vomiting
- Syncope
- Limb weakness/paralysis
- Recent stress, anesthesia, fluids, steroids
 - (esp. long-acting steroids e.g., DepoMedrol)

Physical Examination

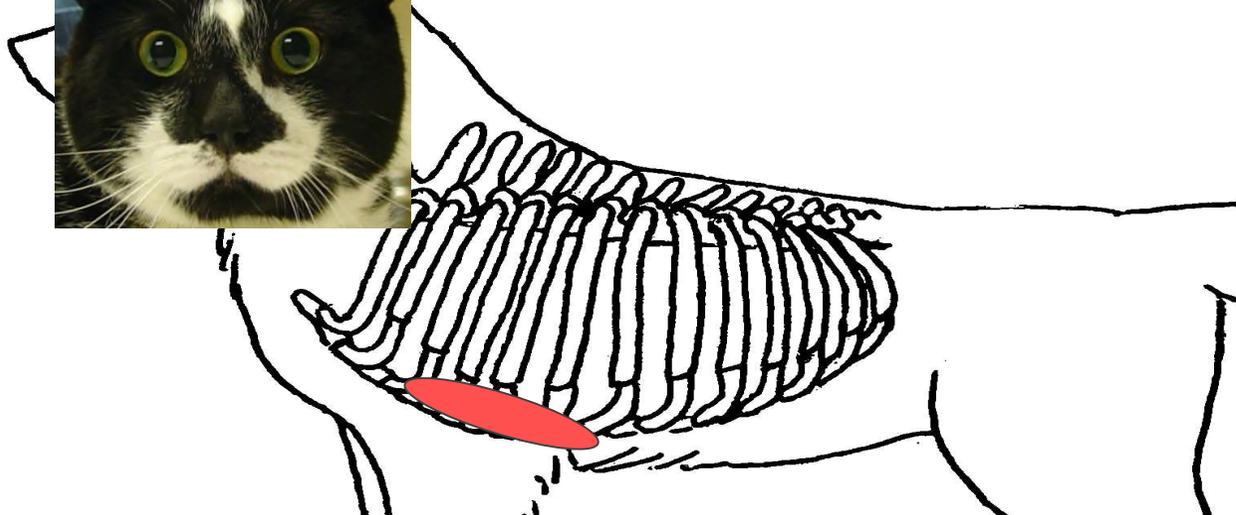
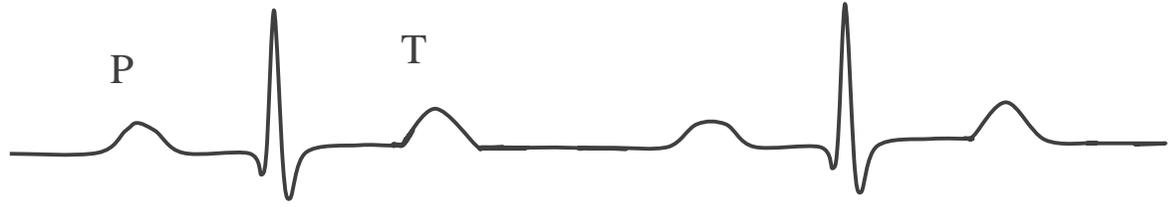
- Cardiac murmur - sternal borders
- Cardiac gallop (S4) - Try the bell!
- Arrhythmia
- Respiratory distress
 - ♥ Pulmonary crackles (pulmonary edema)
 - ♥ Dull lungs ventrally (pleural effusion)
- Jugular vein distention (Pleural effusion, hepatomegaly)
- Variable membrane color and refill time
- Weak arterial pulses
- Hypothermia if CHF or arterial thromboembolism
 - ♥ Heart rate and Temperature related; lower temp slower HR
- Signs of arterial thromboembolism



HSS Slow comes and goes

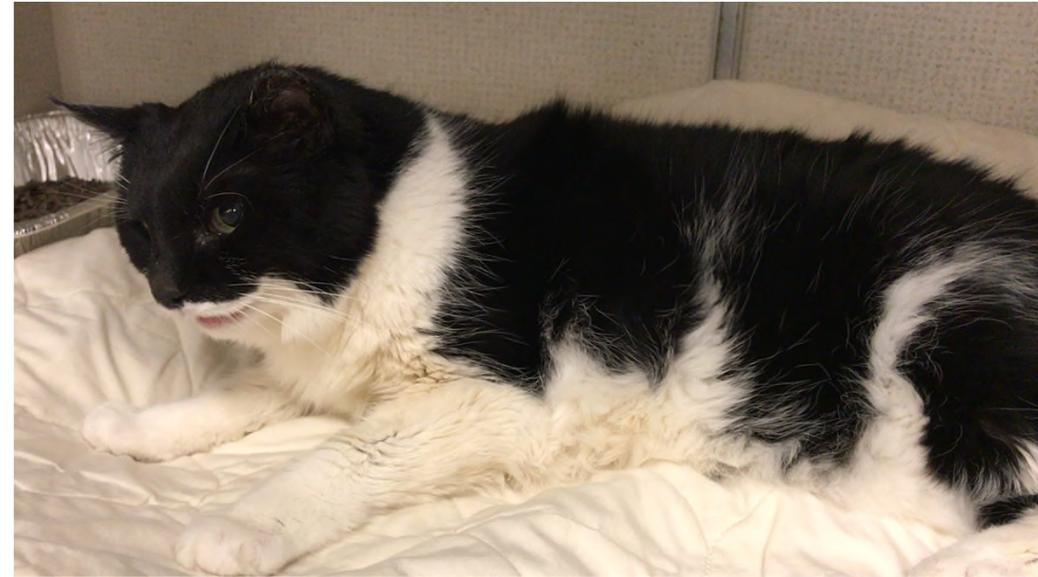


QRS

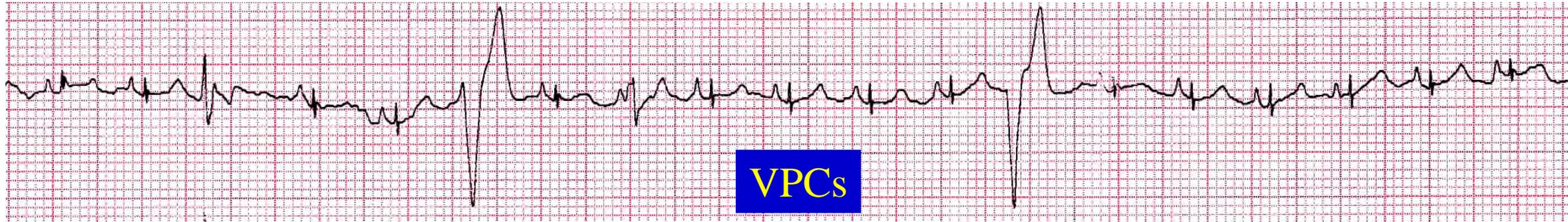


Resting/Sleeping Respiratory Rate and Effort

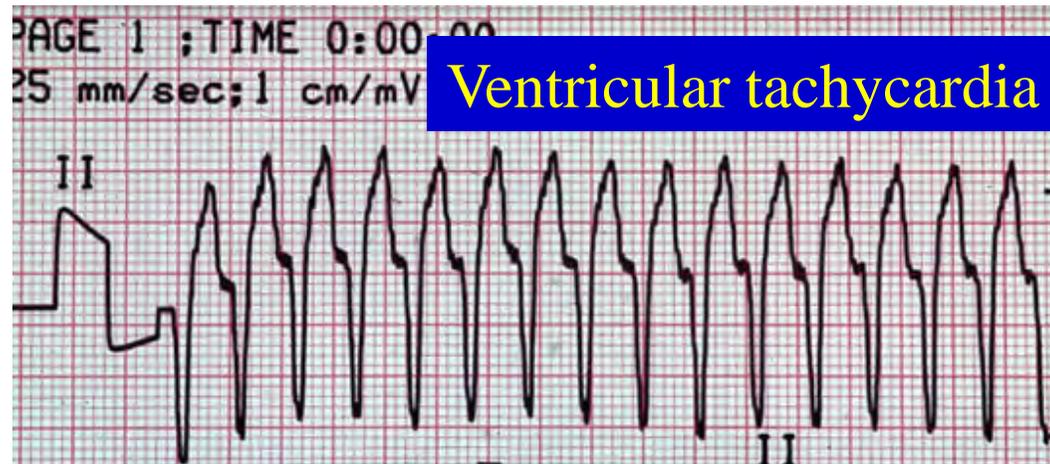
- Most cats < 35 breaths/minute at rest
- Most cats minimal body wall/abdominal effort
- Purring leads to both increased effort and breathing rate
 - Check for no purring before getting RR and effort
- Cats with CHF controlled have RR < 35 /min
 - Cats with RR > 35 /min \gg More diuretics



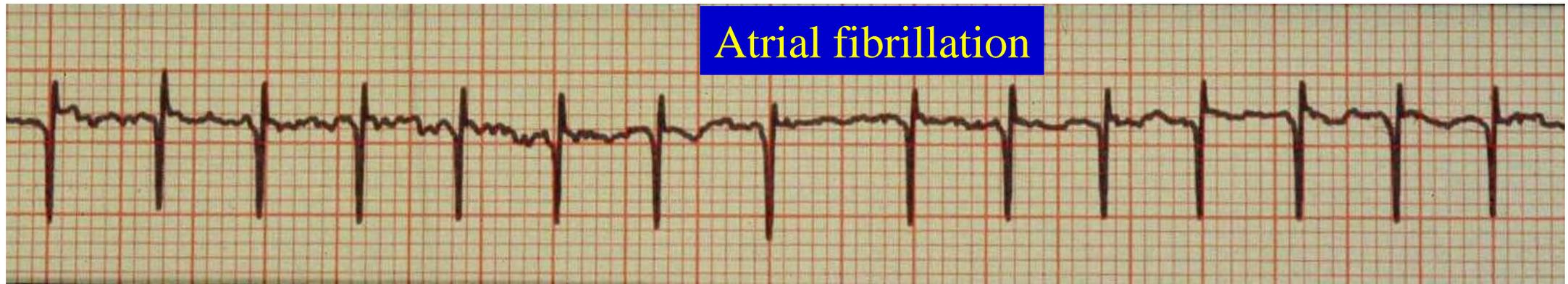
Electrocardiography



VPCs



Ventricular tachycardia

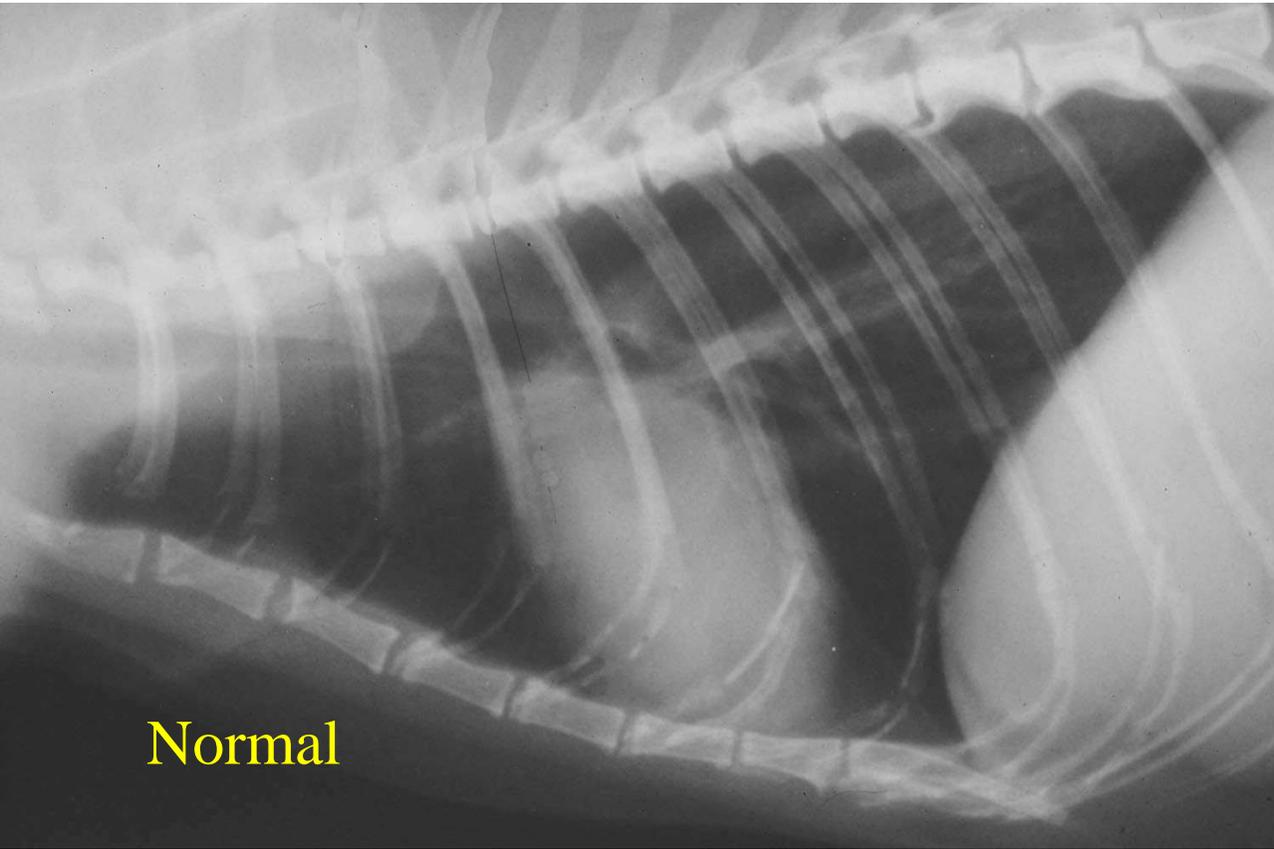


Atrial fibrillation

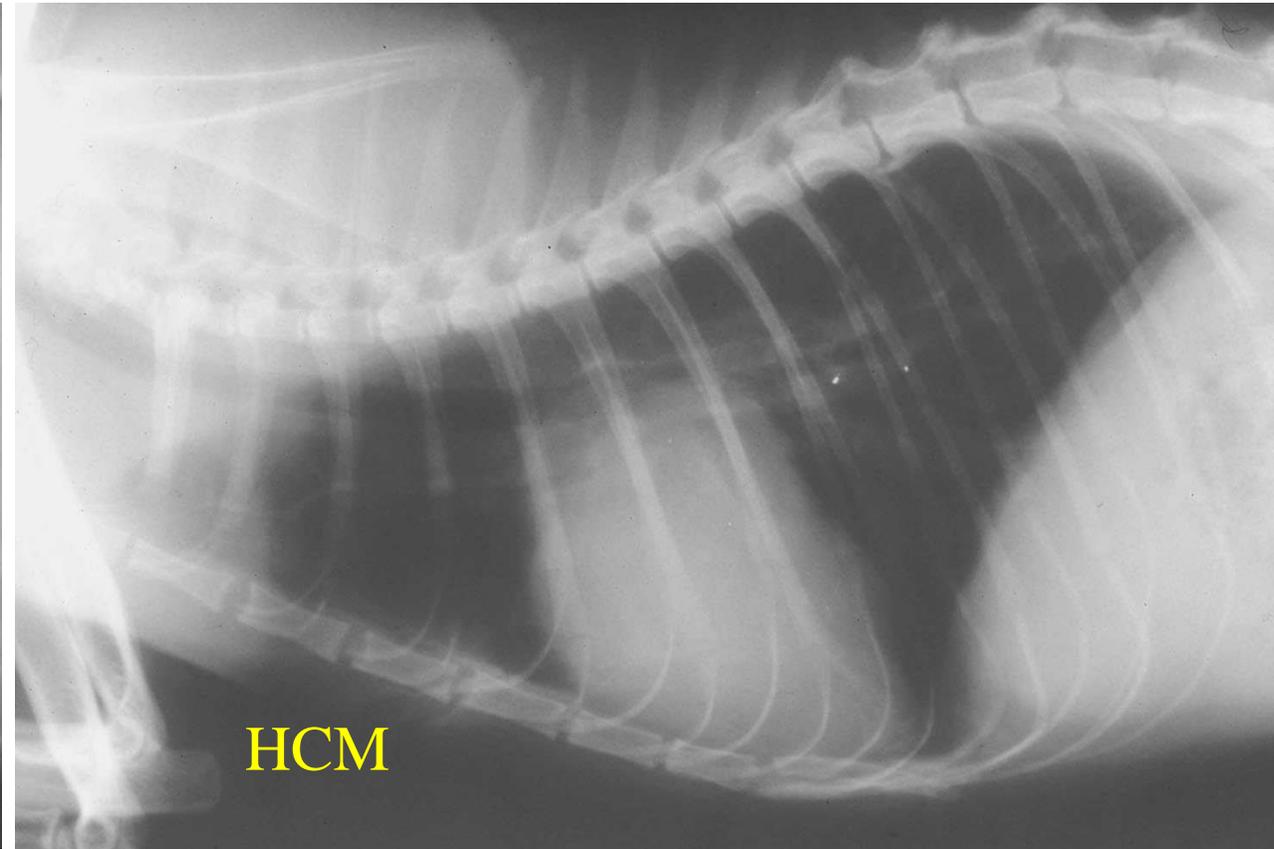
Thoracic Radiographs

- Cardiomegaly
 - DV view helpful
 - +/- Valentine-shaped heart
 - VHS $> 8.5v$ on lateral view if CHF
- Enlarged pulmonary artery and vein if CHF
- Pulmonary infiltrates
 - Variable location
 - Often perihilar and caudodorsal
- Pleural effusion
- Hepatomegaly

Thoracic Radiographs



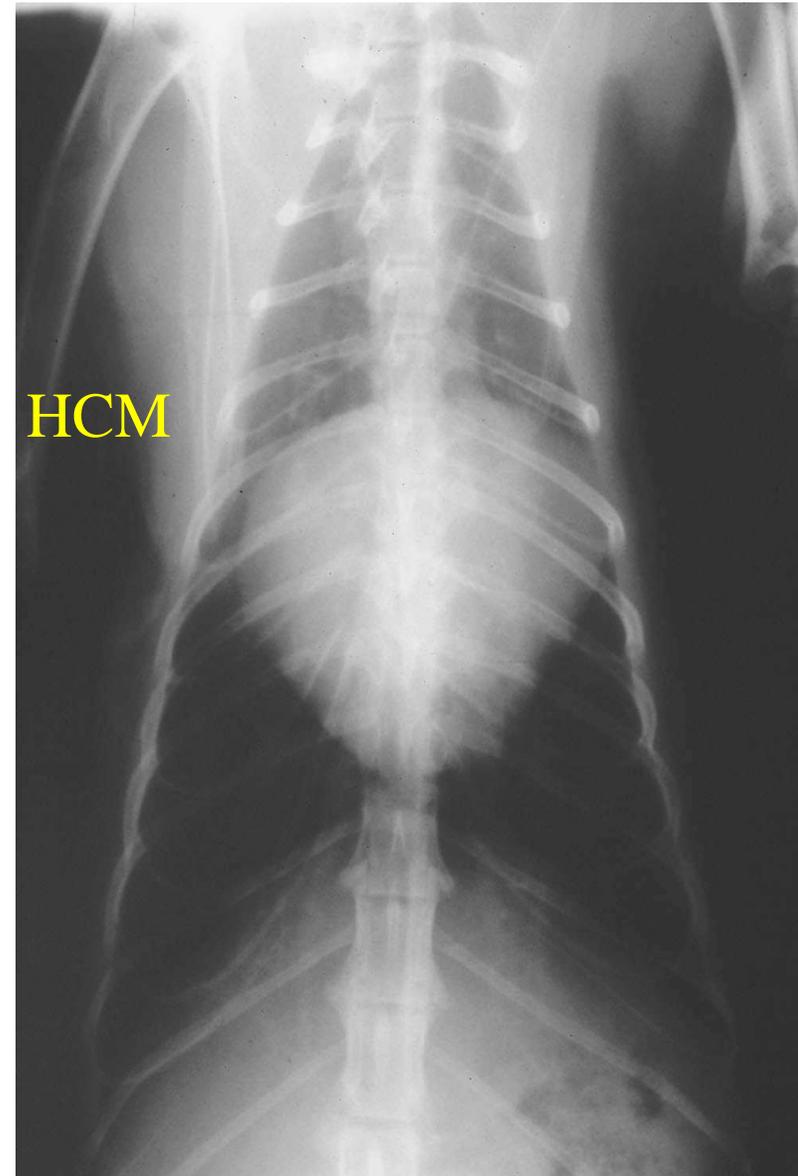
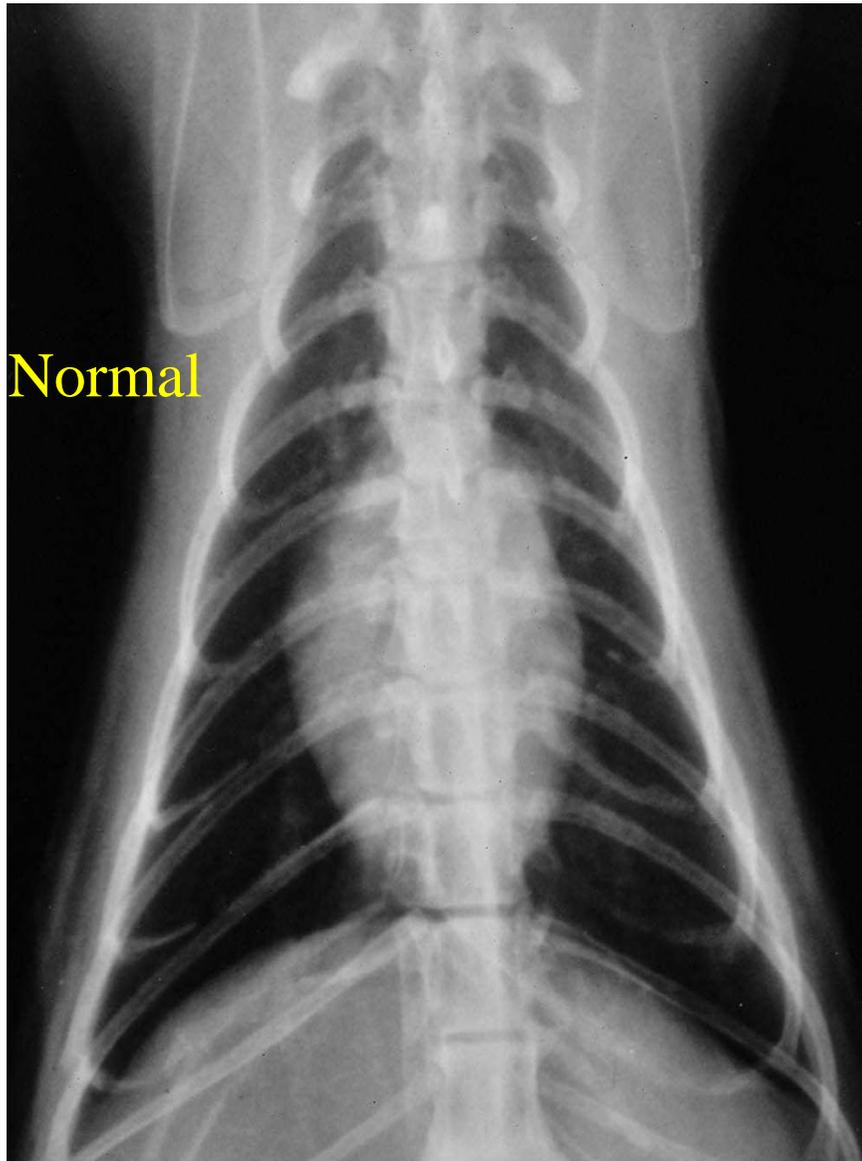
Normal



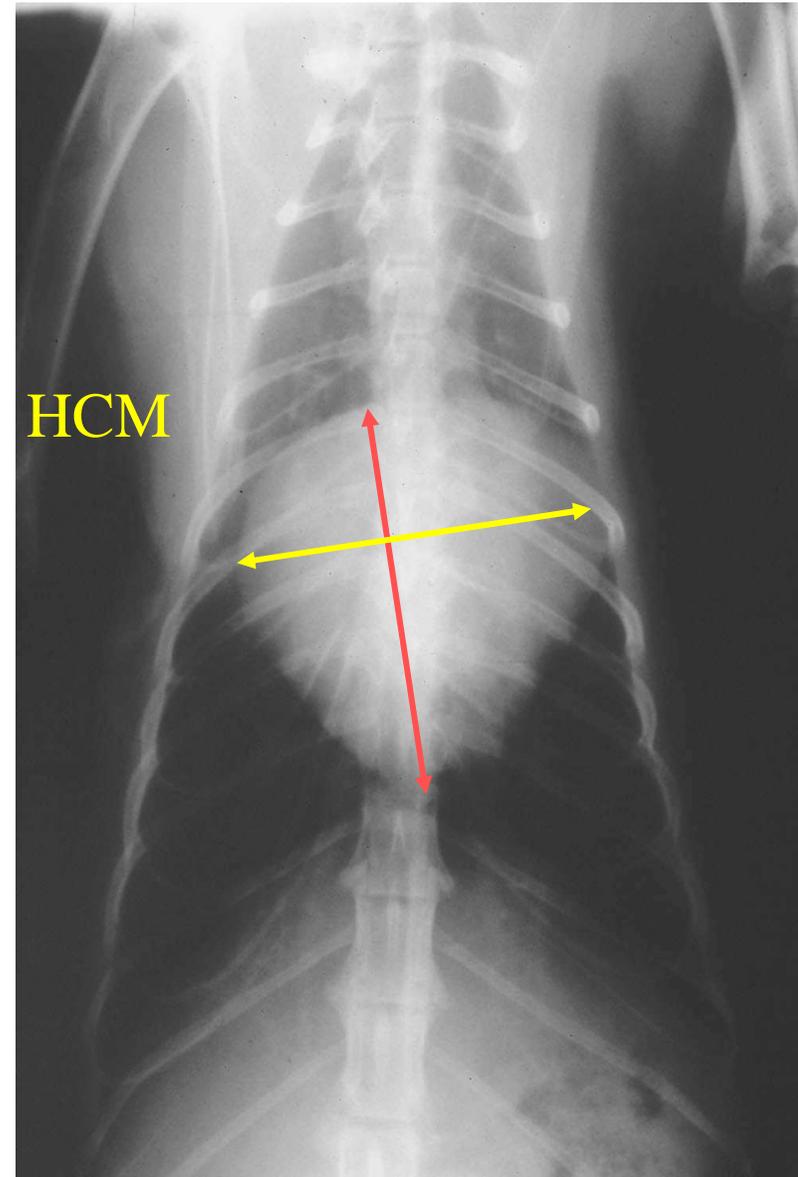
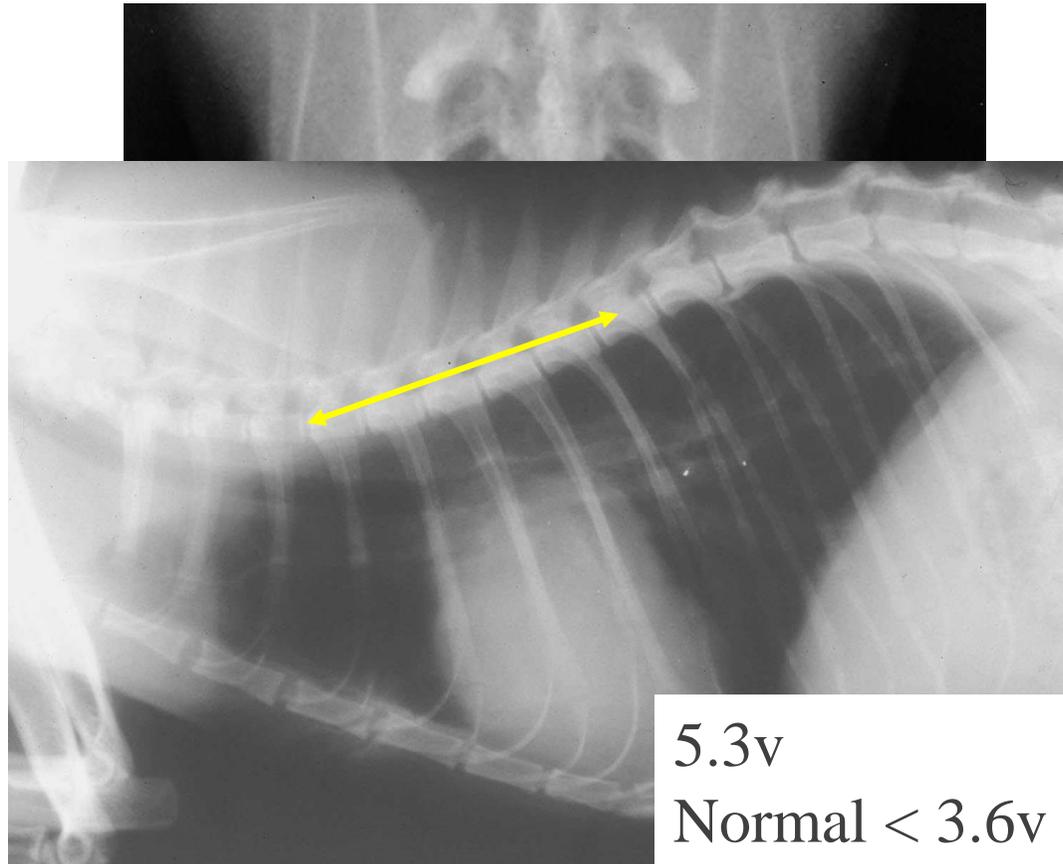
HCM

Cardiomegaly: VHS = 9.8v (> 8.5 v)

Thoracic Radiographs

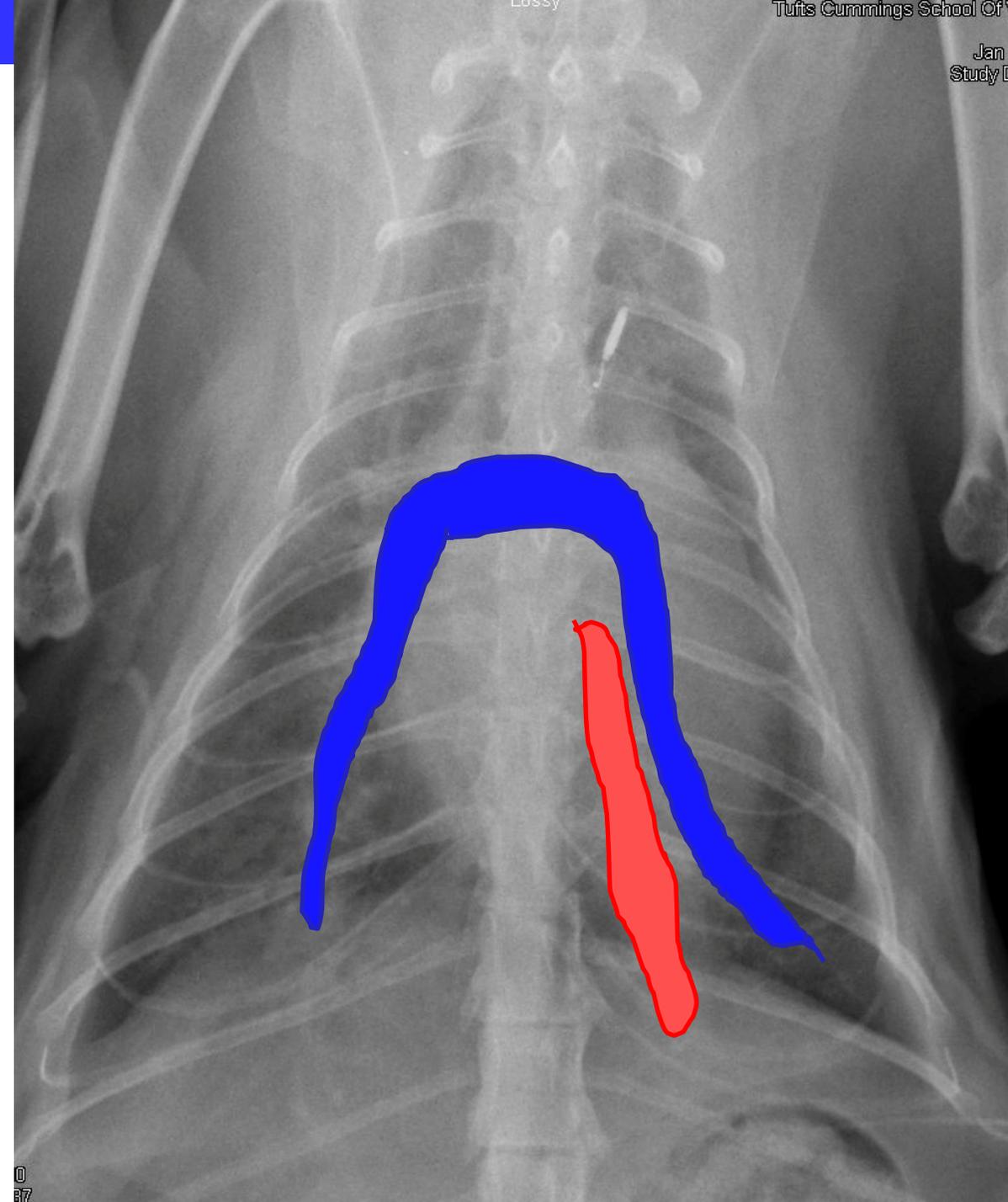


Thoracic Radiographs



Pulmonary Artery and Vein are both enlarged

- Classically, left-sided CHF leads to pulmonary vein distension only
- Cats often have both PA and PV enlarged, especially in chronic CHF



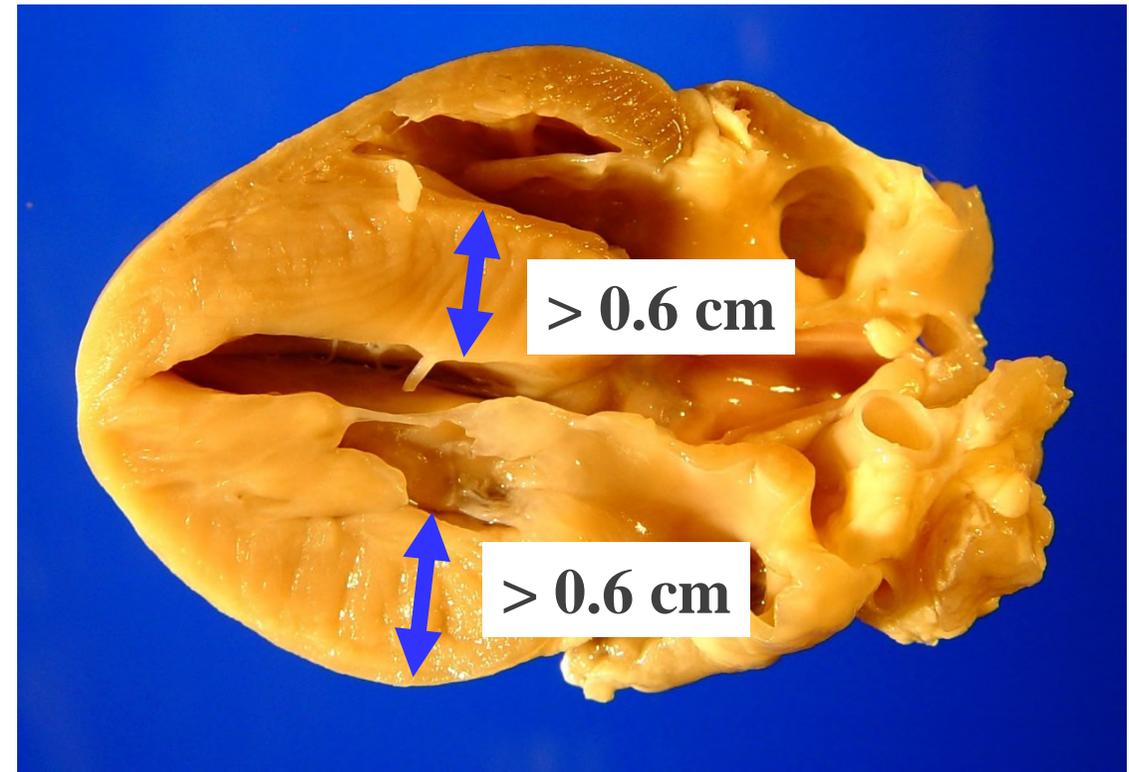
Thoracic Radiographs



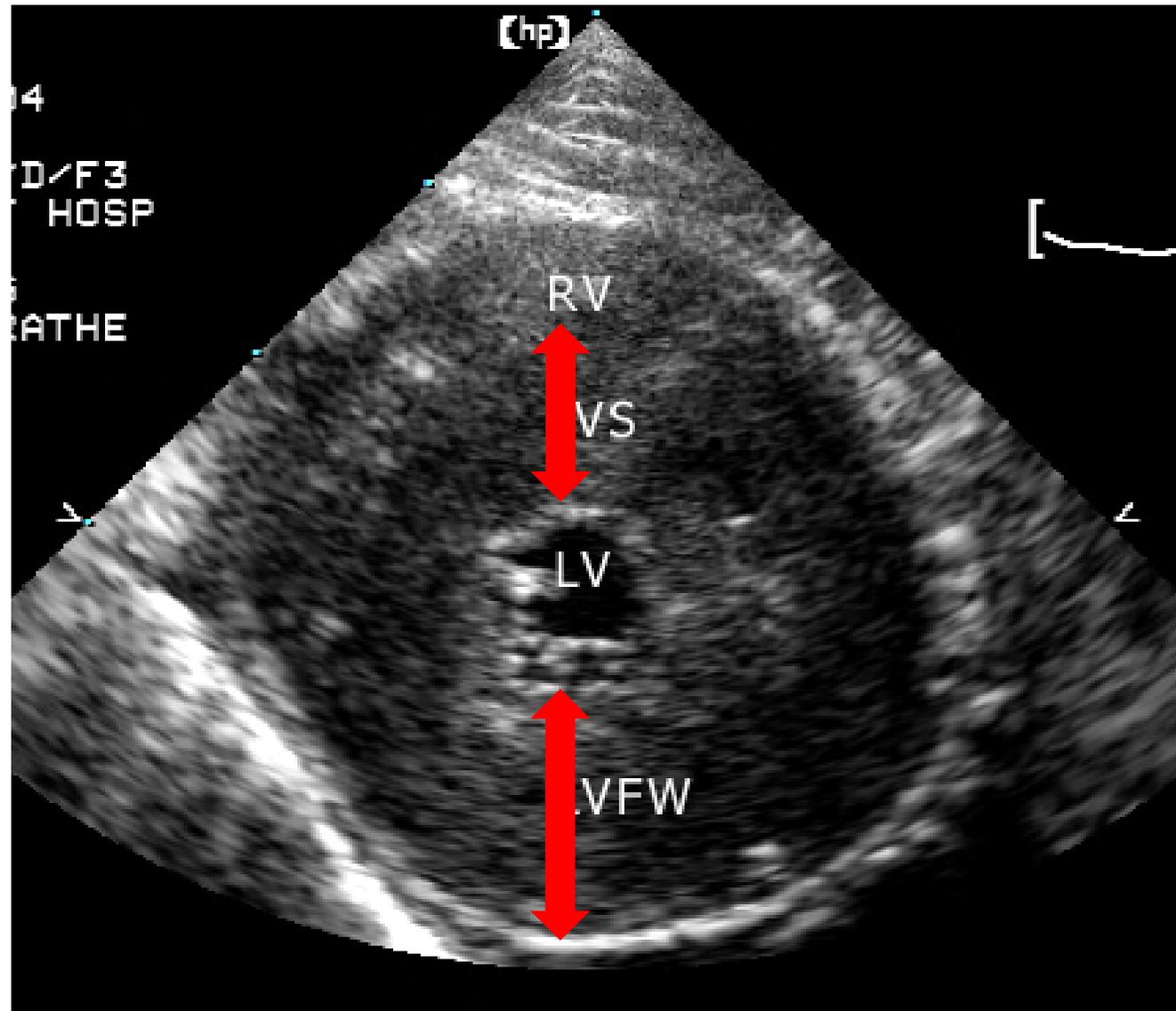
Echocardiography

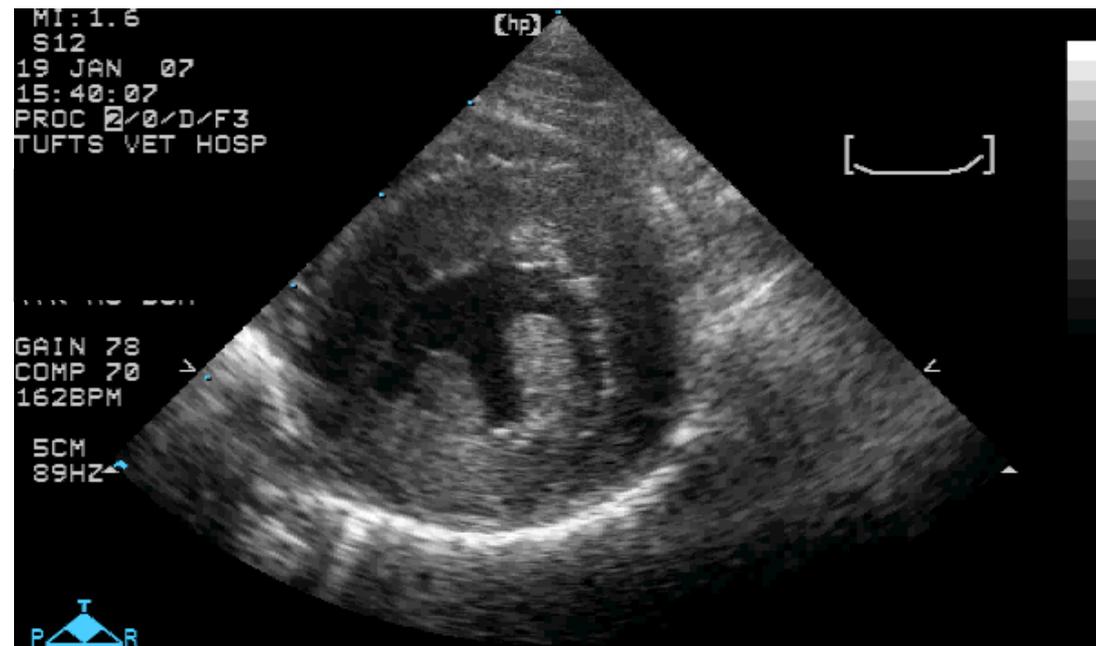
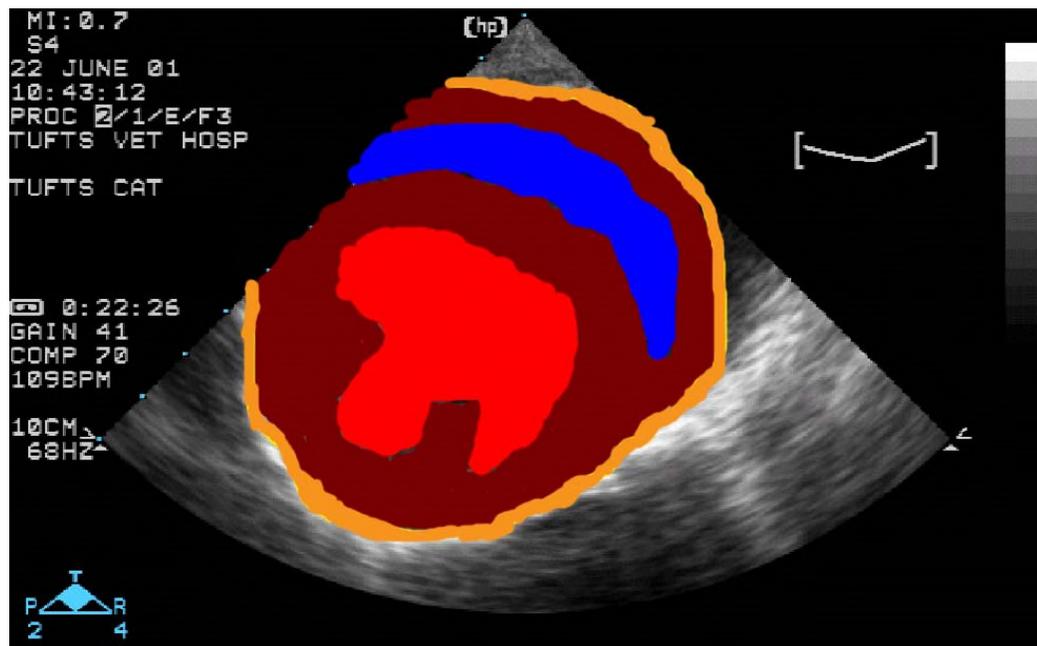
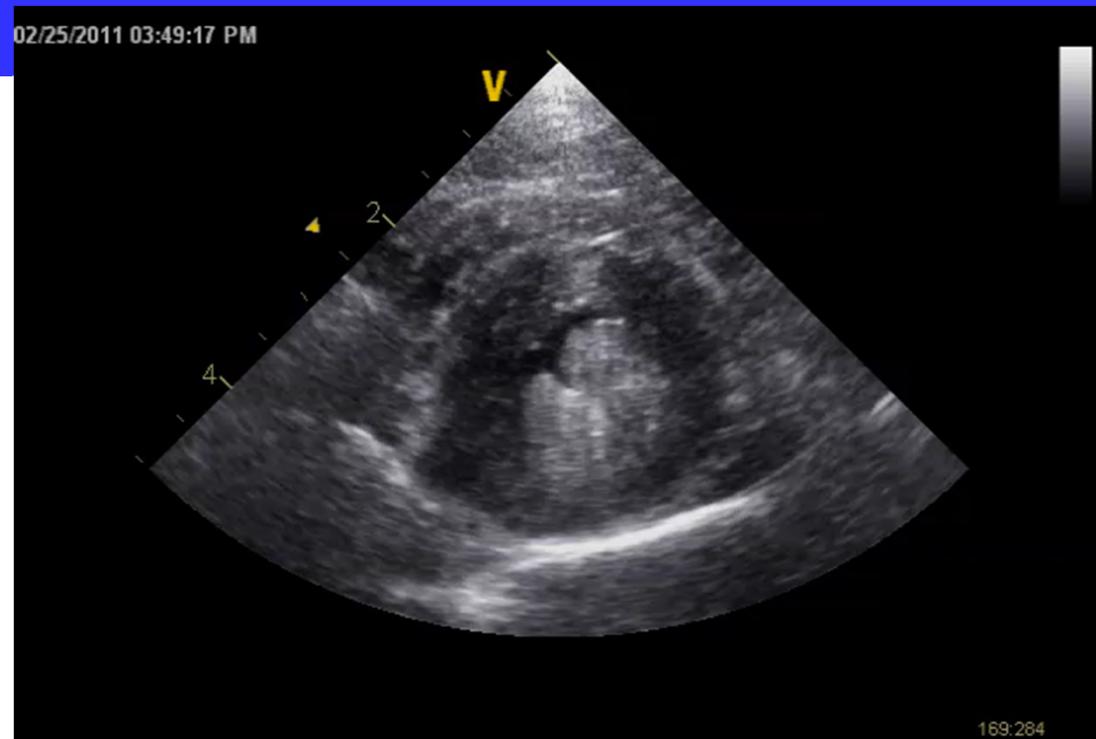
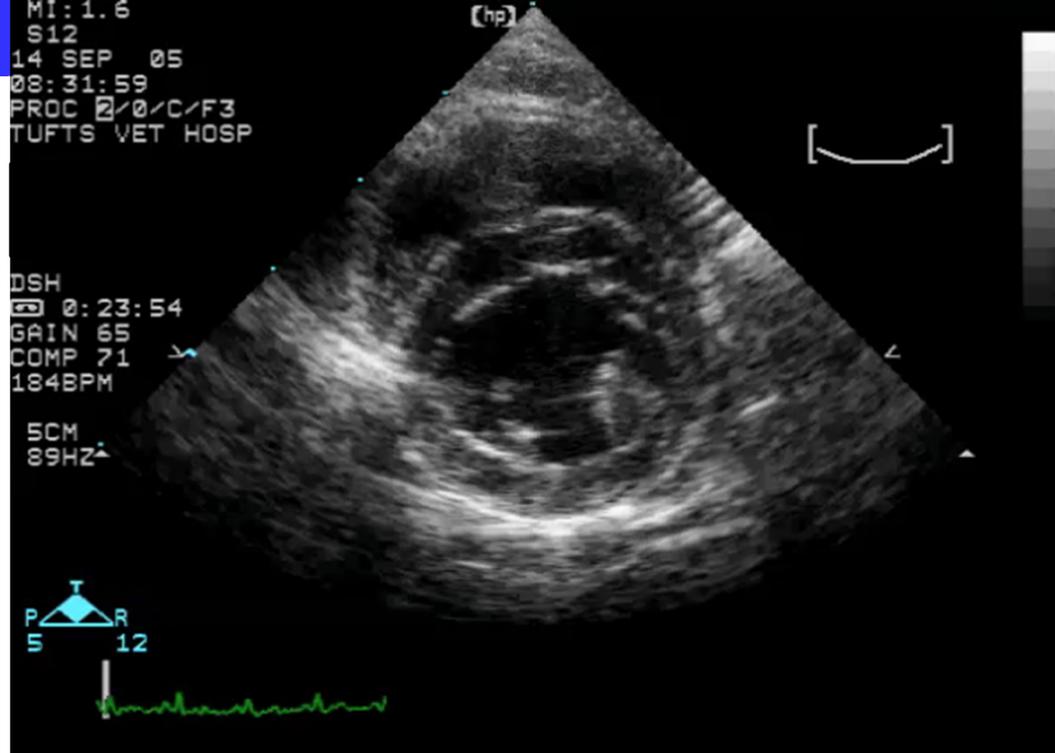
Best diagnostic test for feline HCM

- M-mode or 2-D echo:
 - LVFW or IVS $> 0.55\text{-}0.6$ cm in diastole
 - Or $>$ weight-based echo parameters
- Left atrial size – typically big if:
 - ♥ Left sided CHF
 - ♥ ATE
- LV anatomy
 - ♥ Hypertrophy?
 - ♥ Papillary muscles?
 - ♥ Aorta?
- Right heart
 - ♥ RV/RA enlargement or hypertrophy
 - ♥ Pulmonary artery size
 - ♥ Enlarged if pleural effusion

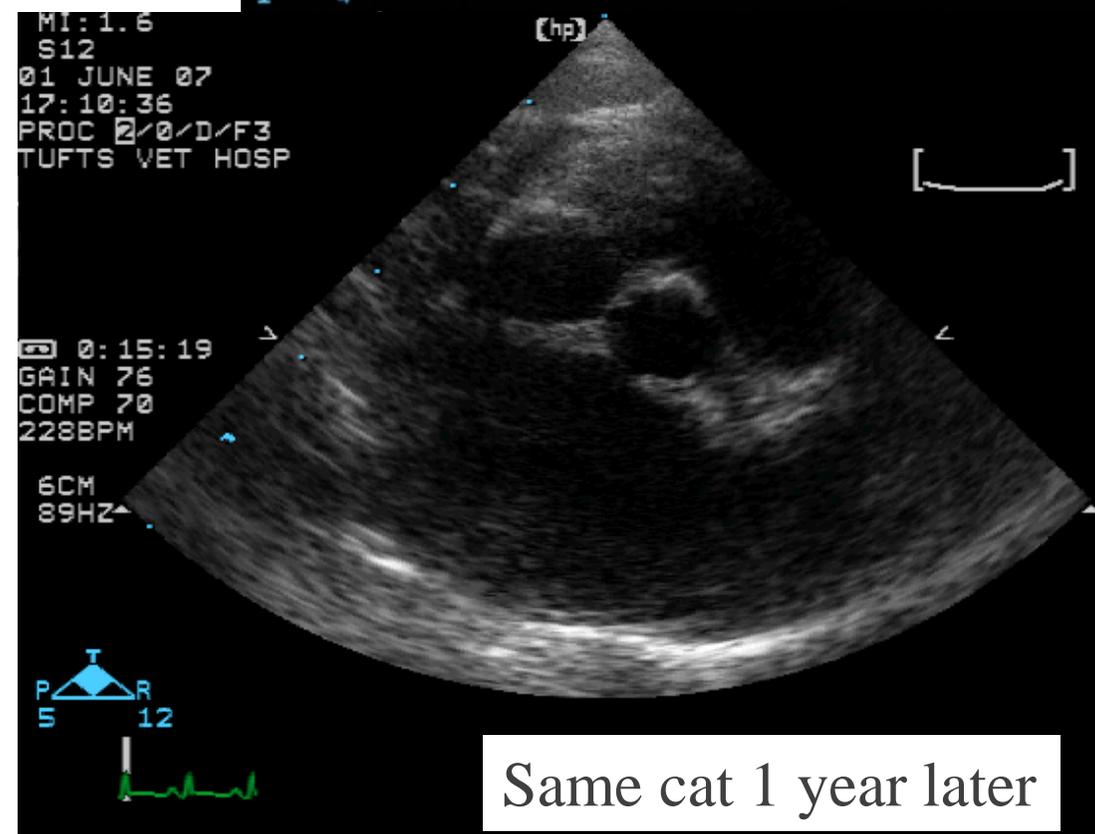
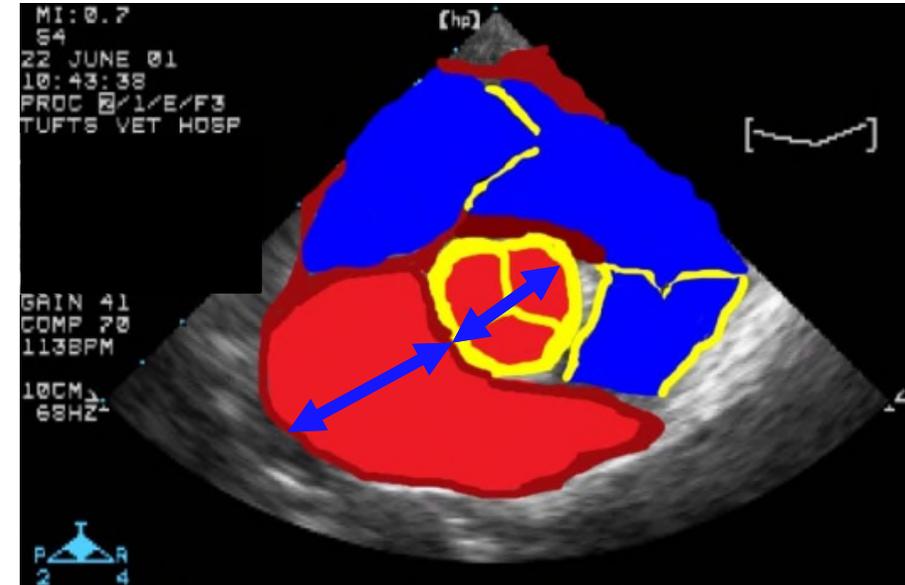


Echocardiography





$La/Ao < 1.6$



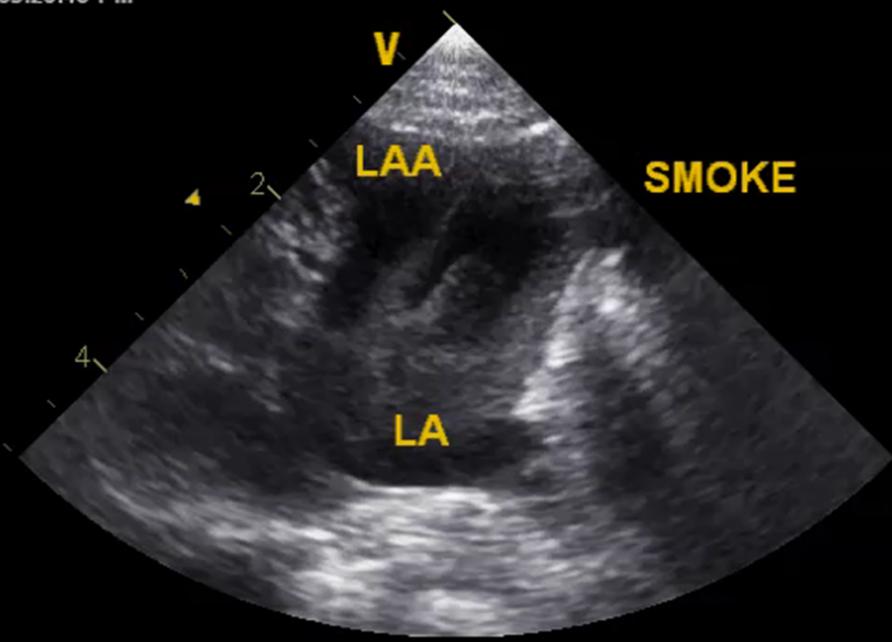
MI: 1.6
S12
11 APR 01
17:34:35
PROC 2/0/D/FS
TUFTS VET HOSP

0:46:00.04
GAIN 85
COMP 70

6CM
89HZ



05/27/2014 03:20:48 PM

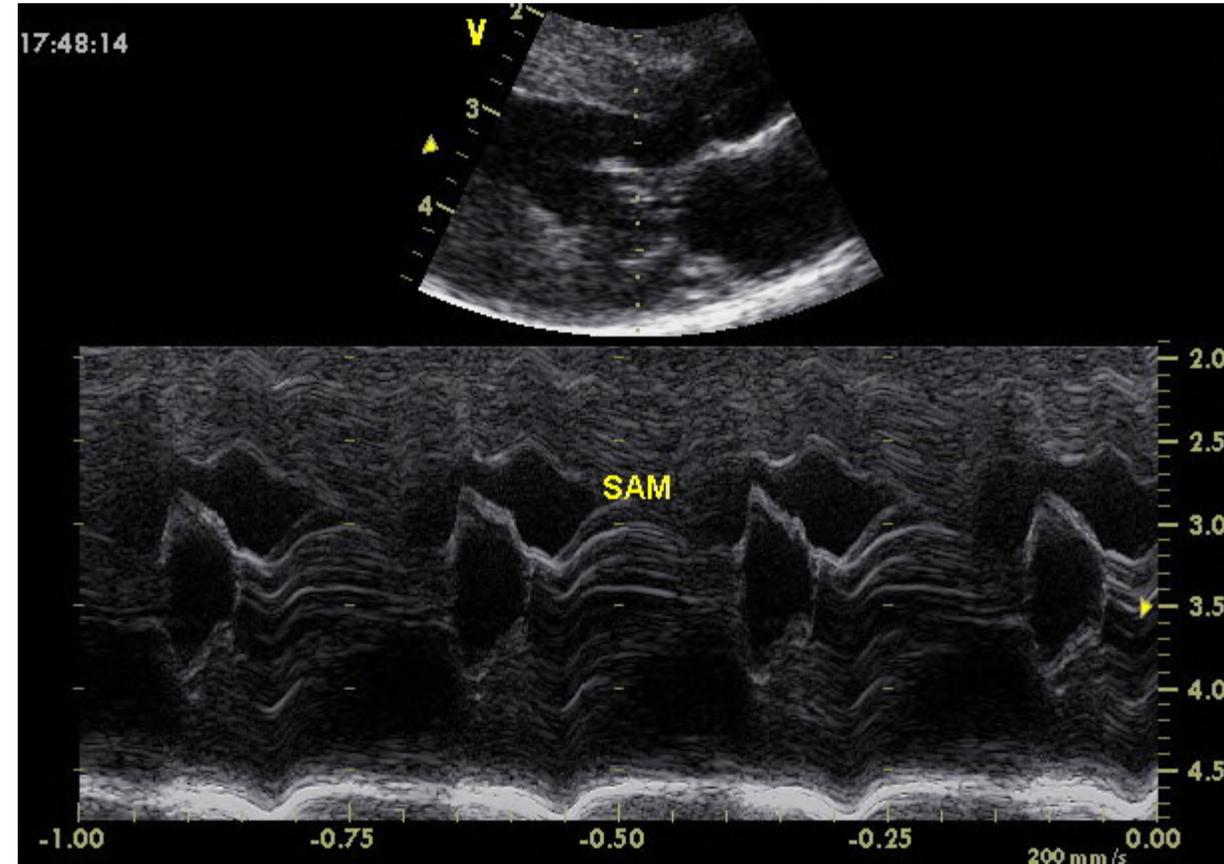
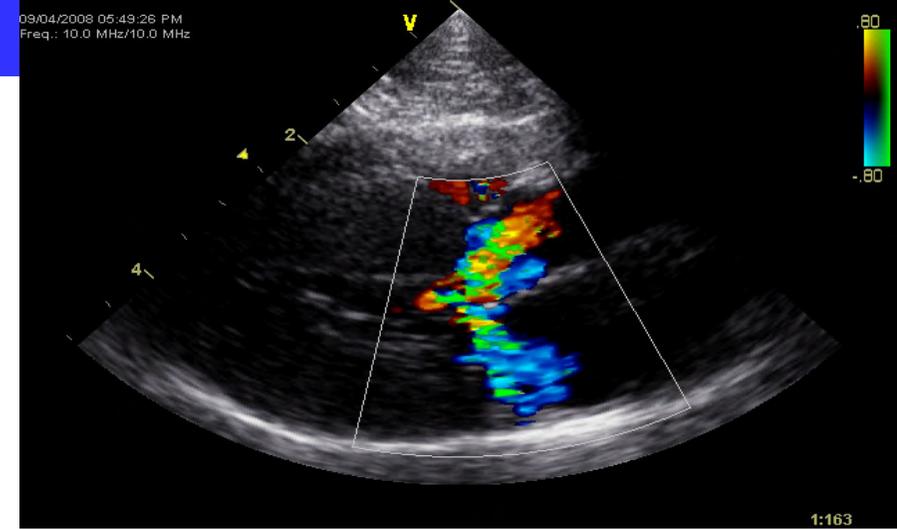


49
1:284 HR

HCM, LVOTO, and SAM

Left Ventricular Outflow Tract Obstruction (LVOTO), Systolic Anterior Motion (SAM) of the Mitral Valve

- 20-60% of cats with HCM
- More common in asymptomatic cats
- Associated with improved outcome in some studies
 - Maybe observed in earlier stages of disease?
- Can be a cause for syncope



FOCUS Echo for Cats

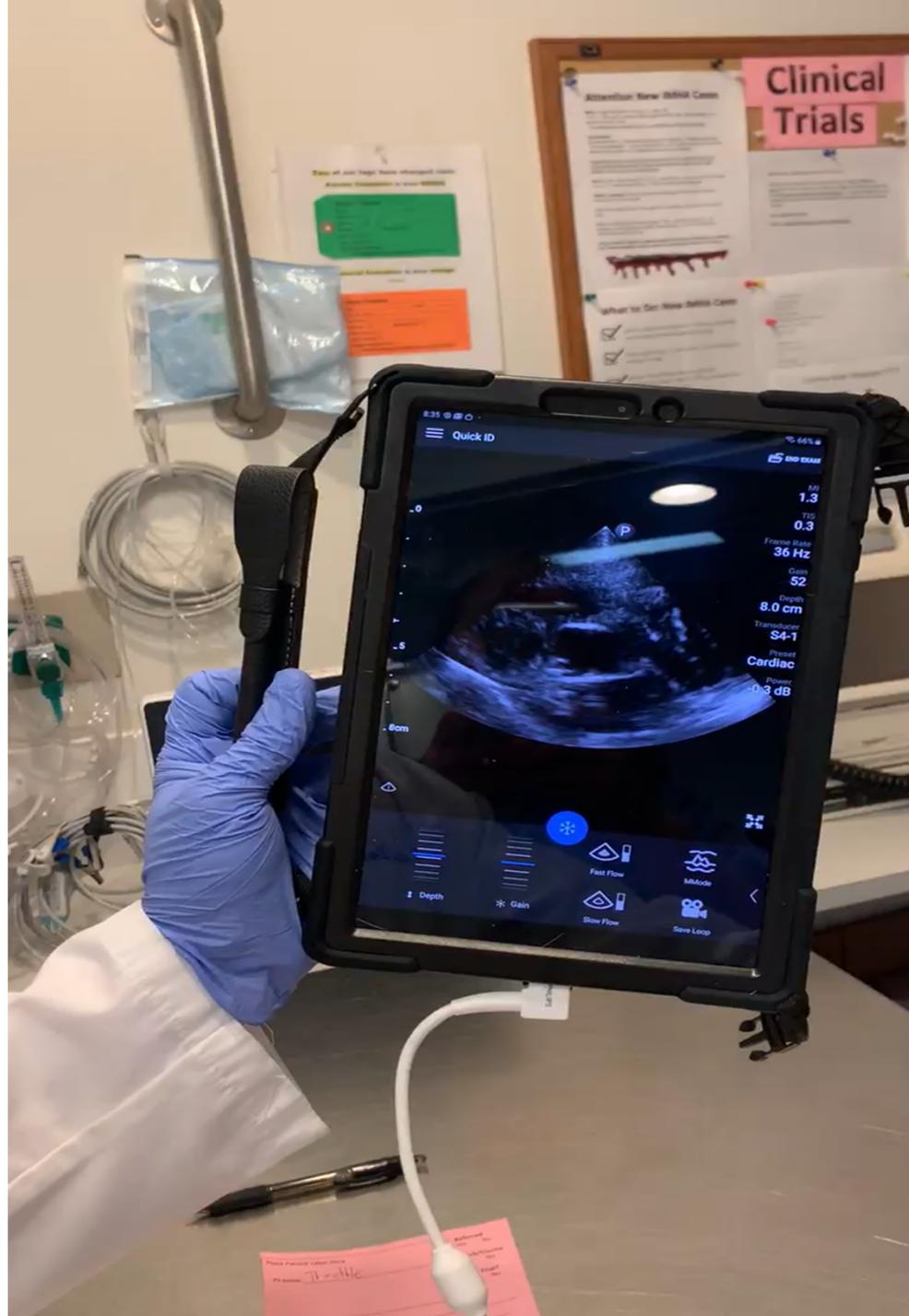
2-minute echo for veterinarians in primary care

- <https://www.youtube.com/watch?v=I4U8AoxYmok&feature=youtu.be>
- Following training/practice on 25-30 cats, most veterinarians can:
 - Identify left atrial enlargement
 - Identify concentric LV hypertrophy
 - Reliably find cats with moderate to severe heart disease
 - More accurately find cats that might benefit from complete echo compared to auscultation alone
 - Less reliably identify cats with mild heart disease

Loughran KA, JVIM 2019 The use of focused cardiac ultrasound to screen for occult heart disease in asymptomatic cats.



The ER Service at Work



Ultrasound and Veterinary Medicine

Highly nuanced exam

Complex congenital disease

Right heart big? Find RA mass

Left atrium big?

LV dilated or thick?

Fluid chest or abdomen

Wicked Expensive Machine, 20-30 min exam

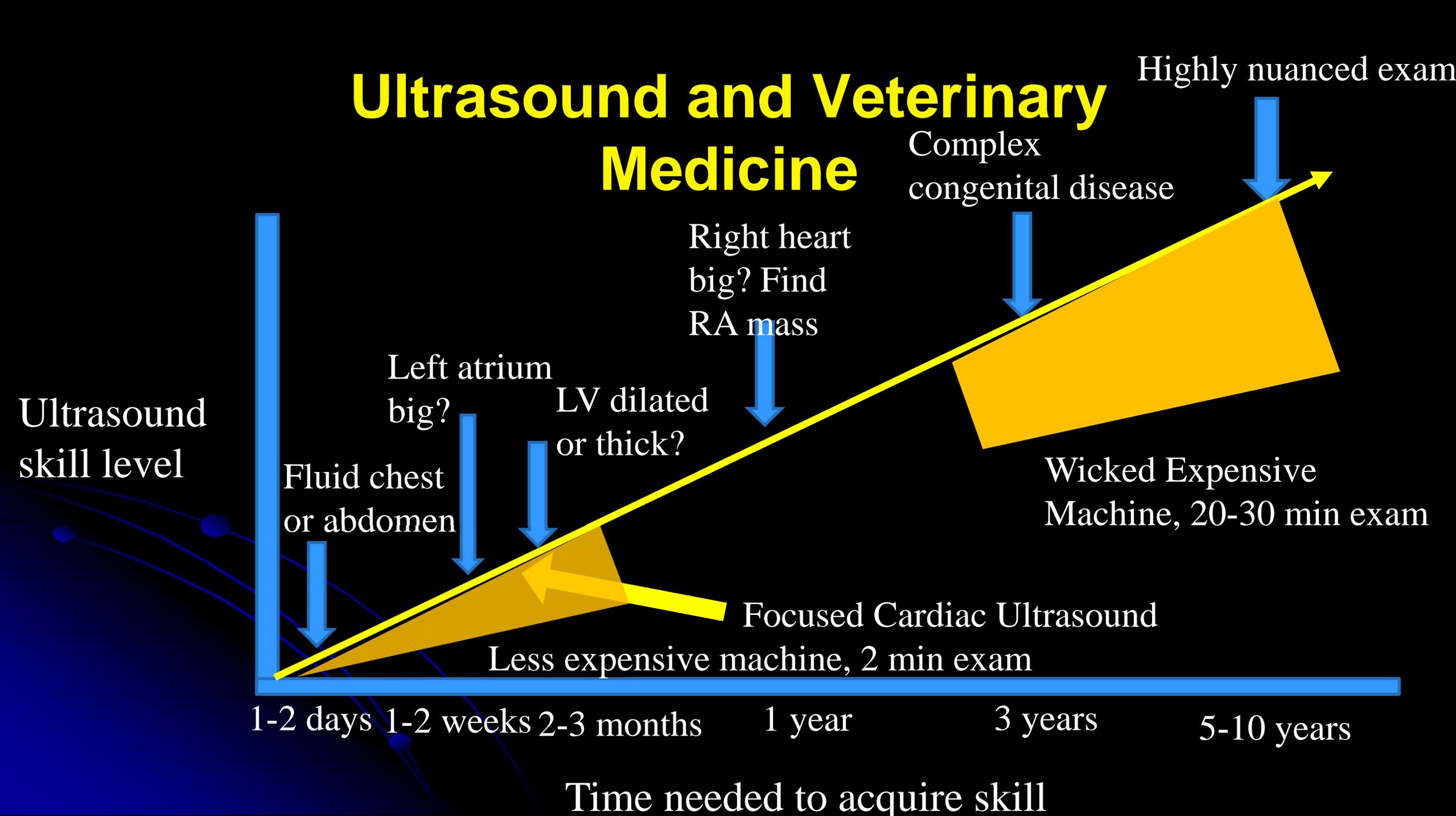
Focused Cardiac Ultrasound

Less expensive machine, 2 min exam

Ultrasound skill level

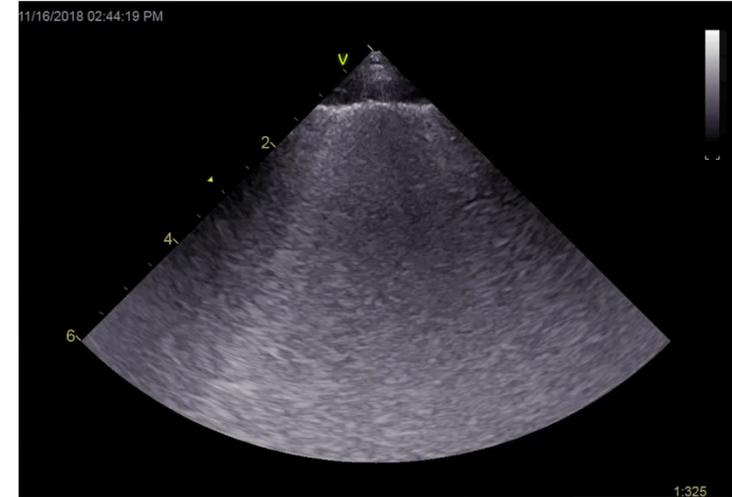
1-2 days 1-2 weeks 2-3 months 1 year 3 years 5-10 years

Time needed to acquire skill



Point of Care Thoracic Ultrasound for Cats with Respiratory Distress (T-FAST)

- Assess the heart and lungs
- Is it CHF or something else?
- Is the LA enlarged?
 - 97% sensitivity and 100% specificity
- Point of care (SNAP) NT-proBNP abnormal?
 - 94% sensitivity and 72% specificity
- > 3 B-lines on more than one US site?
 - 79% sensitivity and 83% specificity
- Pleural effusion also easy to see; pericardial effusion likely CHF

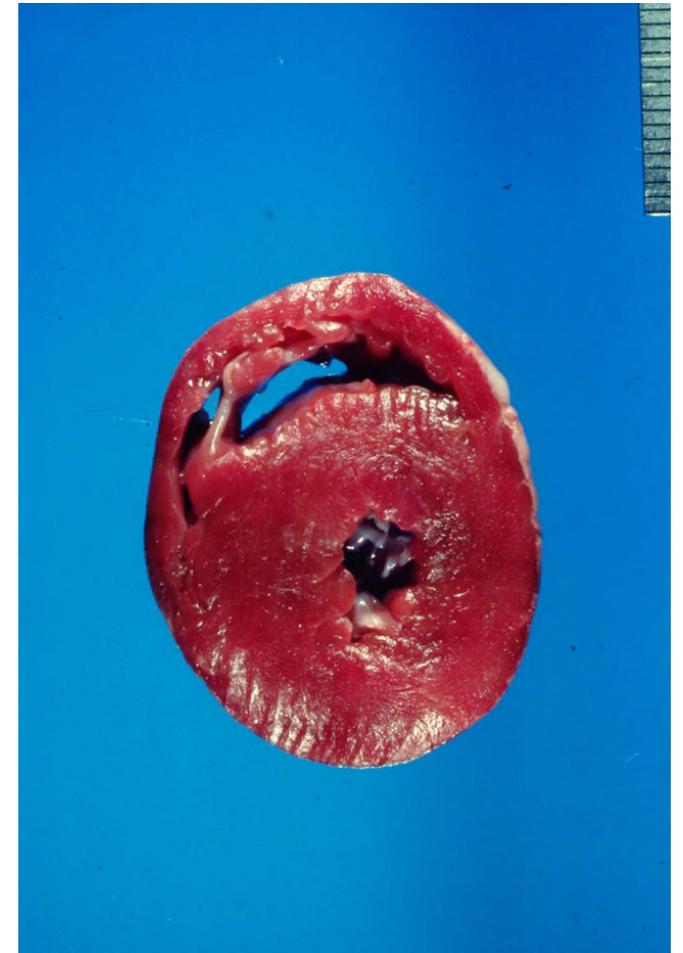


Ward et al JVIM 2017

Feline Concentric Left Ventricular Hypertrophy

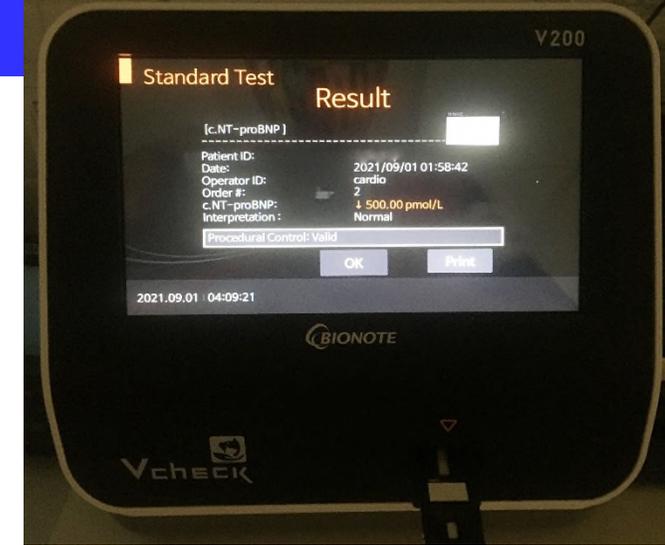
Differential Diagnosis

- Hypertrophic cardiomyopathy
- Systemic hypertension
 - Hypertensive heart disease
 - **Get a blood pressure**
- Congenital aortic stenosis
- Hyperthyroidism
 - Hypertrophic heart disease
 - **Thyroid testing if > 6 years old**



Laboratory Testing

- CBC – often normal or neutrophilic leukocytosis
- Chemistry profile – may be normal or:
 - ♥ Azotemia – esp. if diuretic; prerenal, renal disease
 - ♥ Increased liver enzymes - AST, ALT if CHF
 - ♥ Electrolytes – Diuretics may cause: ↓ Cl⁻, ↓ K⁺, ↓ Na⁺, ↑ tCO₂
- T4 - cats over 6-7 years of age
- NT-proBNP concentration
 - ♥ > 100 pmol/L consistent with heart disease
 - ♥ > 265 pmol/L CHF very likely if shortness of breath
 - ♥ Point-of-Care (SNAP) NT-proBNP positive in most CHF cases
 - ♥ New In-house test available (NT-proBNP, Troponin I, CRP)



Where/When could I use NT-proBNP?

Asymptomatic cat

- Murmur
- Gallop
- Arrhythmia
- Should I do an echo?
- Should I be worried about anesthesia?

- NT-proBNP < 50-100 pmol/L then low chance of major heart disease

Cat with respiratory signs

- Dyspnea
- Cough
- Open mouth breathing
- Is this heart or lung disease?

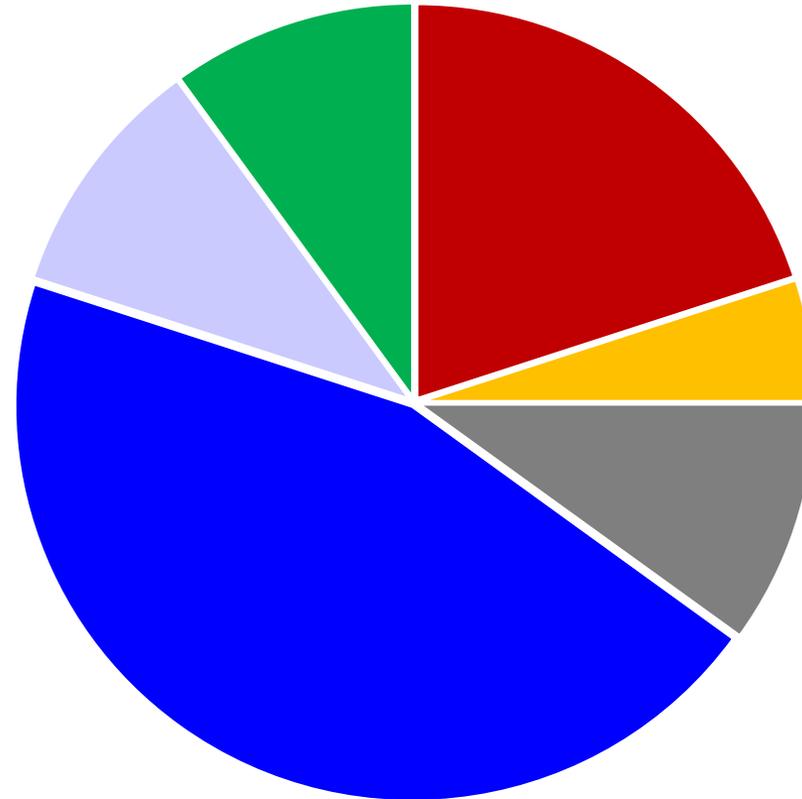
- NT-proBNP > 256 pmol/L indicates high chance clinical signs are due to heart disease

How I Use the SNAP NT-proBNP in Cats

- Cats with cough or dyspnea
 - The SNAP will be positive in most cases with CHF
 - PE, Radiographs, FOCUS Echo compliment Dx
 - The darker the test spot, the more confident the Dx of CHF
- Asymptomatic cats
 - SNAP will find cats with moderate to severe heart disease.
 - SNAP BNP will miss some cats with mild heart disease
 - SNAP BNP elevated in some cats with apparently normal echo
 - Cats with murmur, gallop, arrhythmia, etc.
 - Positive test gets a recommendation for an Echo
 - All cats over 6 years of age?
 - Because most cats with ATE and CHF didn't tell anyone in advance.....

How I Really Use NT-proBNP

Overall Picture of Cardiac Disease



■ Hx and Phys Exam

■ ECG

■ CXR

■ Echo

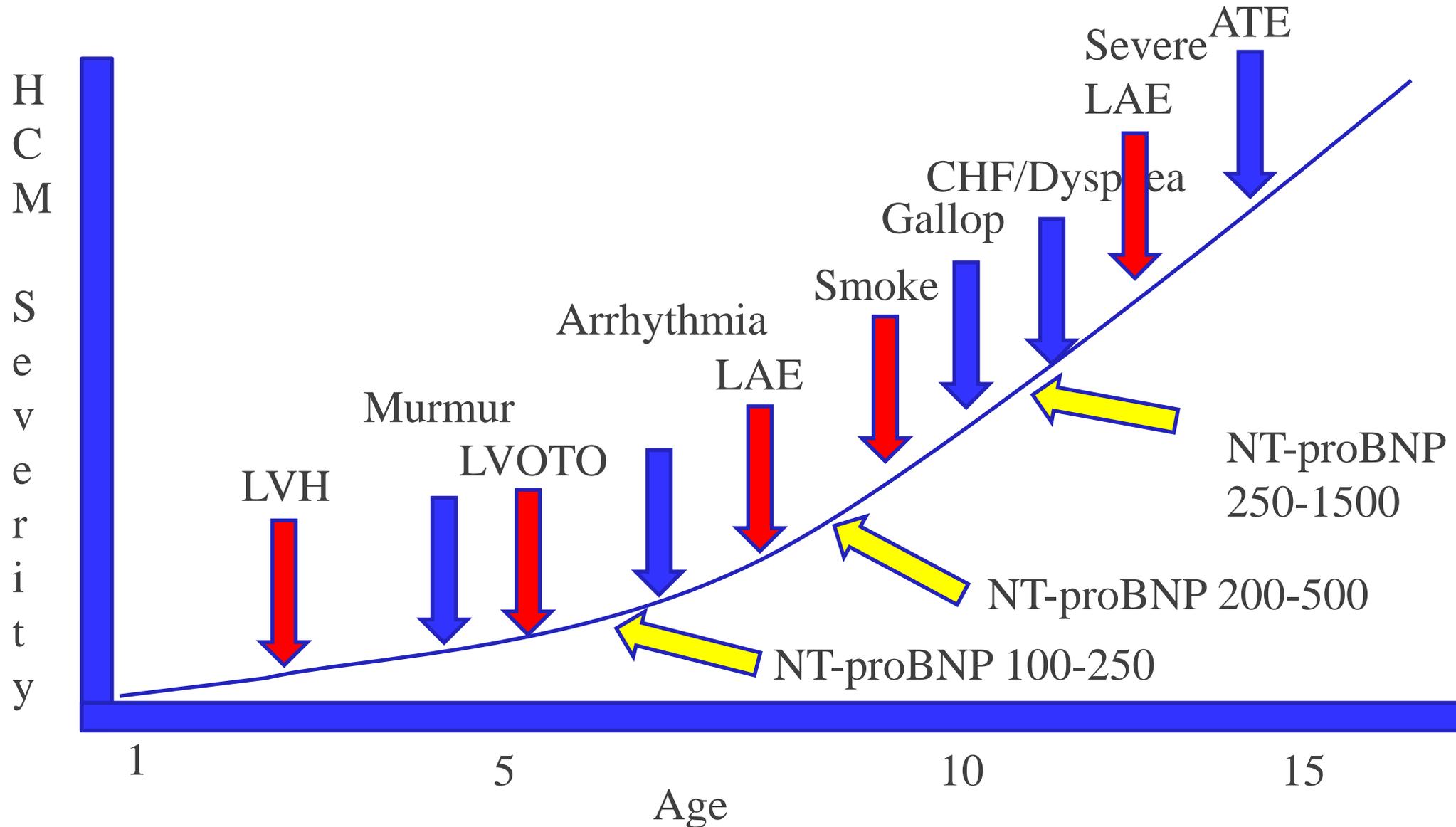
■ Blood Pressure

■ NT-proBNP

Cardiac Troponin I and Feline Heart Disease

- Cardiac troponin I is mildly to moderately elevated in many forms of feline heart disease – HCM, RCM, DCM, Myocarditis, etc.
- May be elevated in cats with asymptomatic disease
 - Works best with high sensitivity cardiac troponin I testing
 - cTnI > 0.163 ng/mL had 62% sensitivity 100% specificity to ID asymptomatic HCM
- May be elevated further in cats with CHF
 - Useful to increase index of suspicion for feline heart disease
 - cTnI > 0.234 ng/mL had 95% sensitivity 78% specificity for assessing CHF
- Various test kits have slightly different normal ranges
- Various test kits have different lower limits of detection

Findings and Clinical Events in Feline HCM



Clinical Scenarios for Feline HCM

- Asymptomatic Feline HCM
 - LV hypertrophy, no outflow obstruction, no LA enlargement
 - LV hypertrophy and LV outflow tract obstruction
 - LV hypertrophy and moderate to marked LA enlargement
- Feline HCM with Congestive Heart Failure
 - Diagnosis and initial management of CHF
 - Management of advanced CHF
- Feline HCM and Arterial Thromboembolism
 - Prevention of ATE
 - Diagnosis and Management of ATE

Asymptomatic HCM

LVH, No LVOTO, No LA enlargement

- R/O systemic hypertension (BP) and hyperthyroidism (T4 if age > 6)
- Most cats will live > 5 years
- Cats are at somewhat increased risk to die from heart disease
- Some cats will never get any problem with the heart
- Most cats do not require treatment
 - Beta-blocker if quite tachycardic or stress prone?
 - Trying to avoid tachycardia-induced CHF
 - Antithrombotics if massive LVH (LVFWd > 0.8 to 0.9 cm) or NT-proBNP > 500 pmol/L?
 - Clopidogrel
 - Weight loss if overweight
- Recheck echo in 1 year (?)
 - Recheck NT-proBNP in 1 year and echo if doubled or > 200 pmol/L (?)

Asymptomatic HCM

LVH, Has LVOTO, Minimal LA enlargement

- Many cats will live > 3 to 5 years
- Cats are at increased risk to die from heart disease
 - CHF and ATE and Sudden death
 - May develop syncope due to LVOTO (uncommon)
- Some cats will never get any problem with the heart
- Hotly debated as to whether treatment is indicated!!
 - No treatment has been proven to improve outcome
 - Atenolol in uncontrolled study failed to improve outcome
 - Beta-blocker ([carvedilol?](#)) if:
 - Significant LVOTO? LVOT velocity > 4 m/sec? LVOTO > 3 m/sec?
 - Treat if syncopal
 - Treat if very young (R/O mitral valve dysplasia)
- Recheck echo in 6 months to 1 year (?)
 - Recheck sooner if alleviation of LVOTO is the endpoint?

Why might you treat with a Beta-Blocker?

- Reduction in LVOT gradient
 - Less progressive LVH, less stress on the heart
- Reduction or elimination of mitral regurgitation
 - Less progressive left atrial enlargement
- Reduction of LV hypertrophy
 - Also seems like a good thing, if it were to happen
- Delay in time until a cardiac event such as CHF or ATE (?)
 - Limited evidence that the drugs can accomplish this goal
 - Atenolol retrospective failed to show any beneficial effect
- Cat feels better after starting atenolol

Atenolol administration to cats with asymptomatic HCM

- Cats with HCM +/- LVOTO
- Evaluated pre- and 14-20 days post-atenolol administration
- Atenolol administration:
 - Reduced heart rate
 - Reduced LVOT velocity
 - Reduced arrhythmia frequency (VPCs)
 - Reduced murmur grade
 - 1 of 3 measures of LA size better
 - 1 cat developed CHF during the study

Effect of atenolol on heart rate, arrhythmias, blood pressure, and dynamic left ventricular outflow tract obstruction in cats with subclinical hypertrophic cardiomyopathy[☆]

**Bethany L. Jackson, DVM^{*}, Darcy B. Adin, DVM ,
Linda B. Lehmkuhl, DVM, MS**

Does Atenolol improve quality of life or biomarkers in cats with asymptomatic HCM?

- 32 cats
- Evaluated before and after atenolol administration
- Blinded and placebo-controlled trial
- Atenolol treatment:
 - Reduced heart rate and murmur grade
 - No effect on biomarkers
 - Quality of Life unchanged
 - Activity scores unchanged

Atenolol in cats with subclinical hypertrophic cardiomyopathy: a double-blind, placebo-controlled, randomized clinical trial of effect on quality of life, activity, and cardiac biomarkers[☆]

A.E. Coleman, DVM^{a,c}, T.C. DeFrancesco, DVM^{a,*},
E.H. Griffiths, PhD^b, B.D.X. Lascelles, BSc, BVSc, PhD^a,
D.J. Kleisch, DVM^a, C.E. Atkins, DVM^a, B.W. Keene, DVM, MS^a

Does Atenolol administration affect 5-year Survival in Cats with Asymptomatic HCM?

- 63 cats with asymptomatic HCM, retrospective study
- 42 cats given atenolol, 21 cats no atenolol
- No difference in all-cause mortality
- No difference in cardiac mortality
- Cats with louder murmur more likely got atenolol
- Cats with higher LVOT velocity more likely got atenolol
- Cats with thicker walls more likely got atenolol
- Did CHF develop?
 - In 6/42 atenolol Rx cats
 - In 0/21 no atenolol Rx cats

Effect of treatment with atenolol on 5-year survival in cats with preclinical (asymptomatic) hypertrophic cardiomyopathy

Karsten E. Schober, DVM, PhD ^{a,*}, Jillian Zientek, DVM ^a, Xiaobai Li, PhD ^b, Virginia Luis Fuentes, VetMB, PhD ^{a,c}, John D. Bonagura, DVM, MS ^a

Does Carvedilol administration affect LVOTO in cats with HCM?

- 50% of the cats had a positive response to carvedilol
- Lower LVOT velocity after carvedilol
- Dose used was 0.2 to 0.5 mg/kg/day
- Certain anatomic features may predict response to carvedilol

Left ventricular geometric characteristics predict response to carvedilol in cats with asymptomatic hypertrophic obstructive cardiomyopathy caused by systolic anterior motion of the mitral valve

Yohei MOCHIZUKI^{1,2)*}, Ryohei SUZUKI¹⁾, Yuyo YASUMURA¹⁾, Takahiro SAITO¹⁾, Takahiro TESHIMA¹⁾, Hirotaka MATSUMOTO¹⁾ and Hidekazu KOYAMA¹⁾

Beta-Blockers for Hypertrophic Cardiomyopathy

♥ Atenolol

- ♥ I do not use any more
- ♥ 6.25 mg/cat or 12.5 mg/cat q 12 hr



♥ Carvedilol

- ♥ 0.2-0.8 mg/kg q 12 hr
- ♥ Most cats: ½ of a 3.125 mg tab PO q 12 hrs for 2 weeks then increase to 1 full 3.125 mg tab PO q 12 hrs
- ♥ Small cats or recent CHF start ¼ tab
- ♥ Titrate to higher dose if persistent LVOTO > 2.5-3 m/sec at the 6 month recheck exam

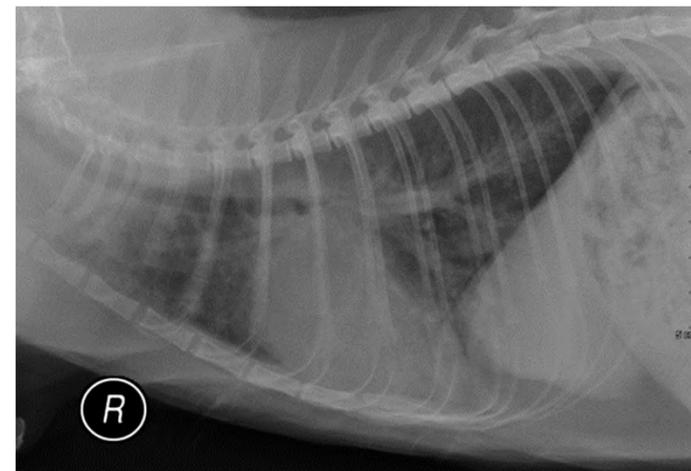
Asymptomatic HCM

LVH with Moderate to Marked LA enlargement

- Cats are at significantly increased risk to die from heart disease
 - CHF and ATE risk is much higher
- Most cats will eventually get into trouble with the heart
- Will treatment affect outcome???
 - Should you use an ACE inhibitor to try to delay CHF?
 - The bigger the LA, the more I might use an ACEi
 - Should you use pimobendan?
 - No LVOTO – **Maybe yes**
 - LVIDd is getting big (> 1.6 to 1.8 cm) – **Maybe yes**
 - Fractional shortening is dropping (< 35%) – **Maybe yes**
 - Should you use an antithrombotic?
 - Yes we would – more likely if Stroke or reduced LA function
 - Send home with a few tabs of furosemide in case dyspnea develops?
- Recheck echo in 6 months (Kidney values/electrolytes sooner if ACEi)

HCM with Congestive Heart Failure (Stage C)

- Most cats with CHF eventually die from CHF or ATE
 - Median survival time varies; owner dedication plus cat factors affect survival
 - Usual message: 6 months is good; greater than 1 year is a big success
- Treatment options
 - Furosemide (dose coming up next)
 - ACE inhibitor
 - Pimobendan (do not give if LVOTO?)
 - Beta-blocker (only give if major LVOTO or bad arrhythmia)
 - Antithrombotic
 - Additional drugs and diet (spironolactone, sildenafil, torsemide, etc.)
 - You should change the diet! Especially if chronically on 1 single diet
- Recheck visits:
 - Recheck exam in 5-10 days plus kidney values, electrolytes, PCV/TS, BP, etc.
 - Recheck cardiac exam and echo in 2-3 months



Furosemide: Dose Titration

Lowest dose needed to control signs of congestion

- Range 1-2 mg/kg EOD up to 4 mg/kg TID or higher
- Severe pulmonary edema – keep giving until breathing better
 - Even 4 mg/kg q 1-2 hours or a CRI
 - After breathing better reduce dose or even stop for 24 to 48 hours
 - Follow BUN, Creatinine, electrolytes, PCV/TS, RR and effort, +/- skin turgor
 - Back off if BUN or creatinine rising more than a few points above the range
- Discharge/Chronic furosemide dose
 - Milder CHF – 1-2 mg/kg (6.25 mg SID)
 - Sometimes go to EOD
 - Almost never stop furosemide once in CHF
 - Severe CHF esp. if pleural effusion tapped – 1-2 mg/kg BID
 - Recurrent pleural effusion needing second centesis
 - More furosemide – 2 mg/kg TID
 - Spironolactone, Pimobendan, ACEi optimized, sildenafil, torsemide



Owner Instructions Regarding Furosemide and RR effort and monitoring

- Ask owner to follow breathing rate and effort
 - Takes some owners a while to get comfortable with this
- Give owners upper and lower limit of furosemide dose
 - “We think he/she will need ½ tablet once a day, but you can give ½ tablet twice a day. Be sure to give at least ½ tablet every other day.”
- For respiratory rate and effort monitoring instruct owners:
 - For labored breathing (extra belly wall or chest wall motion) or if RR > 32-35 bpm: GIVE MORE***
 - If the cat is weak, lethargic, slow, but breathing OK: GIVE LESS
 - Be sure to give at least XX amount as a minimum dose

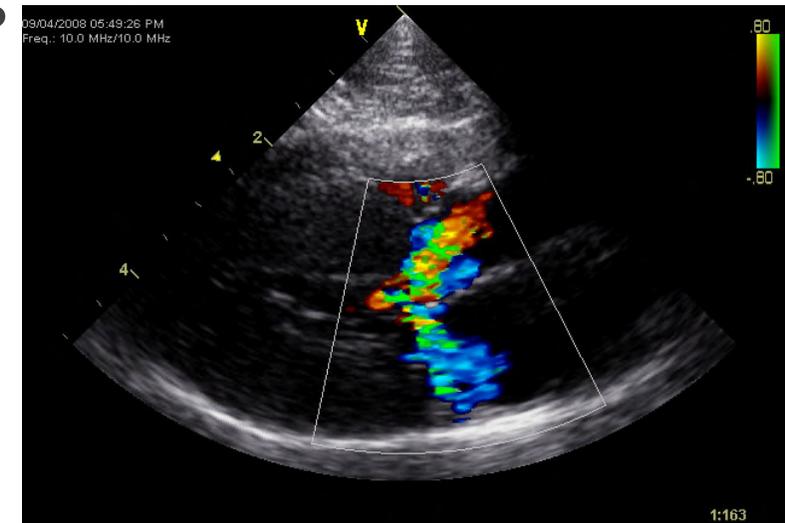


Angiotensin Converting Enzyme (ACE) Inhibitors

- Try to use in all cats with CHF?
- Measure baseline BUN, creatinine and electrolytes
 - Enalapril, benazepril, lisinopril – 0.25 to 0.5 mg/kg q 24 hrs
 - Enalapril 2.5 mg q 24 hours in medium to large cat
 - Enalapril 1.25 mg q 24 hours in smaller cats (< 3.5 to 4 kg) or pre-existing azotemia
 - Lisinopril dosed like enalapril
 - Rarely go to BID in refractory CHF
 - Delay use if dehydrated, azotemic, hypothermic, weak and not eating yet
 - Start on day 3 to 5 after discharge if eating well
 - Recheck kidney values and electrolytes in 5 to 14 days
 - +/- Reduce DIURETIC dose if BUN or creatinine climbing
 - In some cats, very mild azotemia is “the price to pay” for control of CHF
 - Serial total solids/PCV also helpful in diuretic and ACEi dose adjustment (TS rising; less diuretic)
 - Recheck kidney values and electrolytes q 3 to 6 months or shortly after any other diuretic dose adjustment is made

Is Pimobendan Useful to Treat CHF in Cats with Cardiomyopathy?

- Positive inotrope with vasodilator properties
 - Calcium sensitizer
 - Phosphodiesterase III inhibitor
- Documented utility in dogs CHF
 - Improved survival and clinical signs
- Safety and efficacy in cats is unclear
 - Observational clinical reports indicate safe in cats
 - Concerns about LV outflow tract obstruction in HCM
 - One retrospective study showed improved survival



Does pimobendan negatively impact cats with CHF and Cardiomyopathy and LVOTO?

- 260 cats with CM and CHF treated with pimobendan
 - 57 cats with LVOTO
 - 203 cats without LVOTO
- Cats with LVOTO did **not** have more frequent side effects than cats without LVOTO
- Cats with LVOTO were:
 - Younger
 - More likely to have a murmur
 - More likely to have pulmonary edema
 - Less likely to have pleural effusion

Retrospective evaluation of the safety and tolerability of pimobendan in cats with obstructive vs nonobstructive cardiomyopathy

Jessica L. Ward¹ | Efrem Z. Kussin¹ | Melissa A. Tropf¹ | Sandra P. Tou² |
Teresa C. DeFrancesco² | Bruce W. Keene²

J Vet In Med 2020

Does pimobendan affect outcome in a 6-month clinical pilot study?

- 83 cats with HCM and recent CHF randomized to pimobendan or placebo
 - 30 with LVOTO
 - 53 without LVOTO
- “Success” = stayed in study for 6 months
 - LVOTO cats
 - Pimobendan – 28.6%
 - Placebo – 60%
 - No LVOTO
 - Pimobendan – 32%
 - Placebo – 18%

Effects of pimobendan in cats with hypertrophic cardiomyopathy and recent congestive heart failure: Results of a prospective, double-blind, randomized, nonpivotal, exploratory field study

Karsten E. Schober¹ | John E. Rush² | Virginia Luis Fuentes³ | Tony Glaus⁴ | Nuala J. Summerfield⁵ | Kathy Wright⁶ | Linda Lehmkuhl⁷ | Gerhard Wess⁸ | Margaret P. Sayer⁹ | Joao Loureiro⁵ | John MacGregor¹⁰ | Nicole Mohren¹¹

J Vet Int Med 2021

Pimobendan for CHF in cats

- Use in cats with CHF if no LVOTO:
 - An echo that can identify the presence or absence of LVOTO should ideally be done before starting pimobendan
- When to start pimobendan?
 - After the echocardiogram to exclude LVOTO (so not in the Emergency room)
 - As an initial treatment for most cats with CHF?
 - I think it is better tolerated than ACEi
 - Vs. Only in cases with refractory CHF?
- Dose? 0.5 mg/kg/day
 - Most cats 1.25 mg PO q 12 hrs
 - Small cats – ½ of a 1.25 mg tab PO 2 12 hrs
 - Compounding? Stability and absorption unclear
- Side effects: hyperexcitability, weakness, just does not feel right
 - Massive LVH cases more likely to not feel right?

Beta-blockers for Cats with CHF

- We rarely use beta-blockers for cats with CHF
- Possible exception: cats with CHF and marked LVOTO
 - Usually young cat with LVOT velocity > 4 m/sec
 - Usually start after congestion is cleared
 - Usually start low dose and titrate dose upward q 2 weeks
- Possible exception: cats with CHF and concurrent serious ventricular arrhythmia
- What to do if chronically on beta-blocker Rx and develops CHF?
 - Cut dose by 50%
 - If ongoing CHF signs try to stop?
 - Switch from atenolol to carvedilol?
 - Especially if LV dilation or low fractional shortening and no more LVOTO
- Side effects: Weakness lethargy, worsening CHF, syncope

Drug Options for Refractory CHF

Some people use some of these drugs routinely

- Especially likely to try these if furosemide BID does not control congestion or if repeated thoracentesis is needed
- Spironolactone
 - Start low, work up to a higher dose
 - ¼ of a 25 mg tab PO q 48 hours; slowly increase to 1-2 mg/kg q 12 hrs
- Torsemide – 0.5 to 2 mg/cat q 24 hours
- High dose pimobendan (1.25 mg q 8 hrs or 2.5 mg q 12 hrs)
- Sildenafil – Especially if recurrent pleural effusion or big right heart or big PA on echo
- More ACEi (BID)
- Injectable furosemide – especially in cats that hate pills
- Dietary sodium modification (Tufts HeartSmart web site)
<https://heartsmart.vet.tufts.edu/>

Change the diet?

- A few studies documented improvement after a diet change
 - van Hoek 2019 - Diet change in cats with asymptomatic HCM
 - Freeman 2014 - Diet change in cats with HCM
 - Pion 1992 – DCM and taurine deficiency
 - Karp 2021 abstract – DCM and diet
- Indicated most in cats eating a single diet for a long time
- Dietary sodium a consideration
- BCS and MCS are considerations
 - Omega-3 fatty acids?
 - Palatable foods?

Association of diet with left ventricular wall thickness, troponin I and IGF-1 in cats with subclinical hypertrophic cardiomyopathy

Ingrid van Hoek¹  | Hannah Hodgkiss-Geere² | Elizabeth F. Bode² | Julie Hamilton-Elliott² | Paul Mötsküla³ | Valentina Palermo⁴ | Yolanda Martinez Pereira⁵ | Geoff J. Culshaw⁵ | Jeremy Laxalde¹ | Joanna Dukes-McEwan²

Arterial Thromboembolism

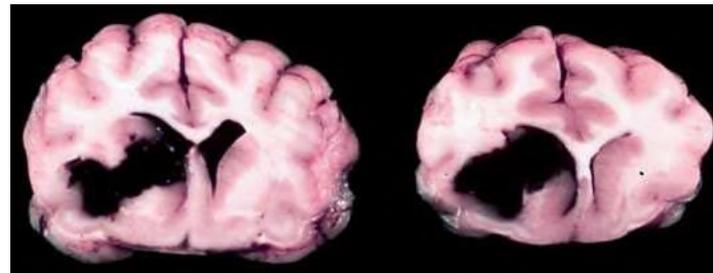
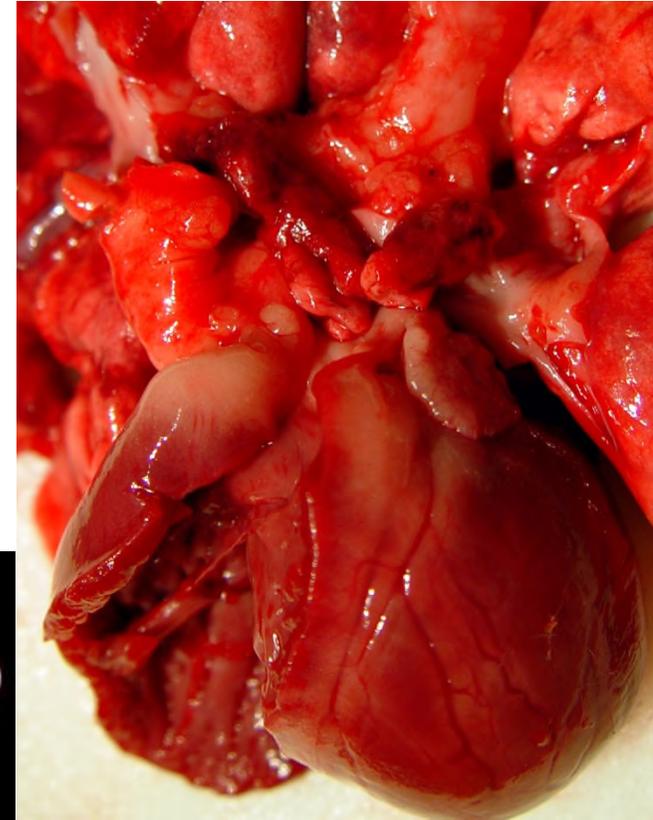
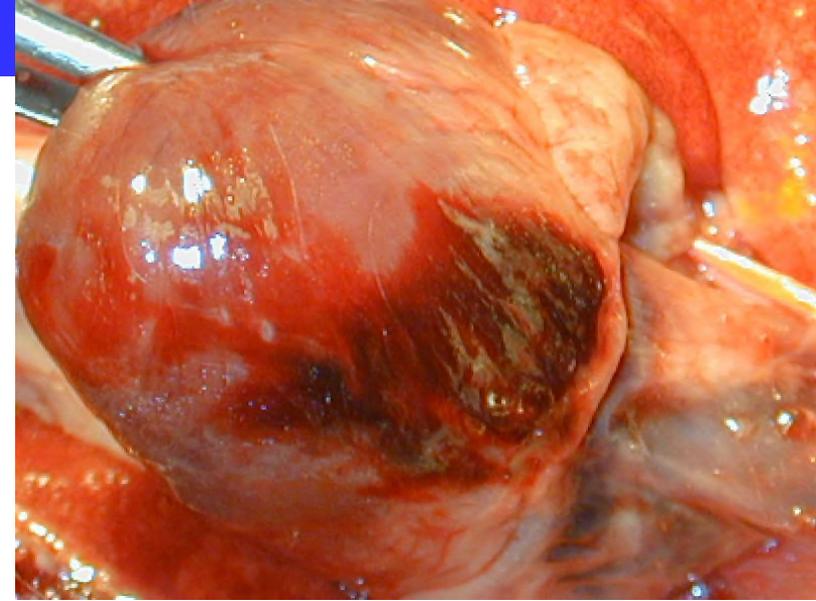
- Occurs in 5-40% of all cats with moderate to severe cardiomyopathy
- Originate in LA or LV; rarely right heart (PTE)
- ↑ LA size, smoke, reduced LA function, Massive LVH associated with ATE
- If minimal cardiac disease look for pulmonary carcinoma



Arterial Thromboembolism

Sites of Emboli

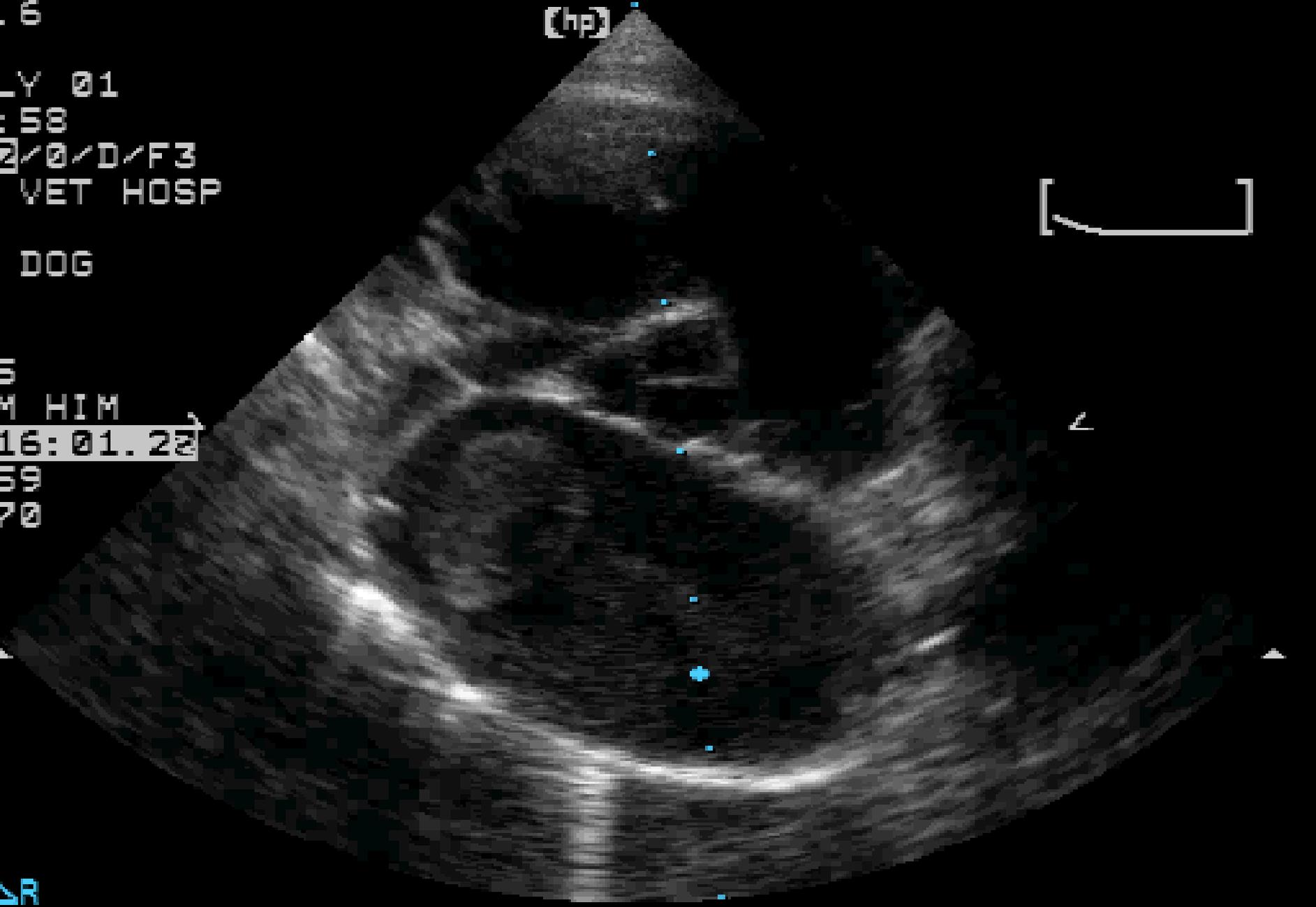
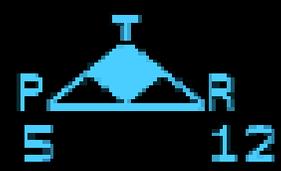
- Rear limbs – 85 to 90%
- Front limb – 5 to 10%
- Other sites:
 - Kidneys
 - GI tract
 - Brain
 - Heart
 - Lungs (PTE)



MI: 1.6
S12
20 JULY 01
12:12:58
PROC 2/0/D/F3
TUFTS VET HOSP

TUFTS DOG
GIBB
SIMON
108025
13Y CM HIM
1:16:01.22
GAIN 59
COMP 70

6CM
89HZ



(hp)

Arterial Thromboembolism

Treatment and Prevention

Treatment of active ATE

- Supportive care, analgesics, oxygen, physical therapy
- Furosemide only if documented CHF; +/- fluids if no CHF(?)
- Antithrombotics (high dose heparin, LMWH, clopidogrel)
 - Start as walk in the door, clopidogrel loading dose 5-10 mg/kg
- Thrombolytics (Streptokinase, tissue plasminogen activator)
- Surgical or catheter thrombolectomy

Prevention

- Clopidogrel
- Low molecular weight heparin (dalteparin, enoxaparin)
- Rivaroxaban or apixaban
- Aspirin – Dose? Frequency?

Clopidogrel



- Antiplatelet drug
- Irreversibly block ADP binding to the P2Y₁₂ receptor on the platelet surface
- Hogan study says that cats with a prior episode of ATE treated with clopidogrel lived longer than ASA Rx
 - Clopidogrel - 346 days
 - Aspirin - 128 days
- Secondary prevention vs Primary prevention

Arterial Thromboembolism Prevention - Clopidogrel

- ¼ of a 75 mg tab/cat PO q 24 hrs
- 2 mg/kg/day (ideally)
 - Use lower dose in small cats (< 3.5-4 kg); Compounding?
- Foaming at the mouth (tastes bad); **capsule** vs. compounding? Marshmallow flavor?
- Hepatotoxicity – idiosyncratic vs dose related?
- When to initiate?
 - Moderate to marked LAE
 - Prior ATE
 - LAE spontaneous contrast (LA “smoke”)
 - Reduced LA contractile function
 - NT-proBNP > 500 pmol/L (?)

Low Molecular Weight Heparins

- ♥ Smaller heparin fragments than unfractionated heparin
- ♥ Longer duration of action
- ♥ Safer than coumadin
- ♥ Less testing than coumadin
- ♥ Anti X-a activity targeting?
- ♥ Unclear efficacy
- ♥ Use with clopidogrel in high-risk cases?



Dalteparin and Enoxaparin

- Dalteparin – 150-175 U/kg Sub-Q q 12 hrs
- Enoxaparin – 1 mg/kg Sub-Q q 8-12 hrs
- No routine monitoring is required
- Costly to use chronically (\$\$\$)
- When to initiate?
 - Moderate to marked LAE
 - Prior ATE
 - LAE spontaneous contrast (LA “smoke”)
 - Reduced LA contractile function



Drug Combinations??

Newer Drugs to replace Coumadin

- Direct Factor Xa inhibitor
 - Rivaroxaban
 - SID dosing in people
 - Initial studies in cats suggest that 2.5 mg SID may be a reasonable dose
 - Anticoagulant effect is not easily reversible
 - Further studies needed
 - Apixaban

Aspirin

- Inhibits cyclooxygenase (COX); blocks production of thromboxane A_2
- Platelet inhibitor
- Is it effective?
- What dose?
 - 2 mg/kg/day?
 - 5 mg/kg/day?
 - 40 mg q 3 days?
 - 81 mg q 3 days?
- Dual antiplatelet strategy (aspirin and clopidogrel)
- Concerns if dehydrated, azotemic or anorexic?

Combination therapies for ATE Prevention in Cats

- Clopidogrel and aspirin
- Clopidogrel and low molecular weight heparin
- Clopidogrel and rivaroxaban (or apixaban)
 - 5/32 cats had bleeding complications
 - Generally better than historical outcomes

Dual therapy with clopidogrel and rivaroxaban in cats with thromboembolic disease

Sara T Lo¹, Ashley L Walker¹, Catherine J Georges¹,
Ronald HL Li² and Joshua A Stern³

J Fel Med Surg 2021

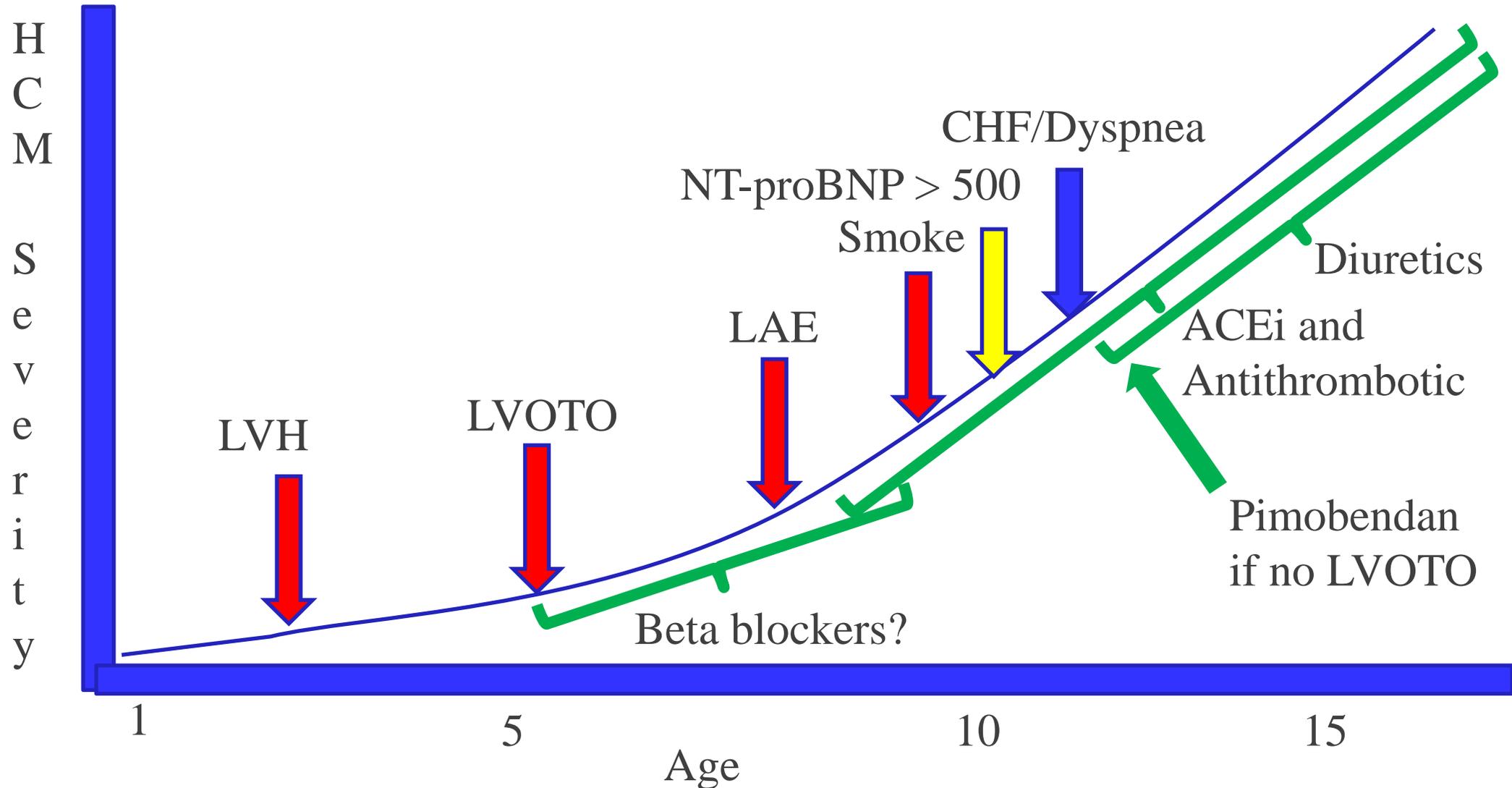
- Something more than clopidogrel post-ATE?
- Combination therapy if there is a thrombus seen on echo?
- Combination therapy for marked LAE and “smoke”?

Overall Treatment Plan for Feline Arterial Thromboembolism

- Heparin (or LMWH) at solid dose
- Clopidogrel on entry (5-10 mg/kg loading dose)
- Analgesics first 24 hours
- Physical therapy
- Rx heart disease
- Avoid non-specific beta-blocker
- Avoid hypotension or dehydration
- Start thromboembolism preventative
- Small volume fluids if no CHF?

Most cats with front leg ATE will walk again and survive to discharge
Only 30-40% of severe back leg ATE cats will walk again

Possible Treatment Approaches for Feline HCM



Diagnostic Checklist Feline Heart Disease

Test	Asymptomatic	CHF	ATE	Syncope
Thoracic radiographs	+/-	√	√	√
ECG	+/-	+/-	+/-	√
Echocardiogram	√	√	√	√
NT-proBNP	√	√	√	√
Chemistry profile	+/-	√	√	√
Complete blood count	-	+/-	+/-	√
Troponin I – esp if arrhythmias or regional wall motion issues	+/-	+/-	+/- or √	+/-

Treatment Checklist Feline Heart Disease

Test	Asymptomatic	CHF	ATE	Syncope
Furosemide	-	√	+/- if CHF	-
ACE inhibitor	-	√	+/- if LAE	+/- if LAE
Pimobendan	-	√ unless LVOTO	+/-	-
Antithrombotic	+/- if LAE	√	√	+/-
Beta-blocker	+/- if HCM	?? Maybe not	-	+/-
Sildenafil	-	+/- if refractory	-	-
Spirolactone		√	+/-	
Change diet	√	√		

Feline heart disease: Fluids and steroids

Can I give fluids?

- ♥ How big is the left atrium? LV cavity size? Diastolic function?
- ♥ Crystalloids
- ♥ Blood transfusion

Can I prescribe corticosteroids?

- ♥ Avoid Depomedrol
- ♥ Dexamethasone preferred (?)

Feline Heart Disease: Anesthesia

Is anesthesia safe?

- ♥ AV block or Ventricular tachycardia? Probably No!
- ♥ Active or recent CHF? No!
- ♥ Myocardial failure? Most likely no
- ♥ Stable disease and on medications; avoid alpha-2 agonists, ketamine and tiletamine?
- ♥ Fluids during anesthesia based on LA size?

How long will cats with ATE live?

- ♥ Many cats: euthanasia in the first 24 hours
- ♥ If no euthanasia in the first 24 hrs:
 - ♥ Most cats with front limb ATE regain function
 - ♥ 61 days (Atkins), 117 days (Smith), 184 days (Rush), 257 days (Lo)
 - ♥ Some cats live a very long time
 - ♥ Concurrent CHF may not impact survival
 - ♥ Recent studies suggest the death from CHF might be more common than death due to repeat ATE

Which cats should be screened for HCM?

- Cat with cardiac murmur or gallop
- Cat with arrhythmia
- Cardiomegaly on thoracic radiographs
- Open mouth breathing/unexplained respiratory distress
- Related cat has cardiac disease
- Breed predisposed to cardiomyopathy

What About the other Feline Cardiomyopathies?

ACVIM consensus statement guidelines for the classification, diagnosis, and management of cardiomyopathies in cats

Virginia Luis Fuentes¹  | Jonathan Abbott²  | Valérie Chetboul³  |
Etienne Côté⁴  | Philip R. Fox⁵  | Jens Häggström⁶  | Mark D. Kittleson⁷ |
Karsten Schober⁸ | Joshua A. Stern⁷ 

Feline Myocardial Disease

Primary myocardial disease

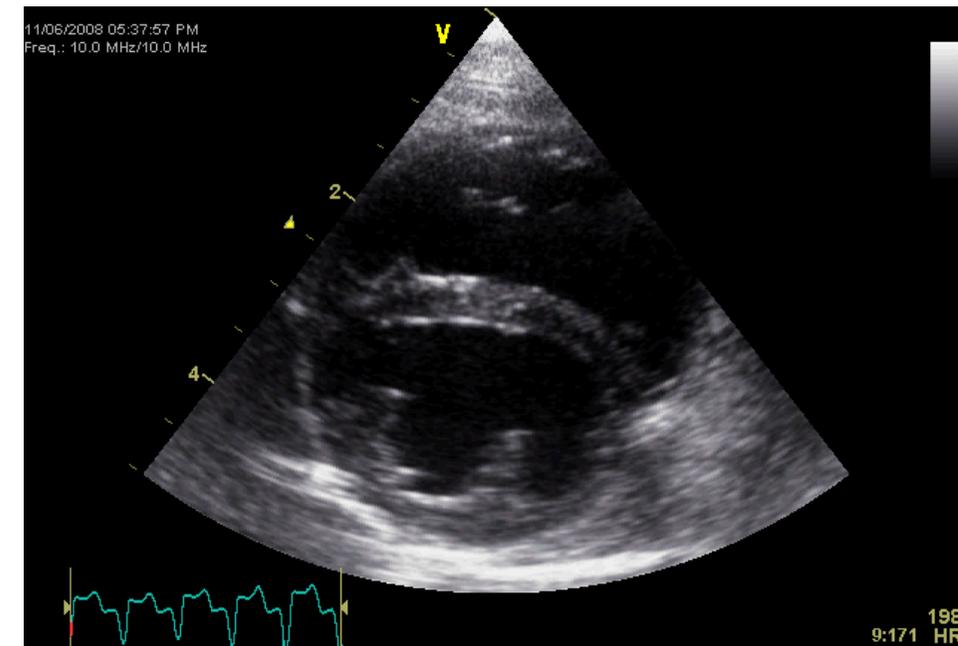
- HCM
 - Includes HOCM
- Dilated cardiomyopathy – DCM
- Restrictive cardiomyopathy – RCM
 - Includes endocardial and myocardial forms
- Arrhythmogenic right ventricular cardiomyopathy (ARVC)
- Nonspecific phenotype CM
 - Includes prior UCM or ICM
- Myocarditis (COVID?)

Systemic disease affects heart

- Systemic hypertension
- Hyperthyroidism
- Acromegaly
- Anemia
- Heartworm disease
- Pulmonary hypertension
- Bacterial endocarditis
- Transient myocardial thickening
- Hypovolemia

Feline Dilated Cardiomyopathy

- Dilation of all 4 cardiac chambers
- Reduced systolic function
- Increased LVIDs
- Often have a loud gallop, +/- soft murmur
- Often develop biventricular CHF with pulmonary edema and pleural effusion
- Taurine deficiency in selected cats
- Possible role for dietary contribution other than taurine (peas, lentils, chickpeas, sweet potatoes, potatoes)



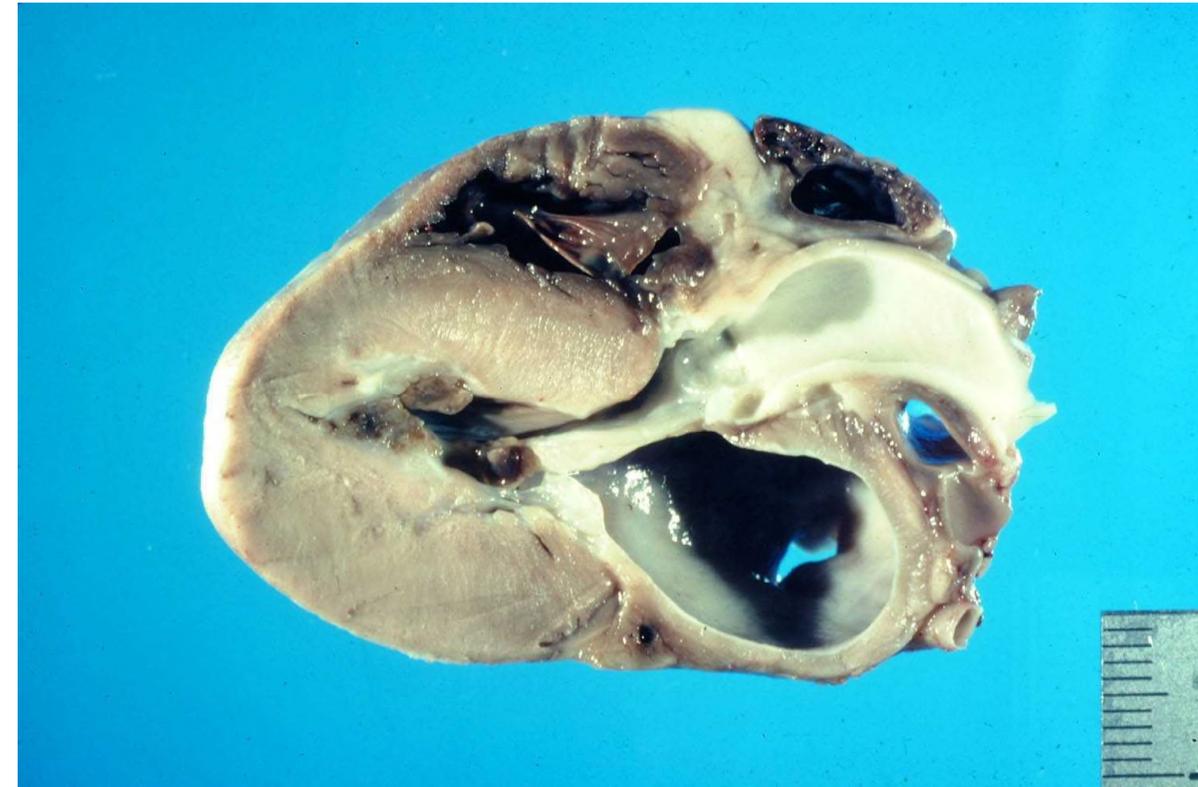
Dilated Cardiomyopathy

- Treat CHF
 - ♥ Avoid excessive diuretic dose
 - ♥ Pimobendan
 - ♥ Low or no initial ACE dose
 - ♥ Thoracentesis
 - ♥ Diet change? What are they eating?
- ATE prevention
- Arrhythmia therapy
- Taurine level; supplementation 250-500 mg BID
- Limit stress

Restrictive Cardiomyopathy

Endocardial Form

- Dramatic fibrosis in the LV endocardium
- Often myocardial inflammation below fibrosis
- Fibrosis restricts LV diastolic filling
- Left atrial enlargement
- Prone to ATE



Arrhythmogenic Right Ventricular Cardiomyopathy ARVC

- Thinning of the RV free wall with RV dilation
- RV wall replaced with fat or fibrous tissue
- Thinning of the RV apex
- Can be confused with tricuspid dysplasia
- Right heart failure
- Arrhythmias or conduction disturbances
- May eventually affect LV as well

Cardiomyopathy with Nonspecific Phenotype

- Do not fulfill diagnostic criteria for DCM or HCM or RCM or ARVC
- No apparent pericardial, coronary, valvular disease or systemic hypertension
- Myocardial disease that defies classification
 - ♥ Walls of variable thickness
 - ♥ Cavity +/- dilated
 - ♥ May have reduced systolic function
 - ♥ Mild valvular regurgitation may be evident
- Suspect that most cases are “Burned out” HCM!



Management of CHF in Cats

- Usual CHF care:
 - Furosemide – 1-2 mg/kg q 12-24 hr
 - ACE inhibitor - Unless side effects
 - Pimobendan - Avoid if outflow tract obstruction?
 - Antithrombotics
 - Diet change - Sodium restriction, +/- fish oil
- Advanced CHF and special circumstances:
 - Spironolactone – repeated pleural effusion
 - Injectable furosemide sub-Q
 - Torsemide
 - High dose pimobendan
 - Entresto? (sacubitril/valsartan)
 - Beta-blocker if LVOTO?

Hyperthyroid Heart Disease

- Scenario 1: Fast heart rate, LVH, murmur, no CHF
 - Treat hyperthyroidism first
 - Most cats do not need cardiac specific Rx
- Scenario 2: CHF, more than mild LAE, serious arrhythmia
 - If CHF, most often concurrent heart disease
 - Lifelong cardiac issue; unlikely resolution with Rx of hyperthyroidism
 - ATE prevention: if CHF or \geq moderate LA enlargement
 - Heart rate and arrhythmia therapy
 - Usually do not need to treat sinus tachycardia
 - Atenolol vs carvedilol vs sotalol for arrhythmias

Recheck of the Cat with CHF: When and what to do?

- Routine recheck 5 to 12 days
 - History and PE - Drugs, response, administration problems?
 - Renal values plus electrolytes
 - **BUN > 35? Creatinine > 1.9? Can furosemide dose be reduced?**
 - PCV, total solids – compare trends
 - **Total solids > 7.5 – can furosemide dose be reduced?**
 - +/- Thoracic radiographs if any dyspnea
 - ECG if arrhythmia
 - Blood pressure is at all lethargic
 - **BP < 110 mm Hg might want a dose reduction?**



*I wonder if she is breathing
Hard??*