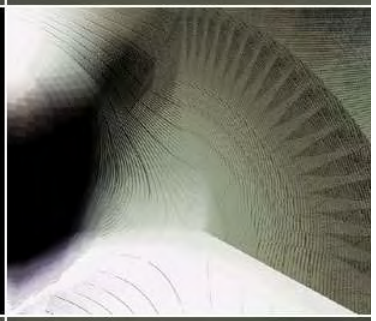
Hypertrofische cardiomyopathie bij de kat in 2019



Nicole Van Israël
European Specialist™ in Veterinary Cardiology

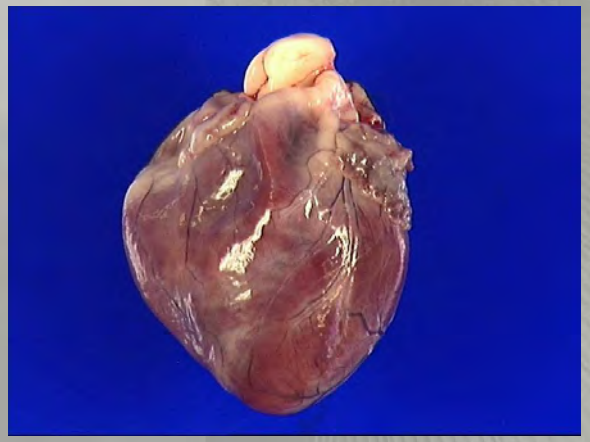
www.acapulco-vet.be

Classificatie

WHO: HCM, RCM, DCM, ARVC, UCM

DGK: primair, secundair

HCM



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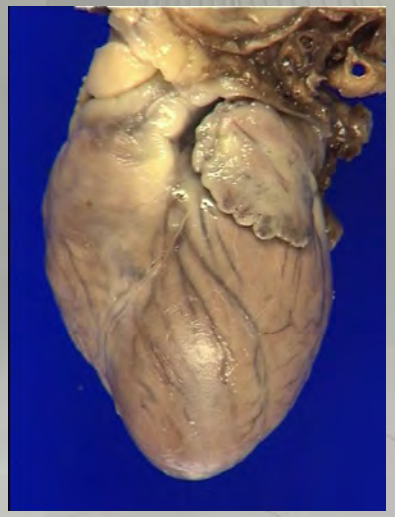
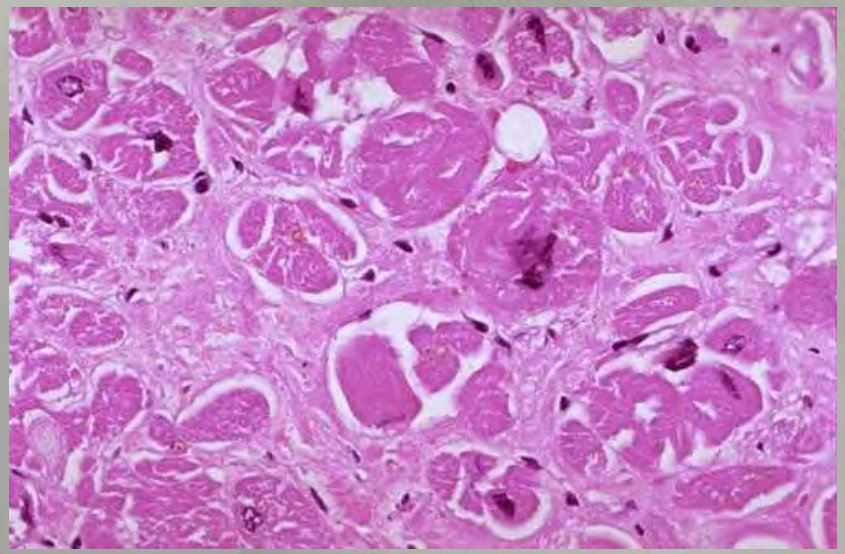
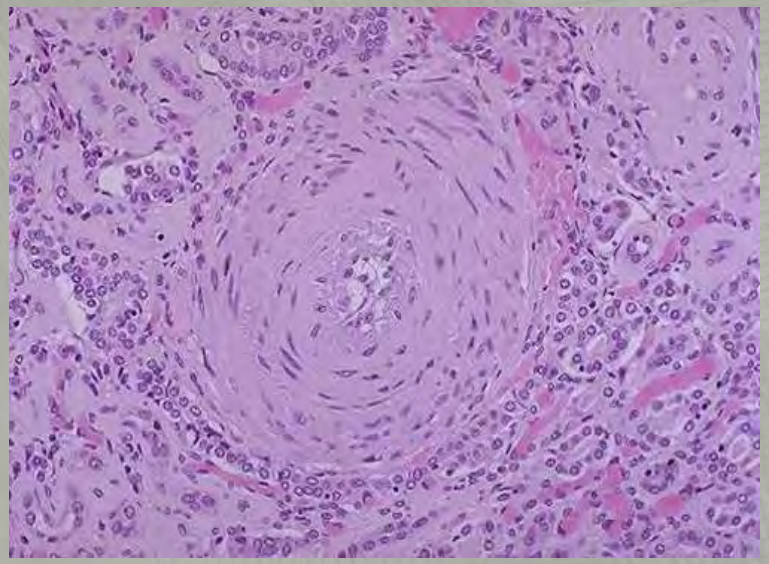


Merci Marianne Heimann

HCM

Definitieve diagnose via histopathologie !!!





©Kittleson

Vet Pathol. **Feline Hypertrophic Cardiomyopathy: The Consequence of Cardiomyocyte-Initiated and Macrophage-Driven Remodeling Processes?**

HCM primair idiopathisch

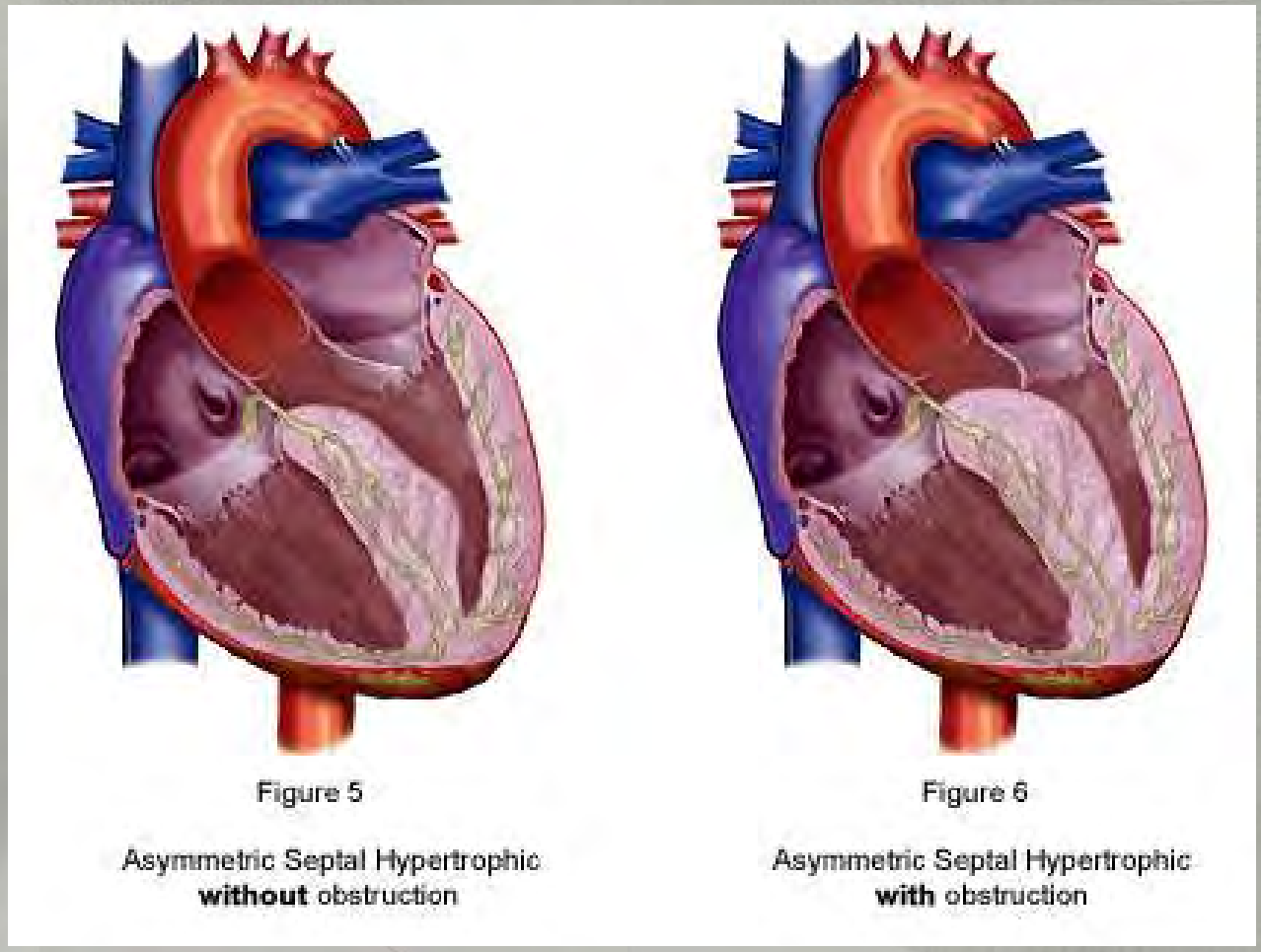


Figure 5

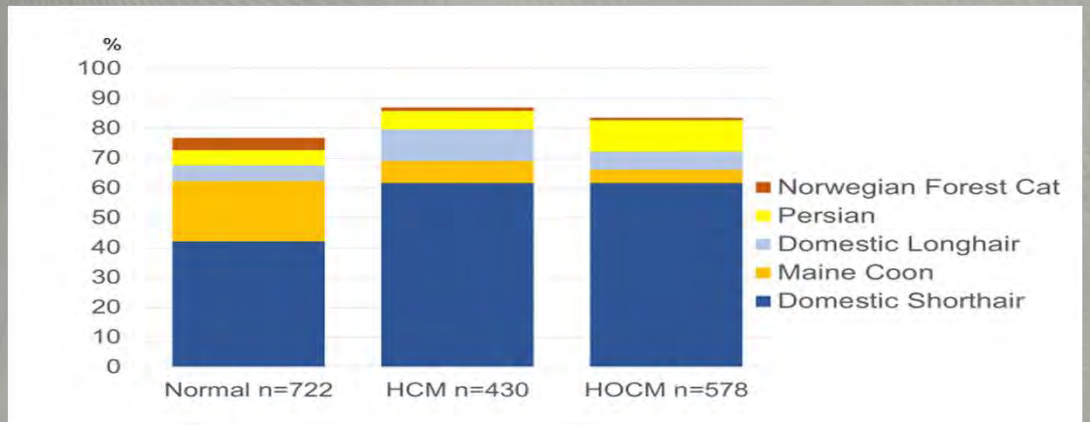
Asymmetric Septal Hypertrophic **without** obstruction

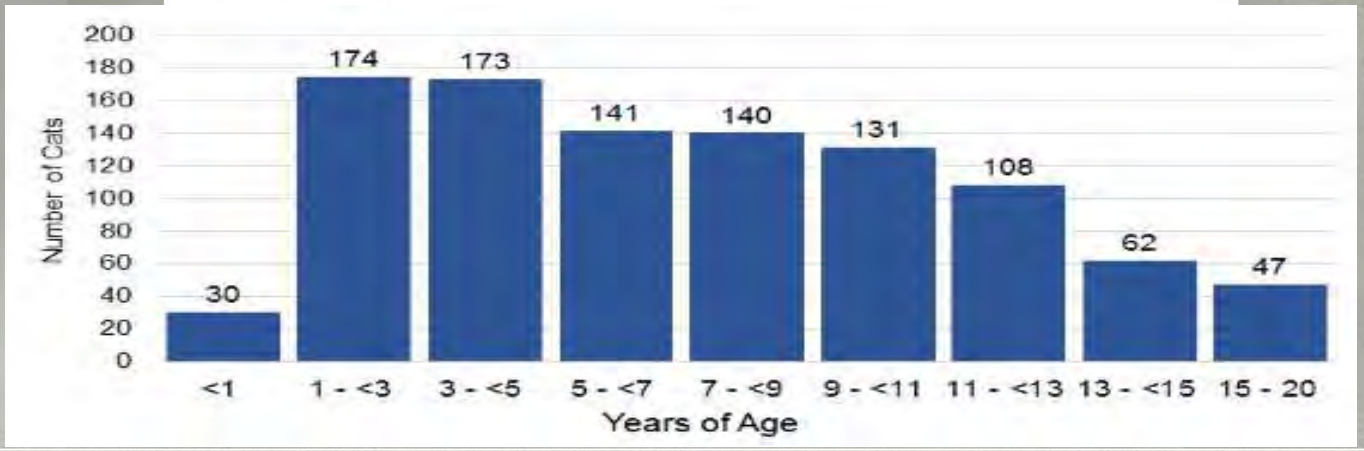
Figure 6

Asymmetric Septal Hypertrophic **with** obstruction

Primaire HCM epidemiologie

- Meest voorkomende CM: 15 % katten aangetast
- Vnl gewone katten, niet altijd raskatten
- Prevalentie verhoogt met de ouderdom
- M>V





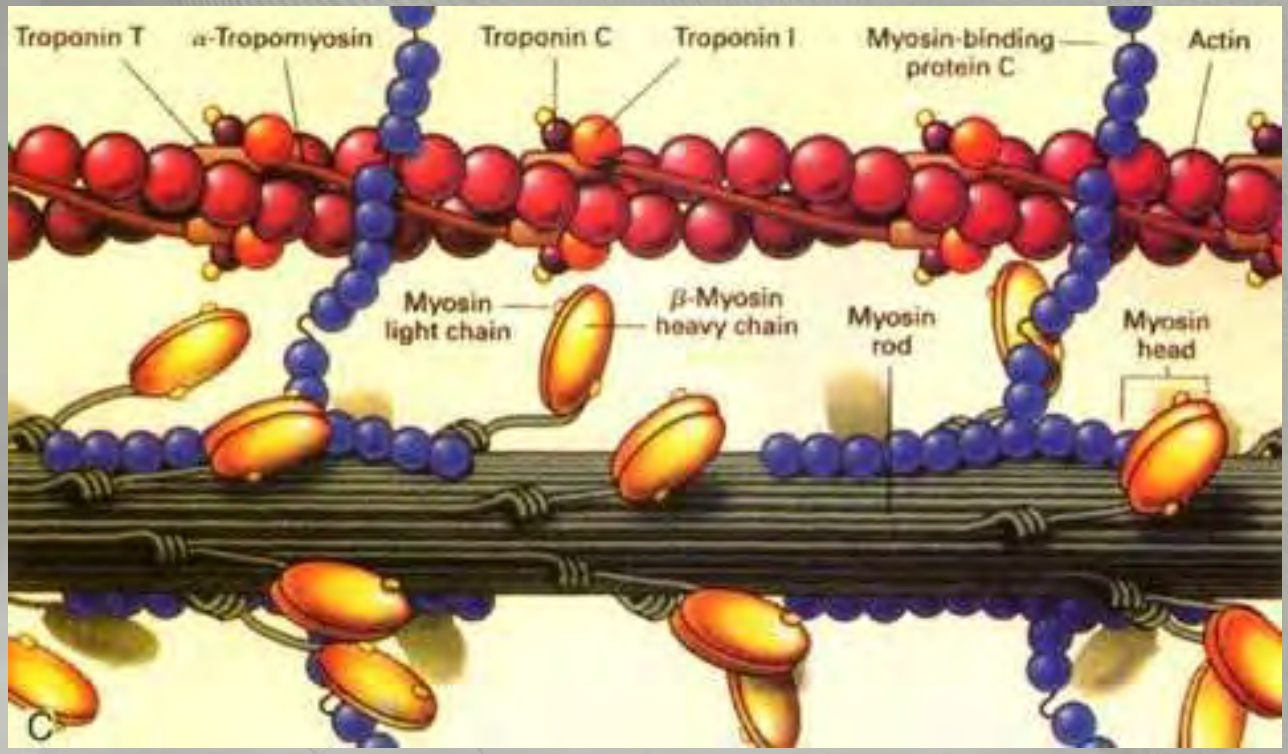
Catscan study 2015 , REVEAL study 2018

HCM genetisch

- Maine Coon, Amerikaanse Shorthair, Britse KH, Pers, Ragdoll, Cornish Rex, Sphynx, NWF, Siberische, Bengaal…
- MI > VI (uitz BKH =)
- Alle leeftijden maar meestal jong
- Progressie is individueel maar bijna altijd fataal
  - homo/heterozygoot
- Sarcomerische mutatie: myosin binding protein C gen
- Autosomaal dominant, incomplete penetratie, variabele expressie

MYBPC3

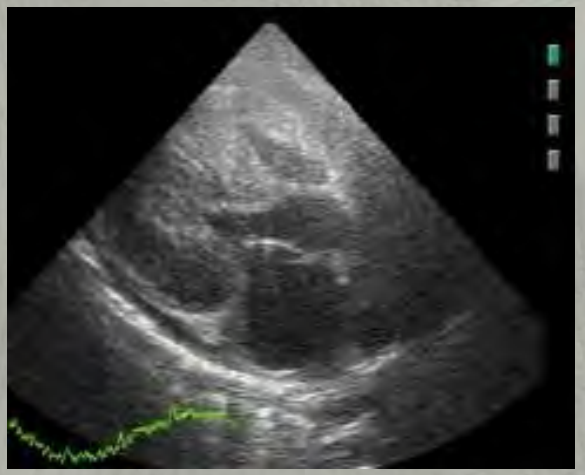
- Maine Coon: A31P, 34 %, relatieve risico x1,8 heterozygoot, x18 homozygoot, niet de enige mutatie, 5% negatief mutatie, M>F, gewicht geassocieerd, meestal voor 4 jr
- Ragdoll: R820W, heterozygoot ontwikkelen de ziekte niet, homozygoot <2jr



Meurs et al 2005 en 2007, Pedersen 2018, Wess 2010

HCM secundair

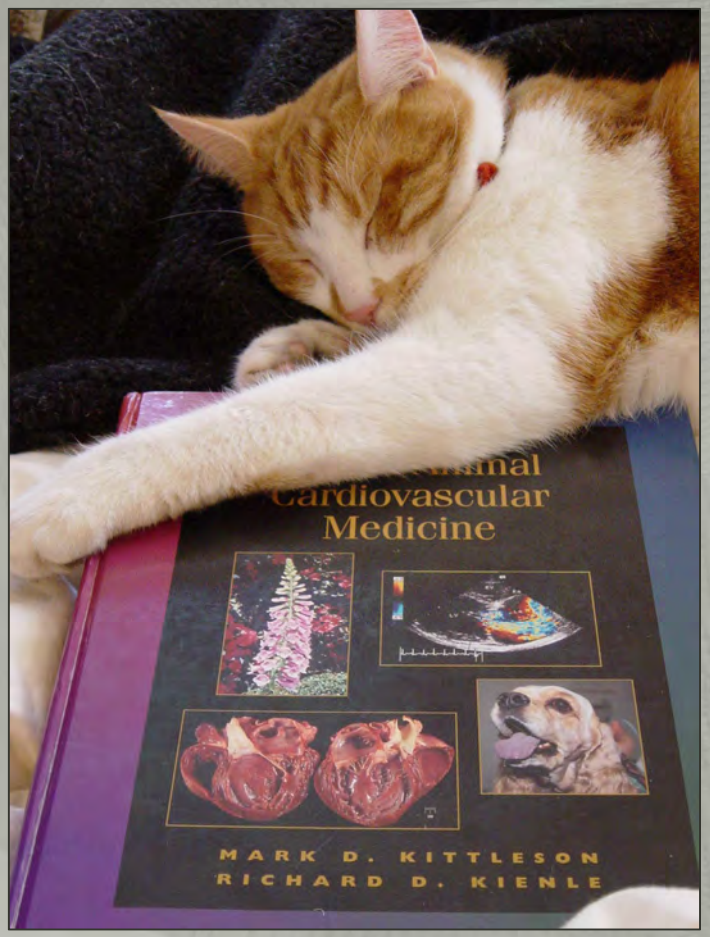
- Hypertensie
- Hyperthyroïdie
- Acromegalie/DM
- Phaeochromocytoma
- Myocarditis
  - FIP
  - Toxo
  - Bartonella
  - FIV/FeLV
- Infiltratie
  - Eosinofiel syndroom
  - Lymphoma en andere neoplasia
  - Obesiteit
- Transient myocardial thickening
- Cortico-geïnduceerd
- Pseudohypertrofie: uitdroging, shock,…



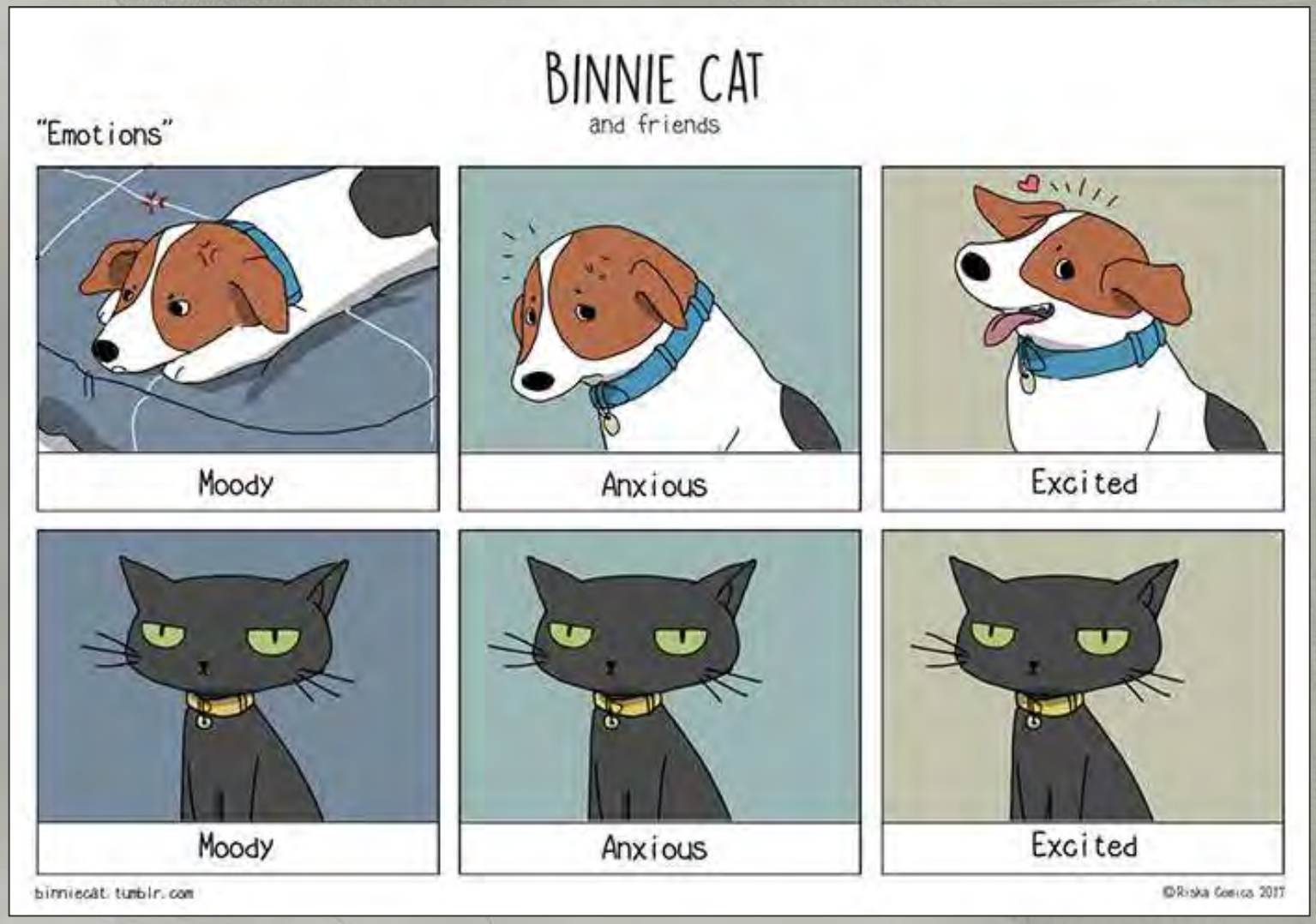
Smith et al 2004; Novo Matos et al 2018, Borgeat et al 2018

HCM DIAGNOSE

- Observatie
- Klinisch onderzoek
- Bloeddrukmeting
- ECG
- Radiografie
- Bloedonderzoek
- Echografie
- Pathologie

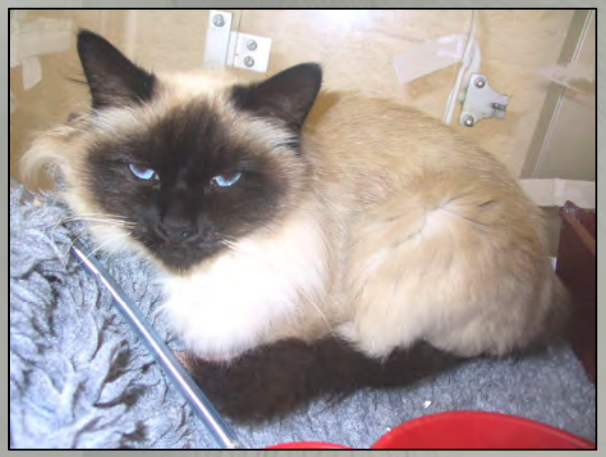


HCM DIAGNOSE observatie



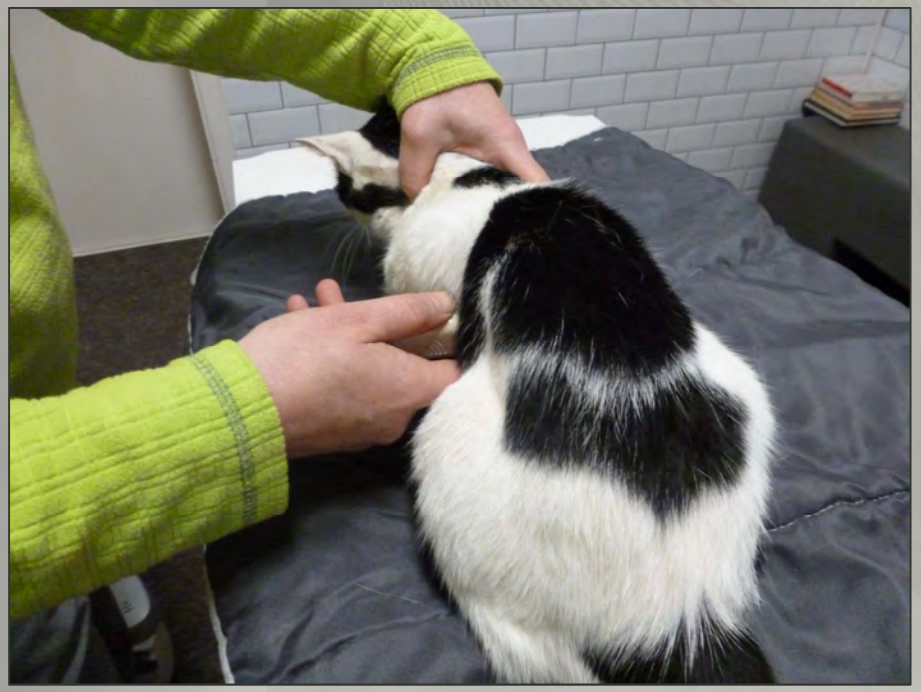
HCM DIAGNOSE observatie

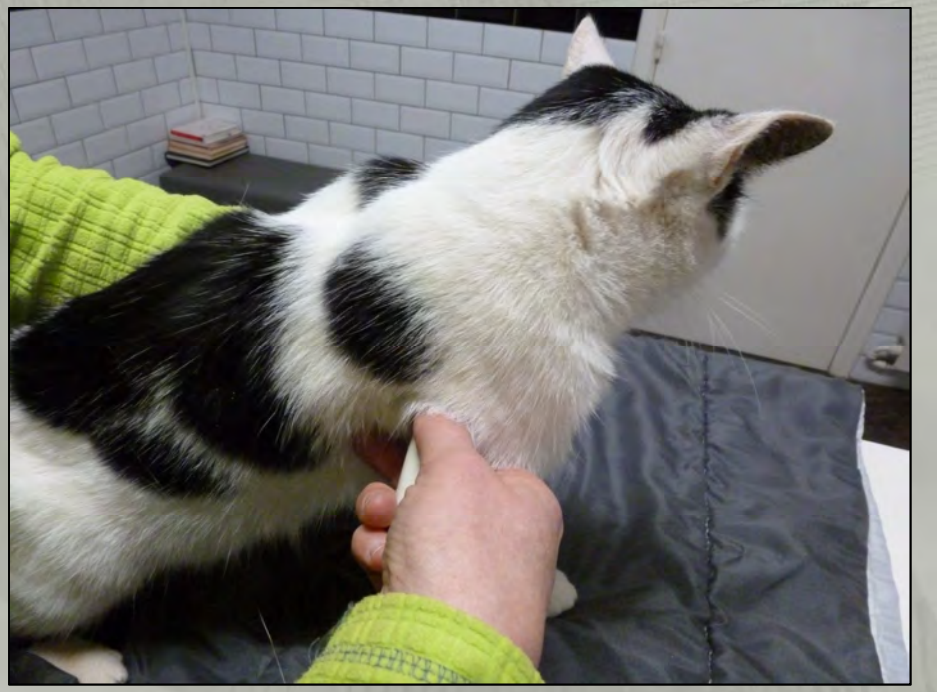
- AH frekwentie ?



HCM DIAGNOSE kritisch?

- FASTx-TFAST- POCUS?

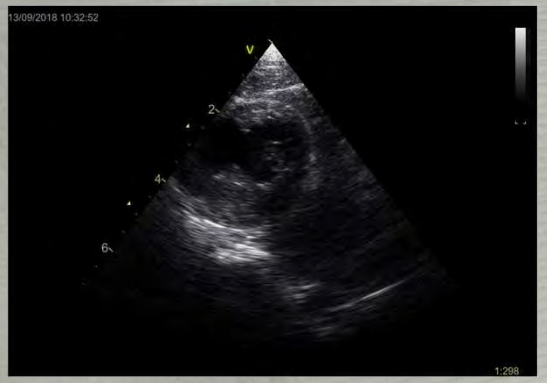


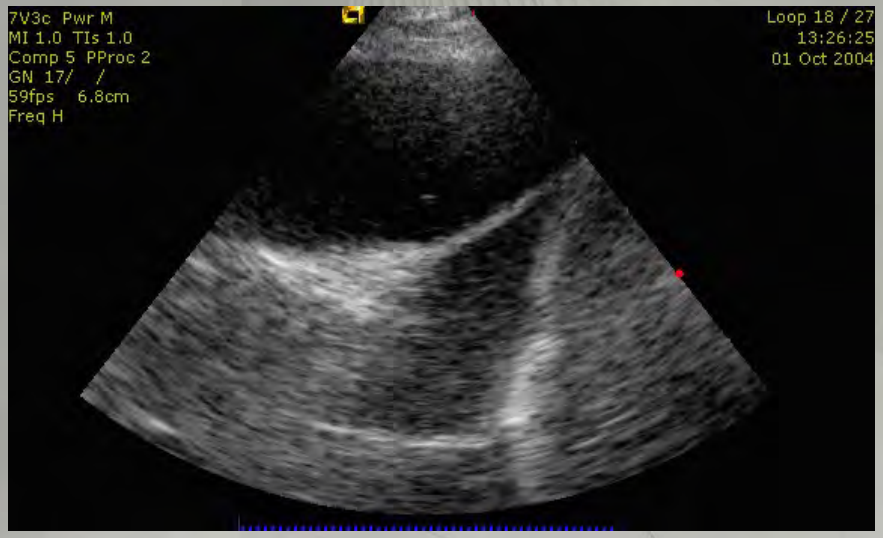


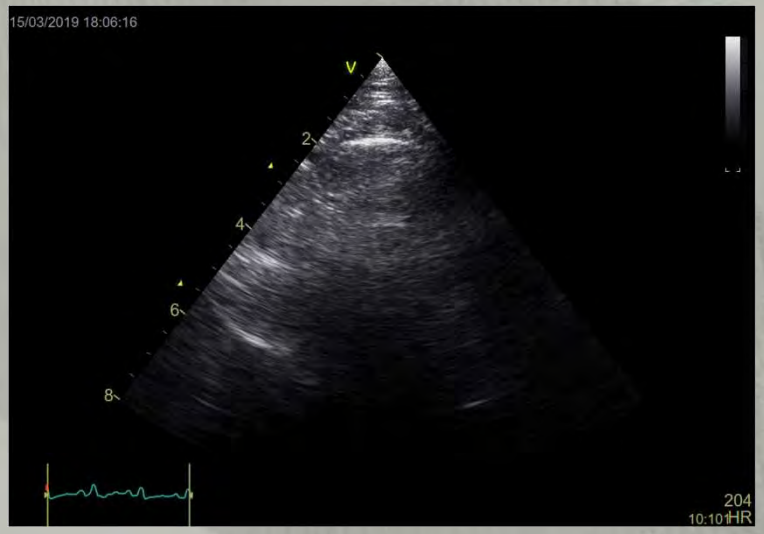
Van Israël 2005, Boysen 2016, Ward 2018

HCM DIAGNOSE kritisch?

- FASTx-TFAST- POCUS?
  - Pleurale effusie
  - Pulmonair oedema: > 3 B lines/site
  - LA-vergroting







Van Israël 2005, Boysen 2016, Ward 2018

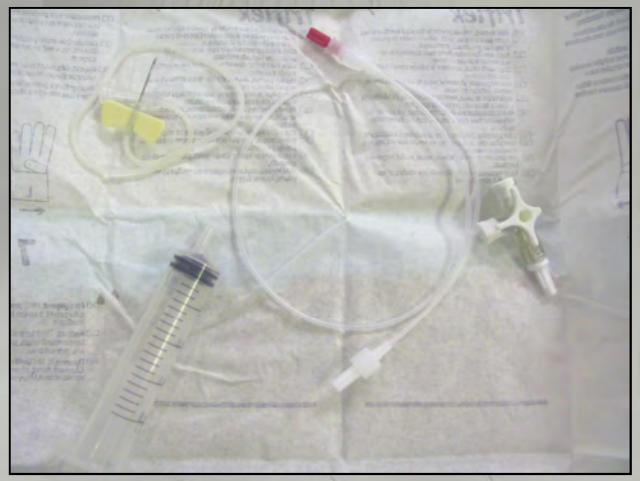
HCM DIAGNOSE kritisch?

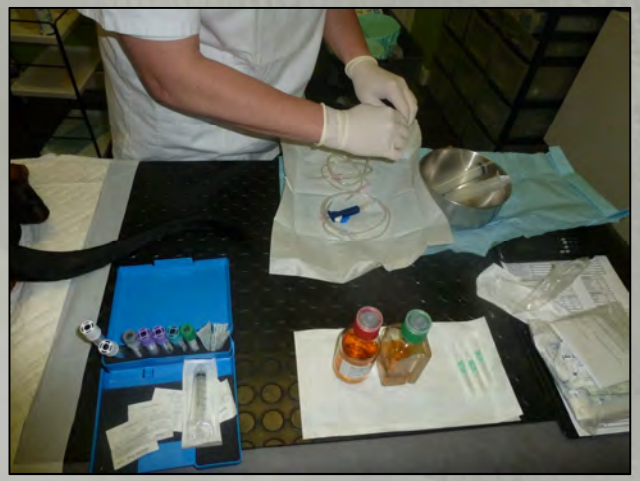
- Thoracocentese ?

KAN EEN LEVEN REDDEN en is diagnostisch

HCM DIAGNOSE kritisch?

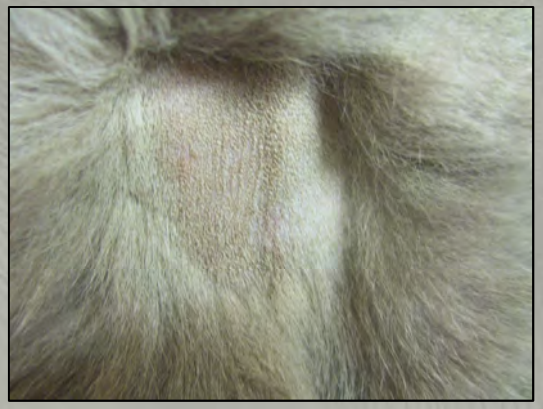
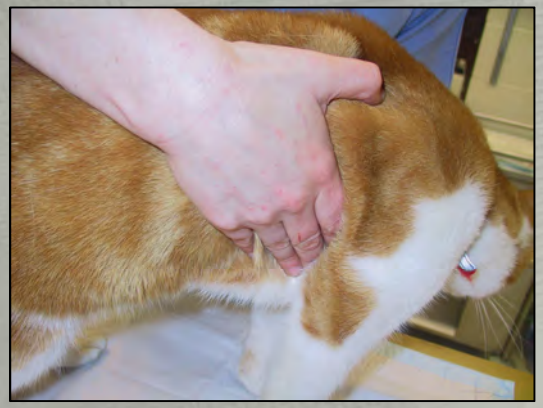
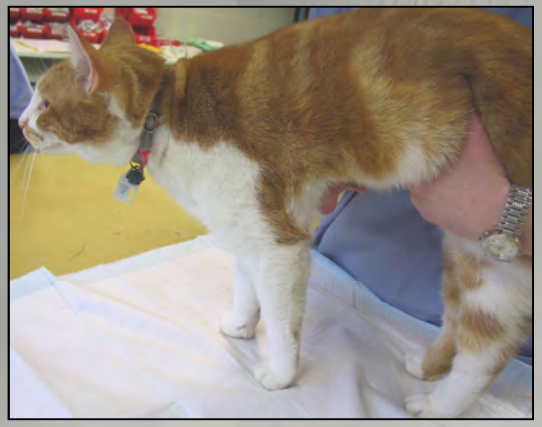
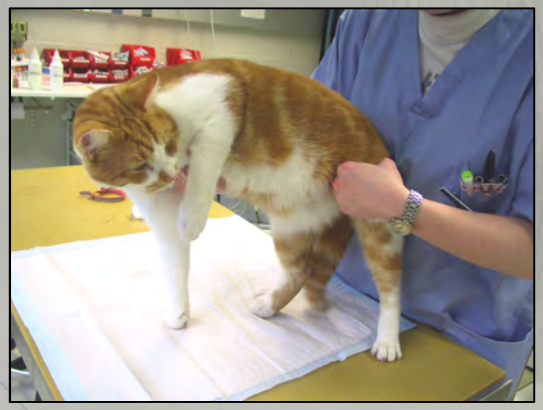
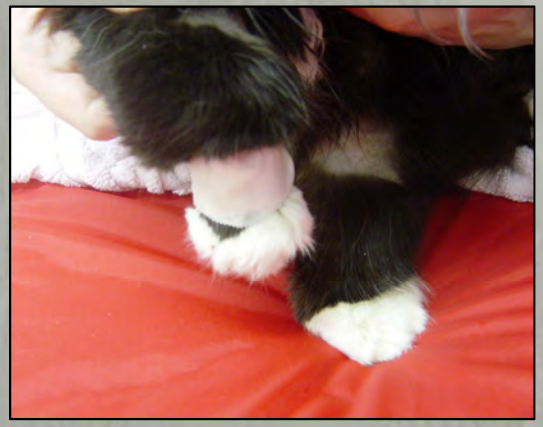
- Thoracocentese
  - Dichtheid
  - TP, alb/glob, TG/cholesterol (serum)
  - Formule (celtelling) en cytologie (EDTA, direct, cytospin)
  - Cultuur aëroben en anaëroben
  - HCT indien bloederig vocht
  - NT-pro BNP bedside: moet verdund worden 1/1
    100 % sens, 86 % spec
    Cut-off 229pmol/l (onverdund 467 pmol/l)





HCM DIAGNOSE klinisch

- Klinisch onderzoek

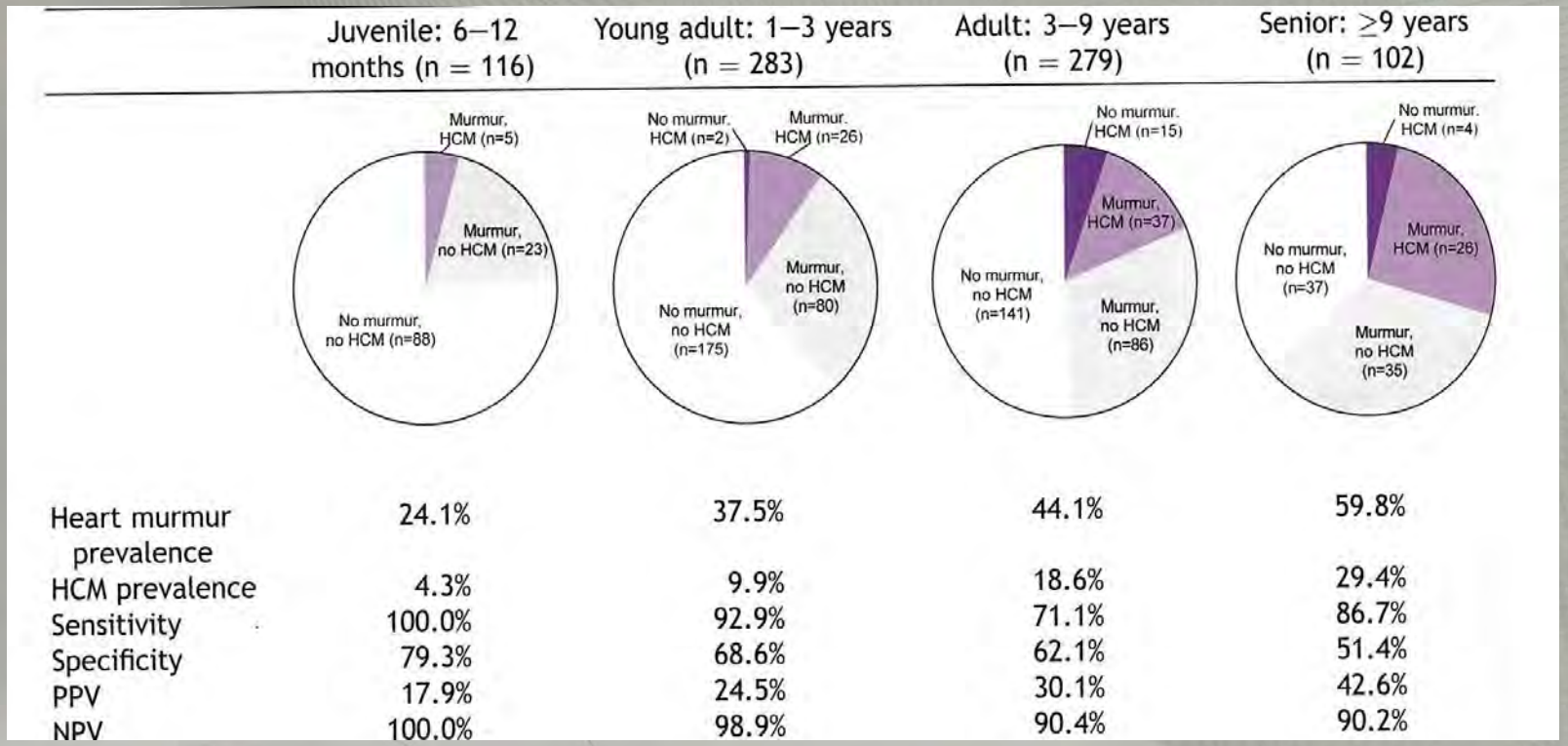







HCM DIAGNOSE klinisch

- Auscultatie
  - Hartfrekwentie
  - Bijgeruis
  - Gallop
  - Ritme: VPC's, AF

HCM DIAGNOSE klinisch

- Bijgeruis
  - PPV 17-40 % (jong-oud)
  - NPPV 90-100 % (oud-jong)

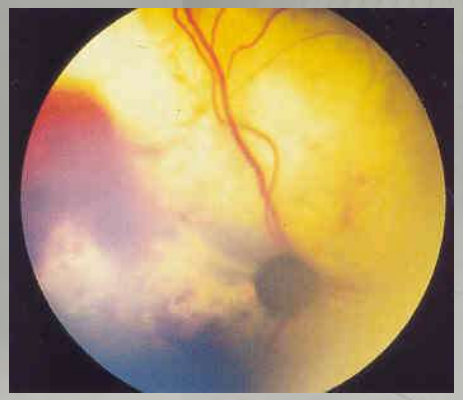


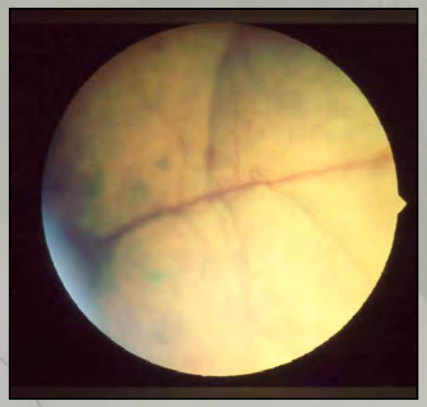
	Juvenile: 6–12 months (n = 116)	Young adult: 1–3 years (n = 283)	Adult: 3–9 years (n = 279)	Senior: ≥9 years (n = 102)
Heart murmur prevalence	24.1%	37.5%	44.1%	59.8%
HCM prevalence	4.3%	9.9%	18.6%	29.4%
Sensitivity	100.0%	92.9%	71.1%	86.7%
Specificity	79.3%	68.6%	62.1%	51.4%
PPV	17.9%	24.5%	30.1%	42.6%
NPV	100.0%	98.9%	90.4%	90.2%

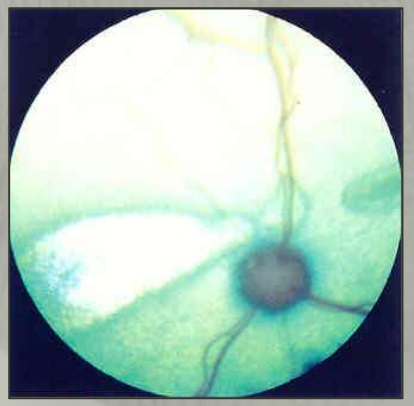
Catscan study 2015

HCM DIAGNOSE klinisch

- Oftalmologisch onderzoek
  - Hoge bloeddruk
  - Myocarditis
  - Taurinedeficiëntie (DCM)

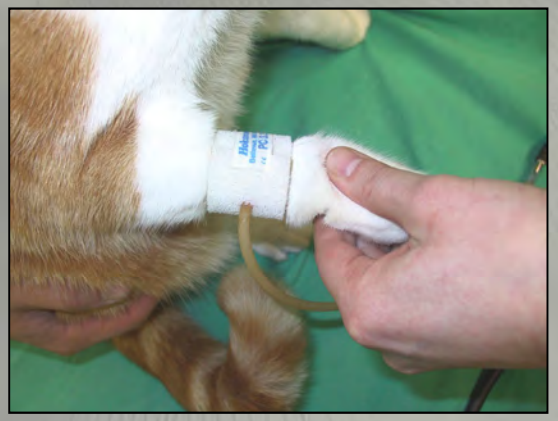


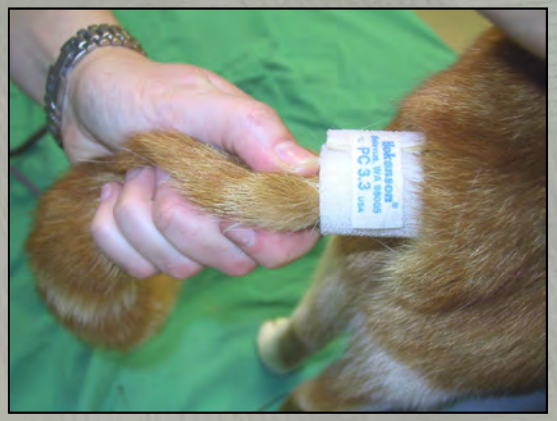




HCM DIAGNOSE bloeddruk

- Doppler





ACVIM Consensus 2017

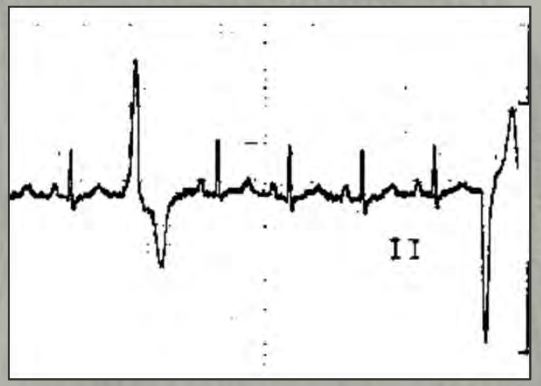
Risk for Target organ damage

Category	Systolic	Risk
Normotensive	< 140	Minimal
Prehypertensive	140-159	Low
Hypertensive	160-179	Moderate
Severely hypertensive	≥ 180	High risk

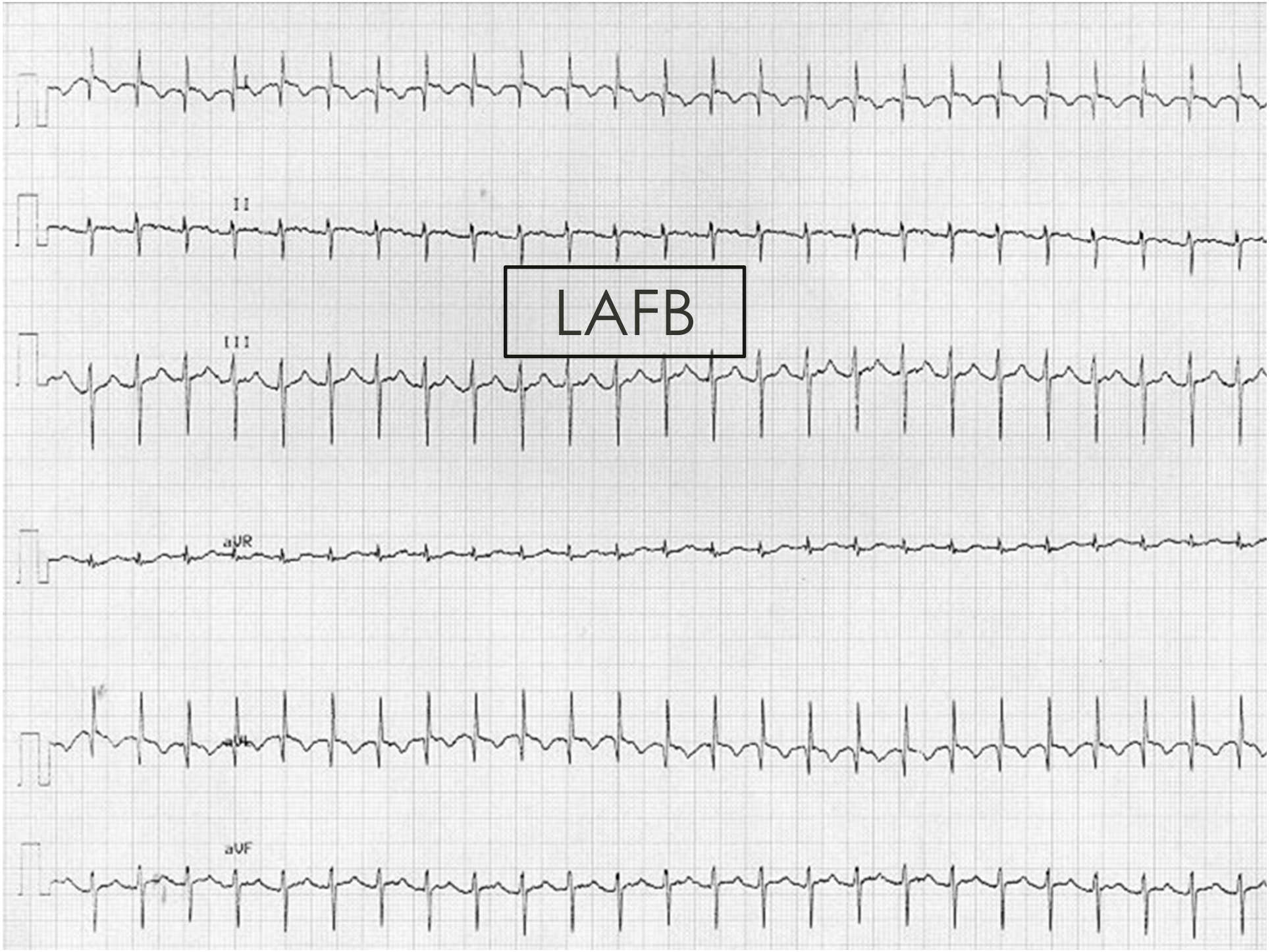
HCM DIAGNOSE

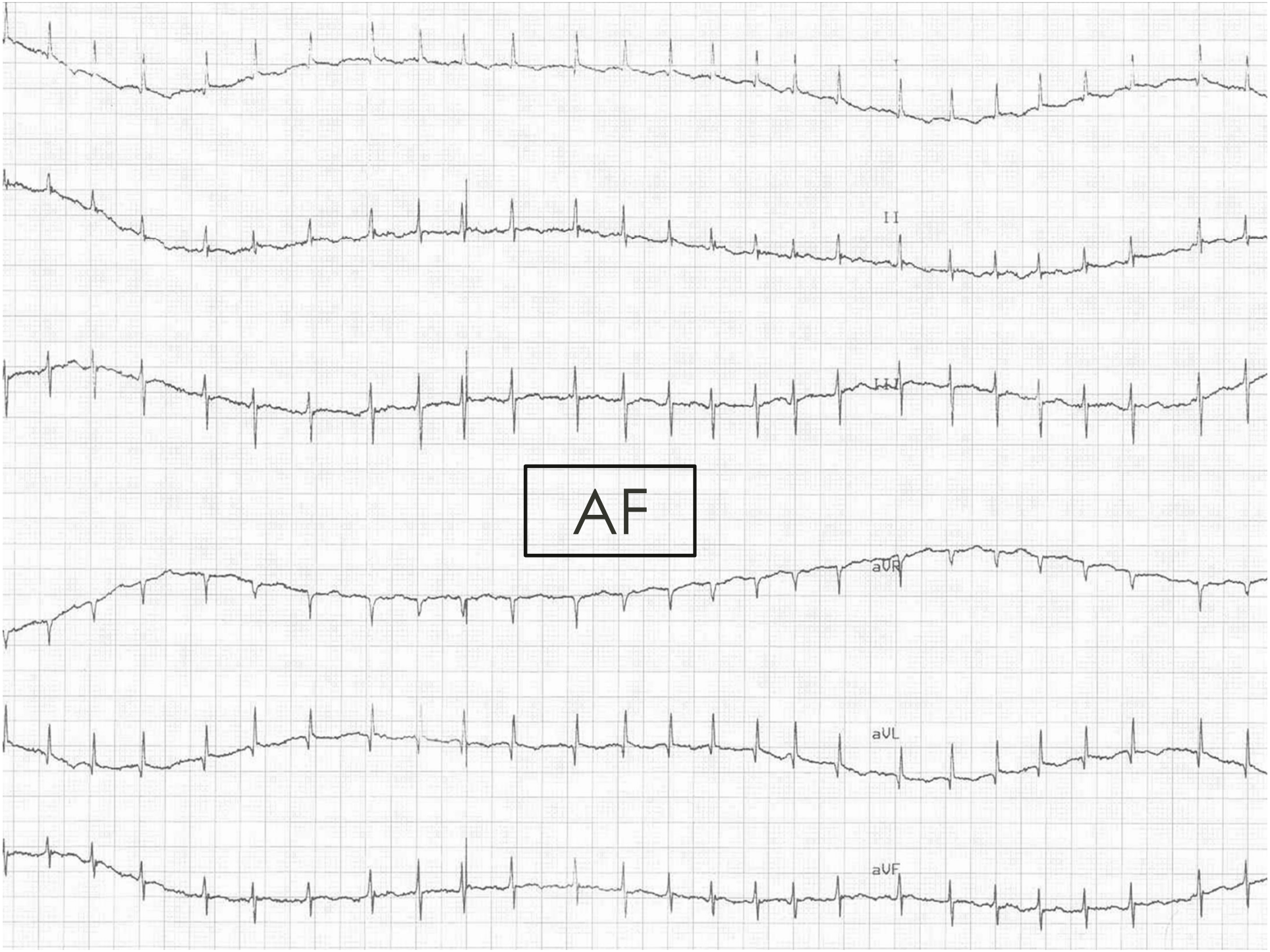
- ECG

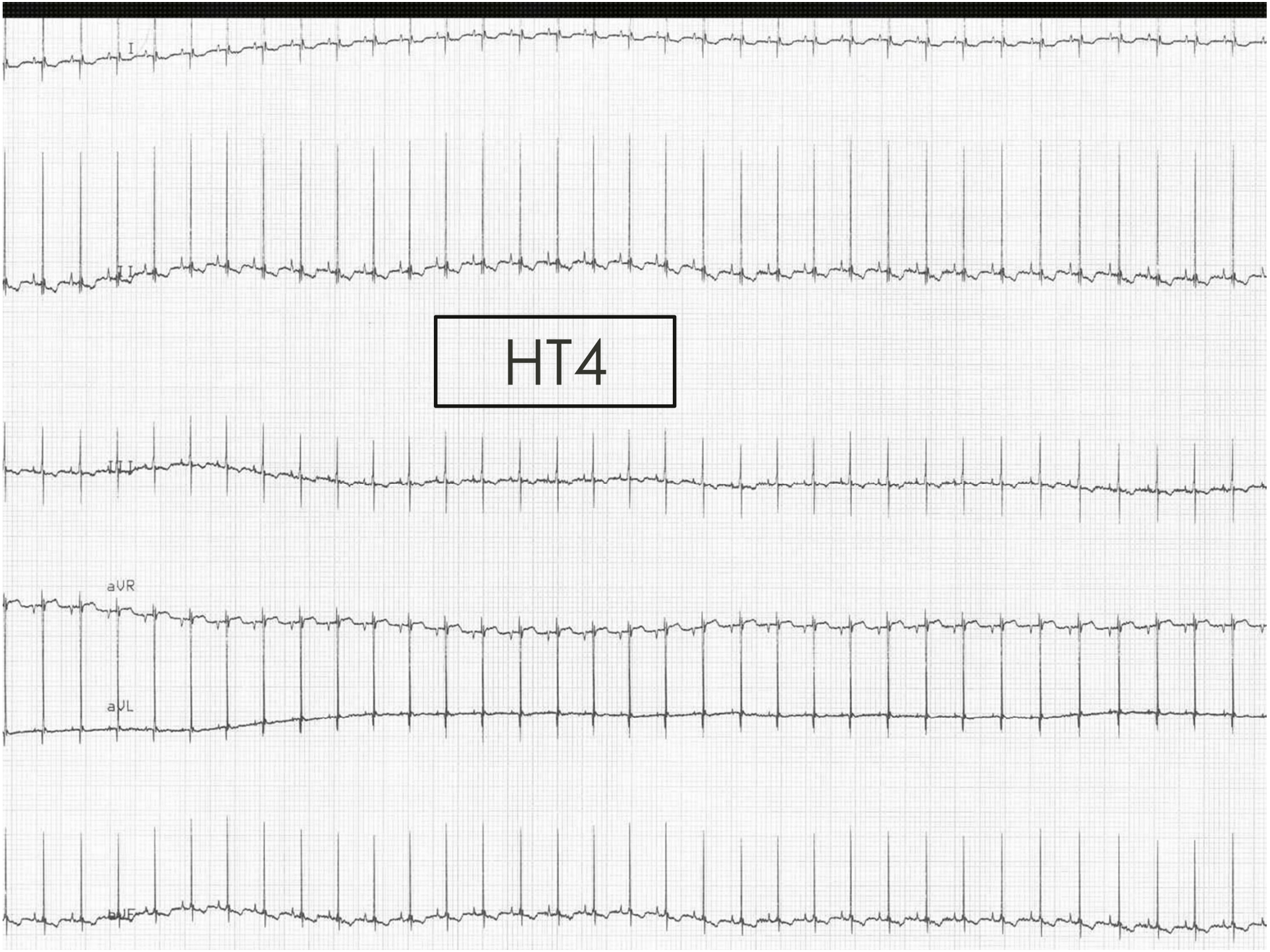
  - LAFB
  - VPC's
  - SVT
  - AF: advanced disease
  - Grote R > hyperthyroïdie
  - Q-T verlenging (>170 ms)
    - sens 62 %, spec 91 %



Romito et al 2018

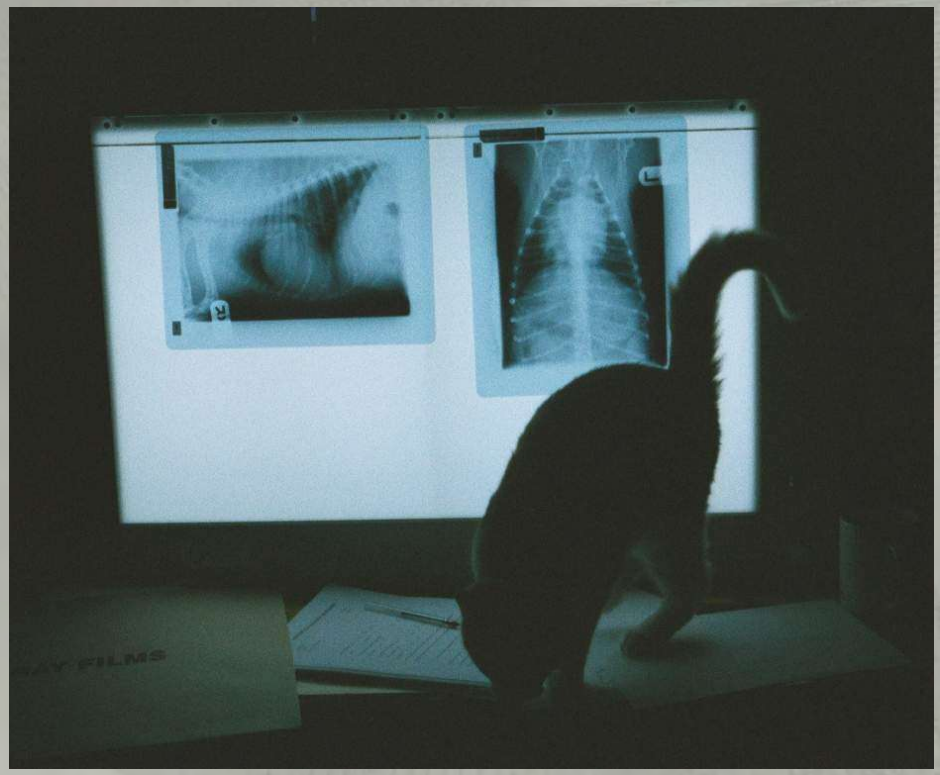

II
III
aVR
aVF
LAFB


II
III
AF
aVR
aVL
aVF

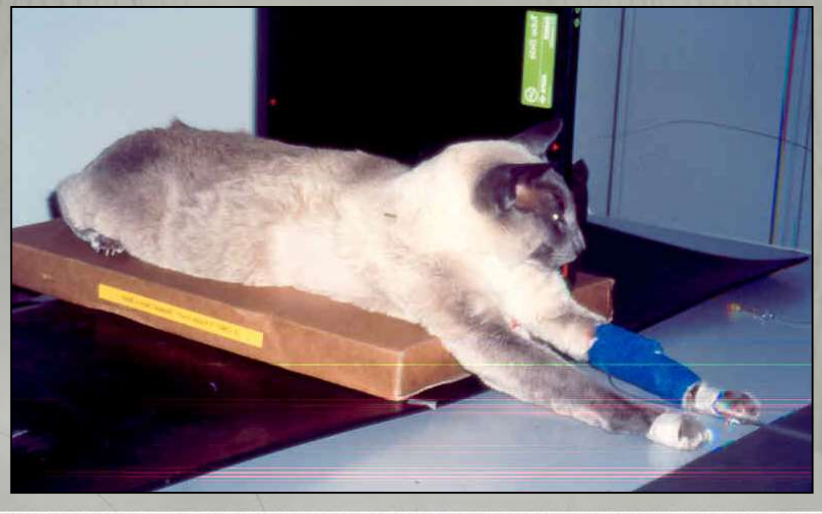

I
II
HT4
III
aVR
aVL
aVF

HCM DIAGNOSE

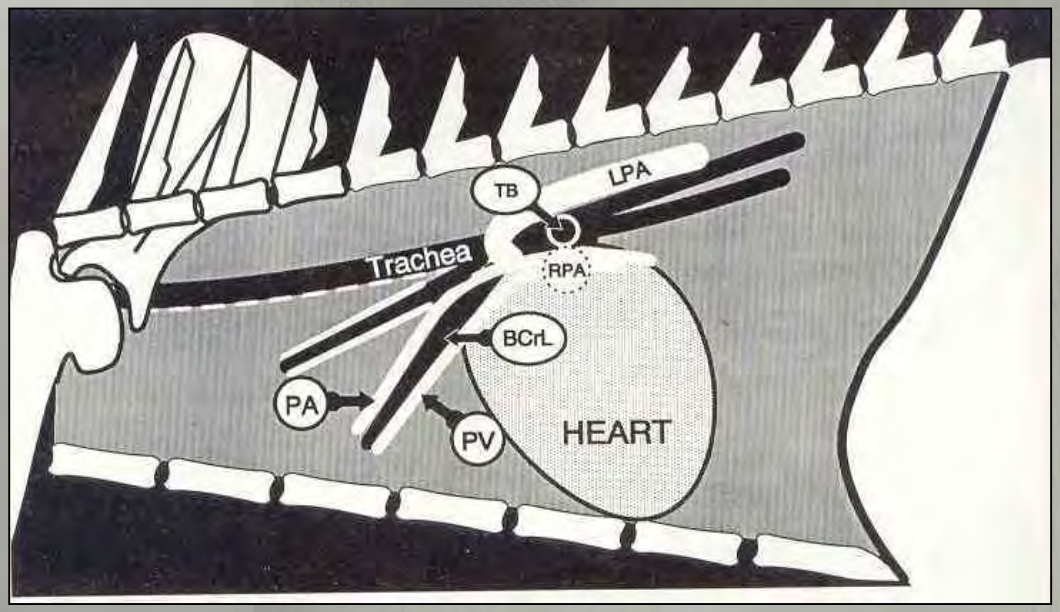
- Radiografie
  - DV en R-Lat
  - Valentijnshart
  - Hartfalen
  - Aorta

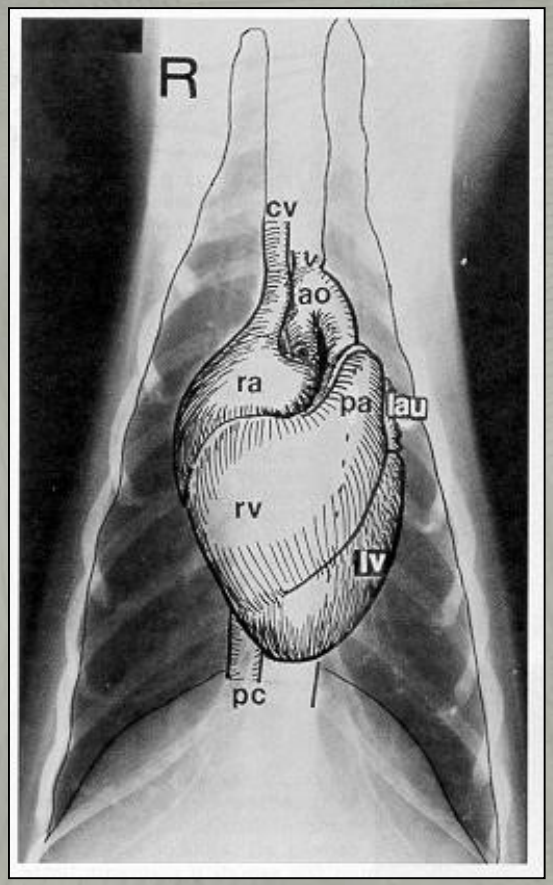


HCM RX



HCM RX VHS

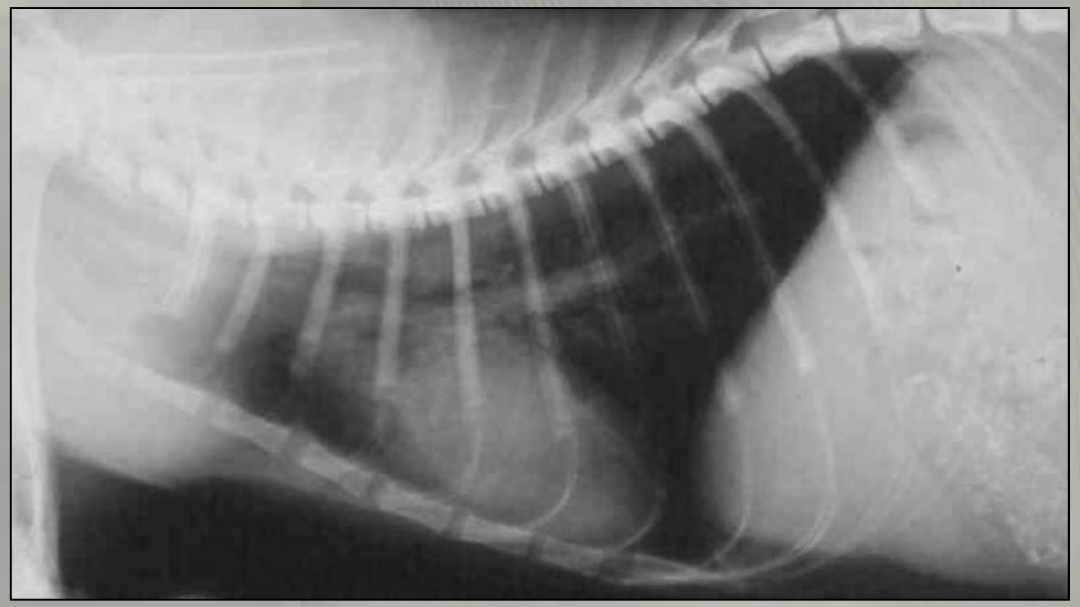


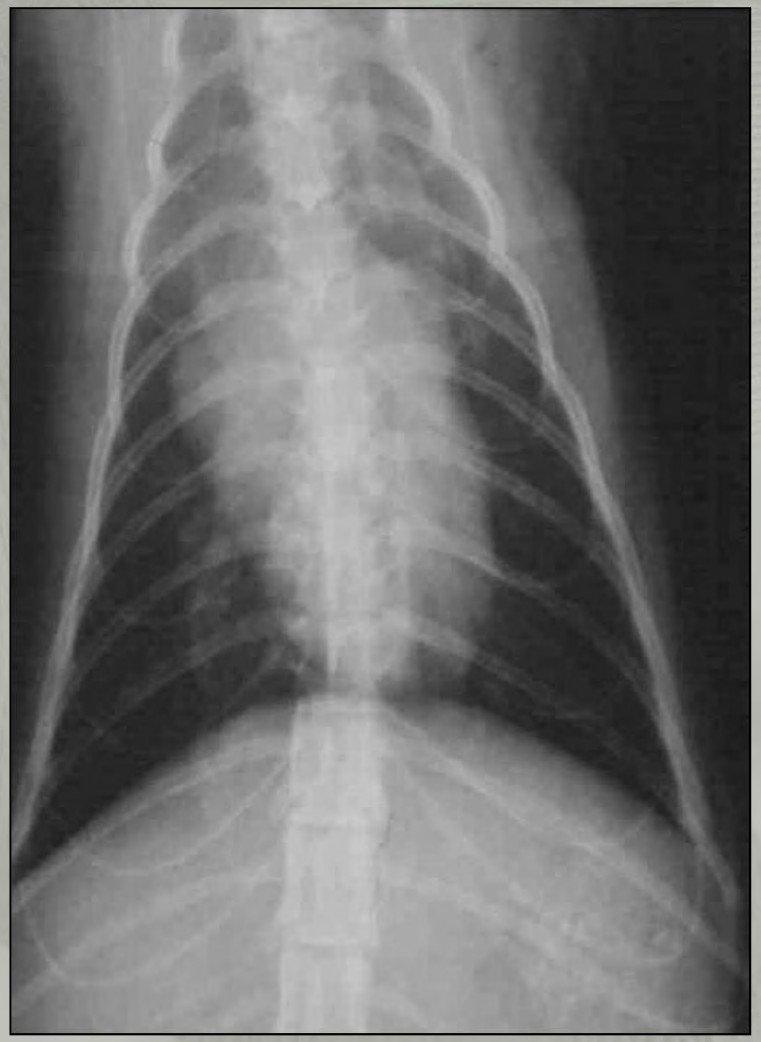


VHS < 8v

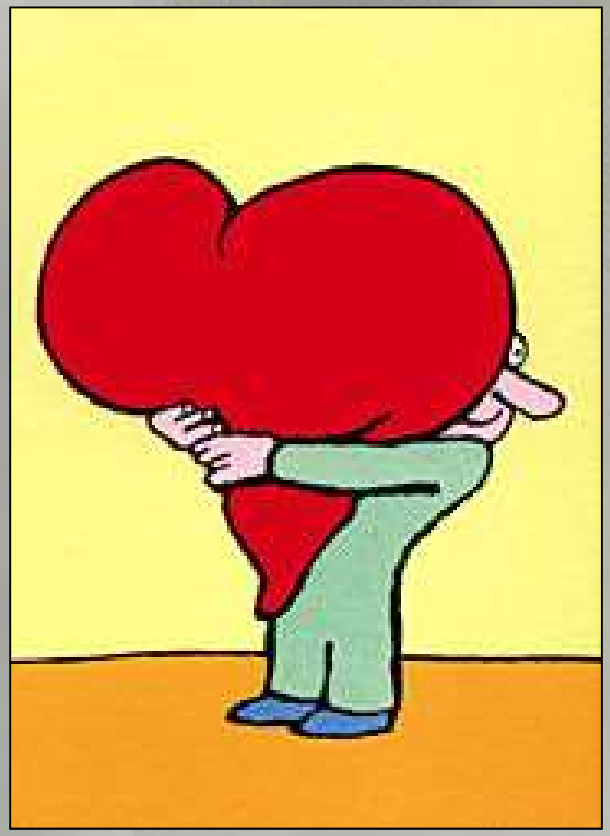
Suter 1997

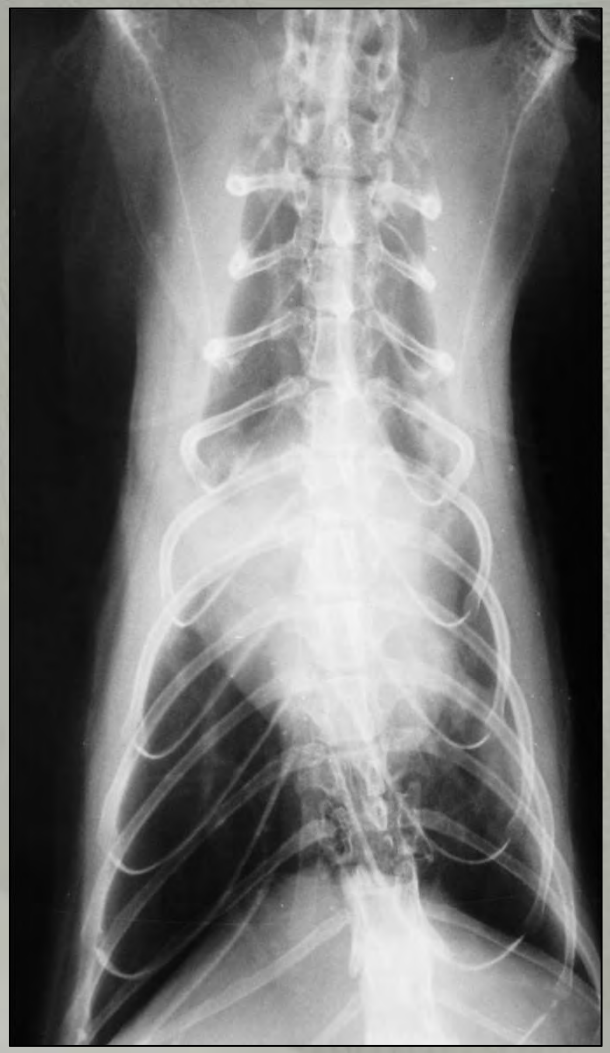
HCM RX cardiomegalie



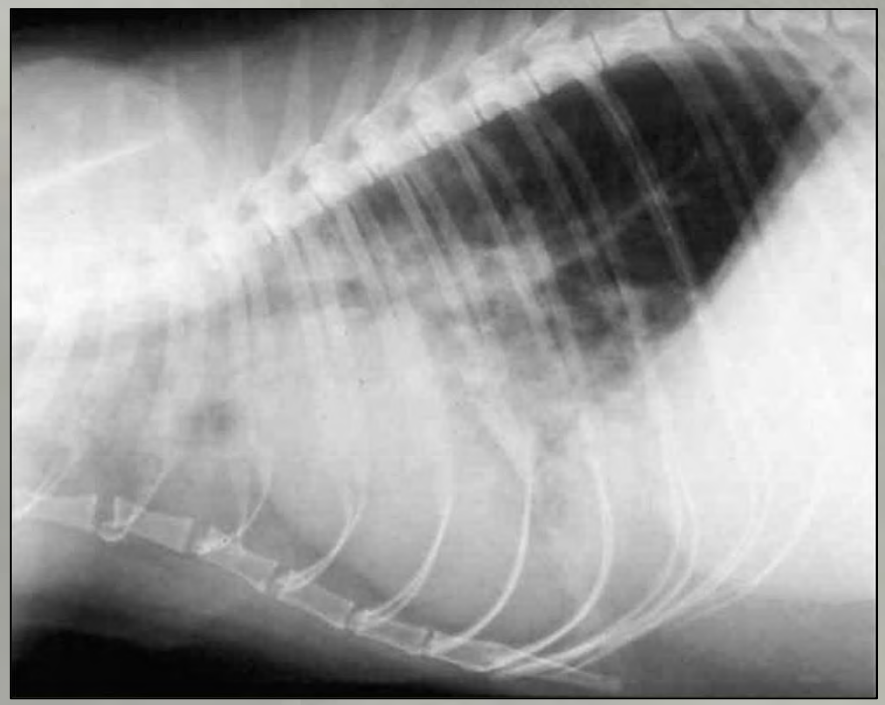


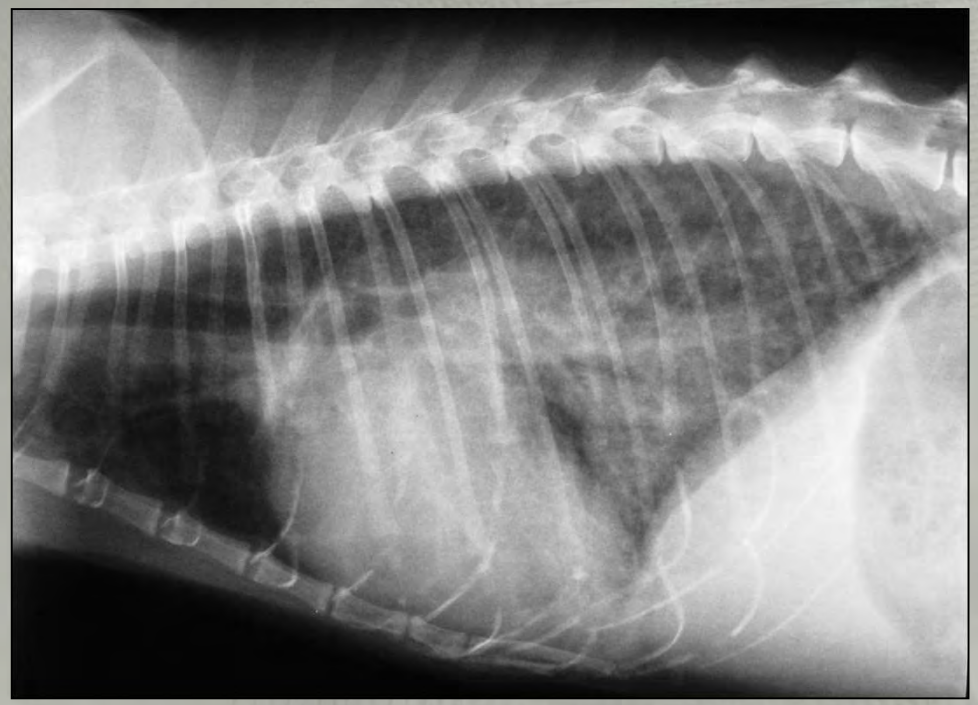
HCM RX LA vergroting



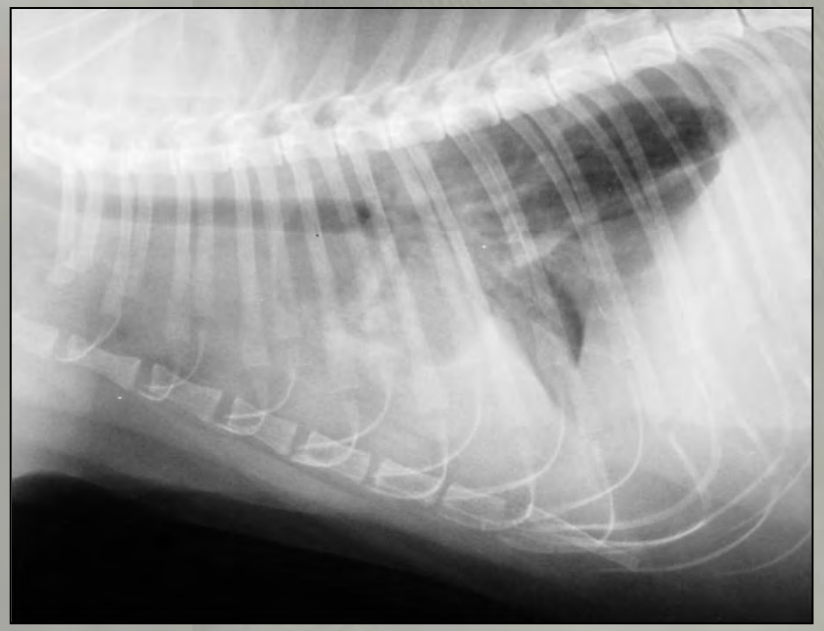


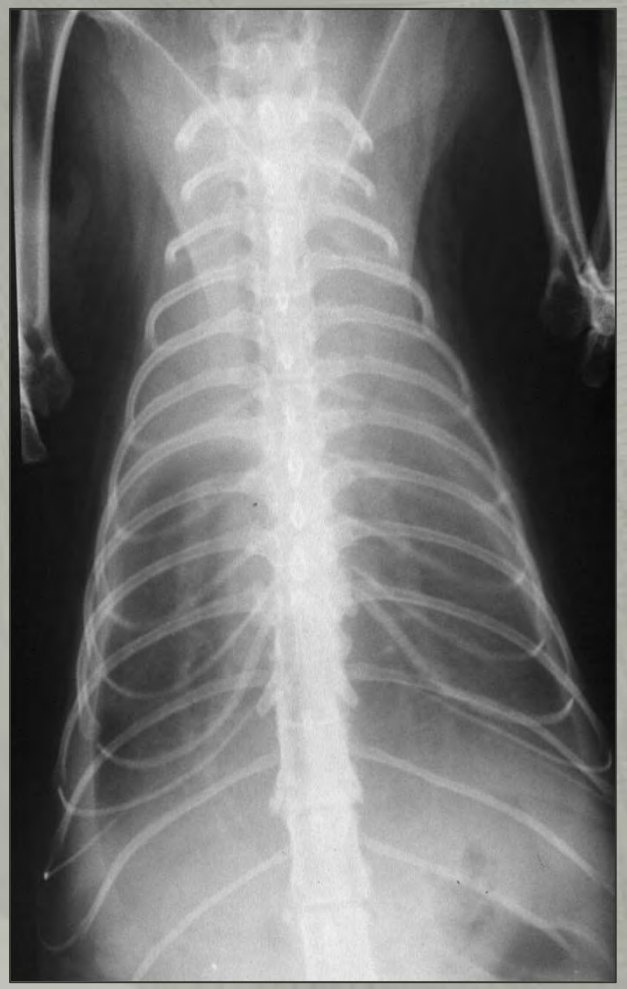
HCM RX longoedeem





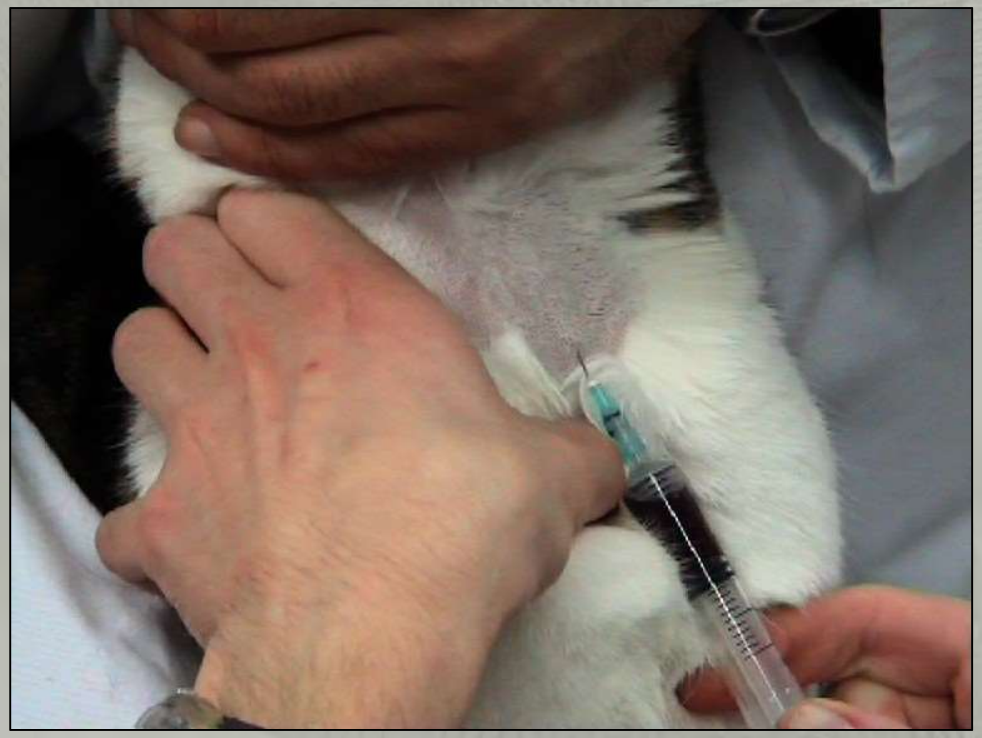
HCM RX pleurale effusie





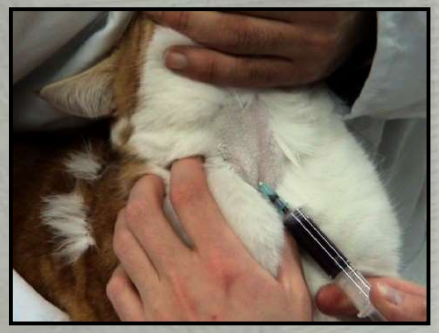
HCM DIAGNOSE

- Bloedonderzoek
  - HCT
  - Nierfunctie
    - **Ureum**
    - **Crea**
    - **SDMA♥**
    - **Electrolyten**
    - **iCa**
  - TP, alb
  - DNA testing
  - Biomarkers
    - **TnI**
    - **NT-proBNP**
- Urineonderzoek
  - Dichtheid
  - Prot/crea

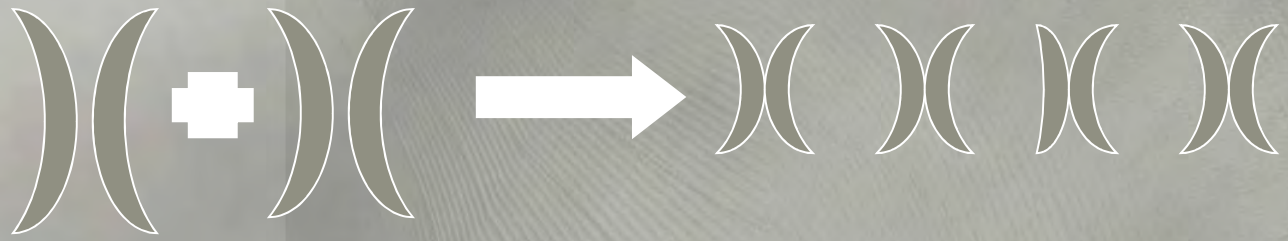


HCM DNA testing

- Myosin Binding Protein C3 Mutatie
- Prof Meurs Kate
  - http://www.cvm.ncsu.edu/vhc/csds/vcgl/index.html
- Maine Coon: 34 % heterozygoot
- Ragdoll: 35 % heterozygoot
- WAARDELOOS BIJ ANDERE RASSEN
- Bloedprik (EDTA)/ buccale swab (niet na zuigen)
- Identificatie imperatief
- Vanaf de geboorte
- Homozygoot/heterozygoot : prognose
- Opgelet een negatieve kat kan nog steeds HCM ontwikkelen (mens > 1400 genvarianten)
- Reproductie homozygoten niet aanbevolen
- Reproductie heterozygote enkel met een negatieve kat



Genetica (1)

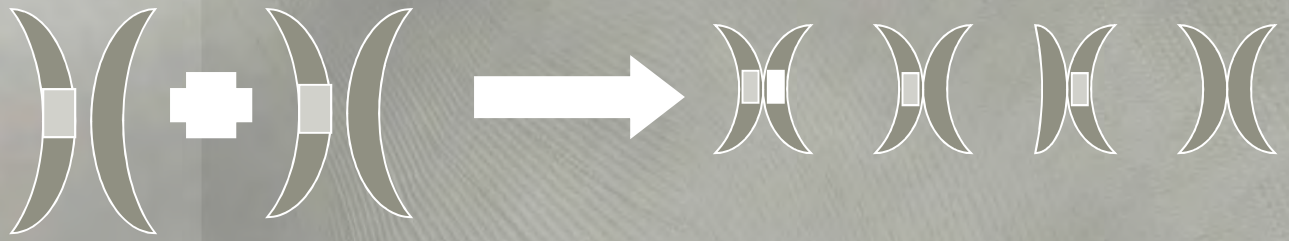


100 % gezond

50 % aangetast heterozygoot

100 % aangetast heterozygoot

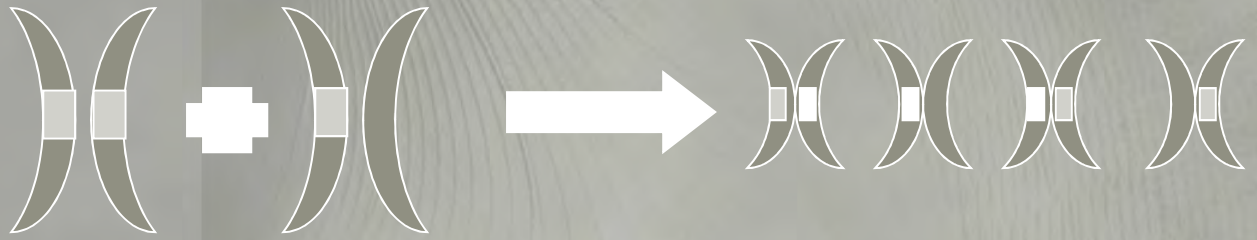
Genetica (2)



25 % gezond

50 % heteroz

25 % homoz



50 % heteroz

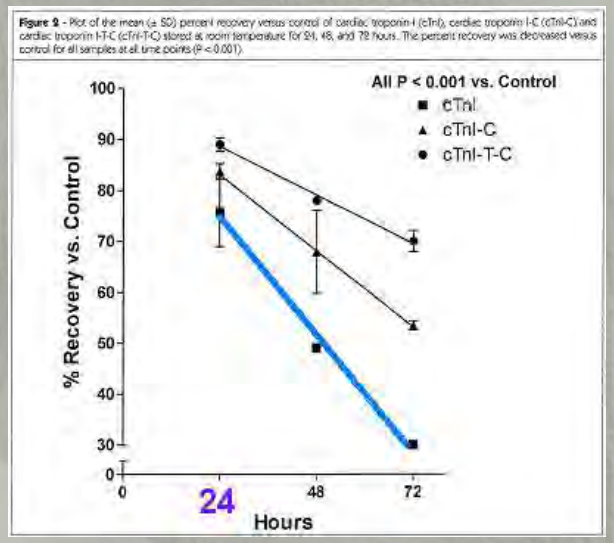
50 % homoz

100 % homoz

HCM Biomarkers

- TnI
  - Komt vrij met myocardischemie en necrose
  - Myocarditis >>> HCM (x10)
  - BSH >> MC/NWF: 0,13 versus 0,08 ng/ml
  - MC MYBPC3 homo >> hetero: 0,11 versus 0,04
  - Geen leeftijdscorrelatie
  - Geen geslachtscorrelatie
  - Gewichtscorrelatie
  - Helpt echodata
  - Lage sens/spec:

    kan niet gebruikt worden voor prognose



Langhorn et al 2014-2016

HCM Biomarkers

- NT- pro-BNP
  - Vooreinde van BNP
  - Vrijgelaten door ventriculaire myocard bij wandstress
  - Eerste, tweede generatie en nu POC bedside
  - NT-proBNP is relatief specifiek maar niet heel sensitief (weinig vals positieven)
  - Identificatie van katten met matige tot erge HCM indien > 100pmol/L
  - Differentiatie tussen cardiale of resp dyspneu
  - Nooit als alleenstaande test gebruiken

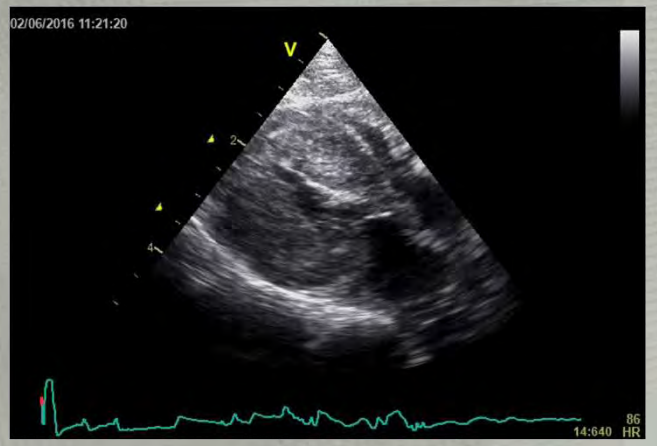
Conolly 2008 Wess 2011 Fox 2011 Machen 2014

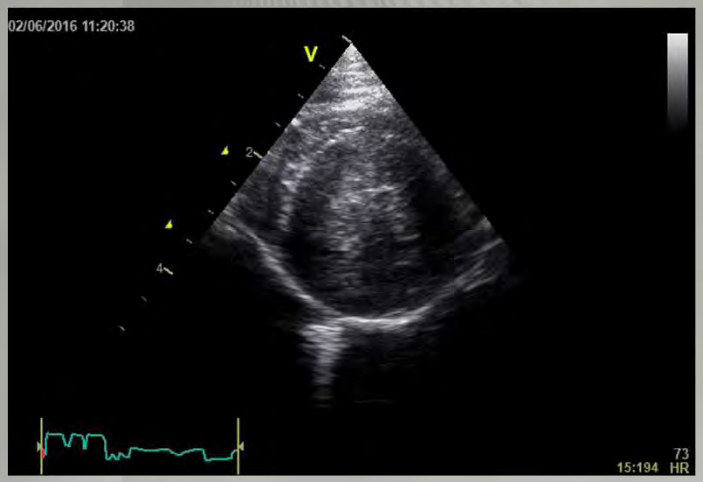
HCM Echocardiografie

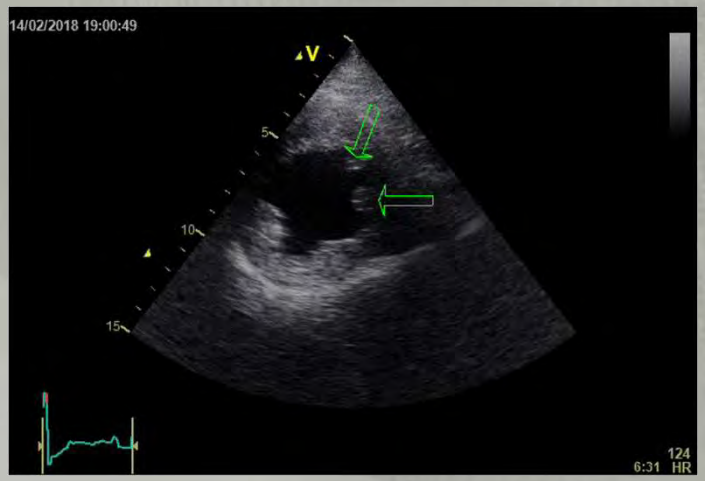
- Classificatie
- LA dilatatie
- Predispositie voor thrombusvorming
- Wanddikte
- Dynamische obstructie
- Diastolische en systolische functie
- Screening
- Pseudohypertrofie

HCM Echocardiografie

- Classificatie
  - Links/rechts/beiden
  - Symmetrisch-asymmetrisch

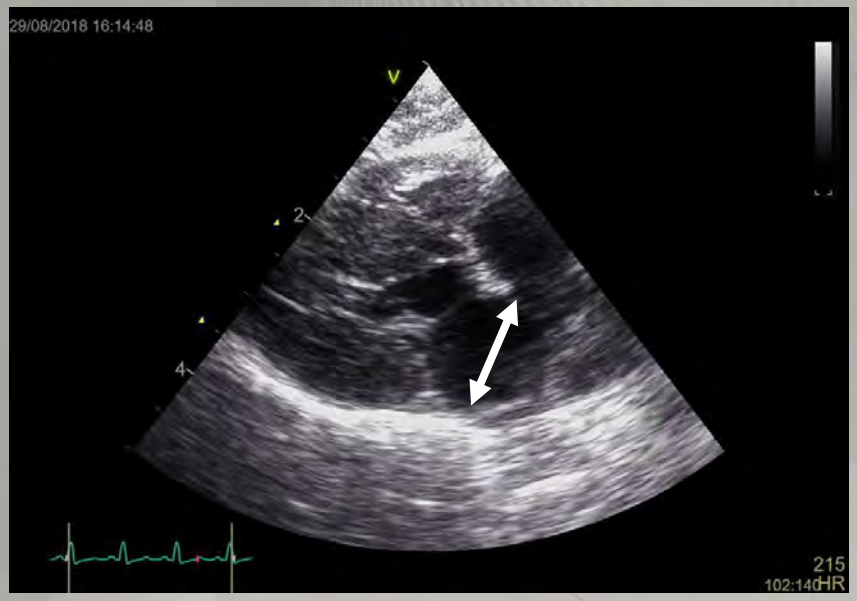


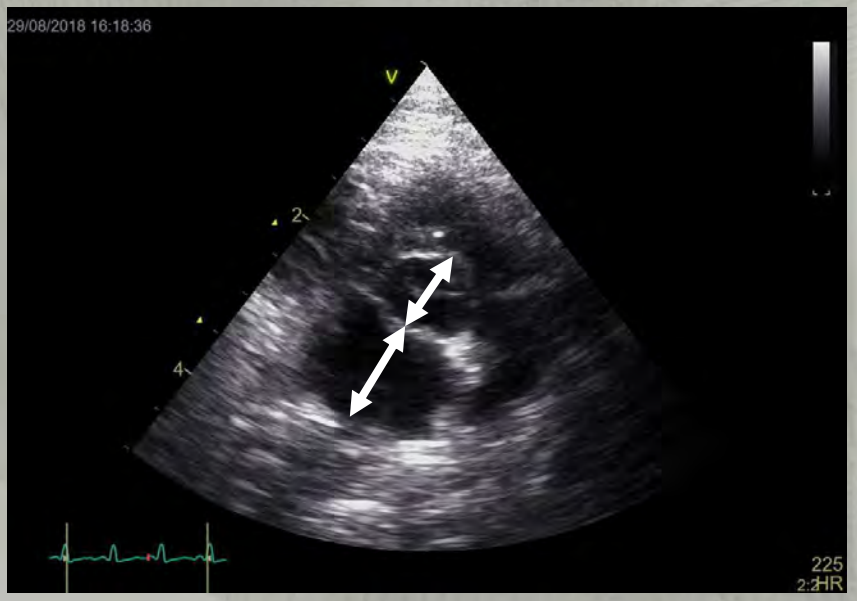




HCM Echocardiografie

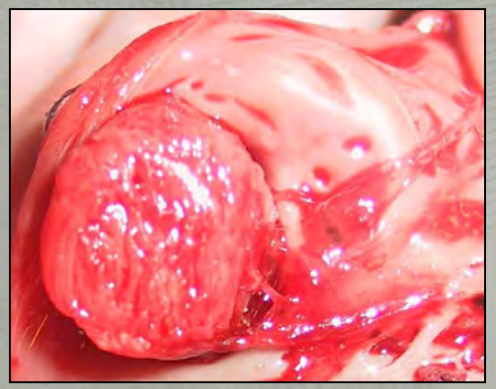
- LA dilatatie
  - Lange as (Rishniw) < 16 mm
  - Korte as (Hansson) < 1,6

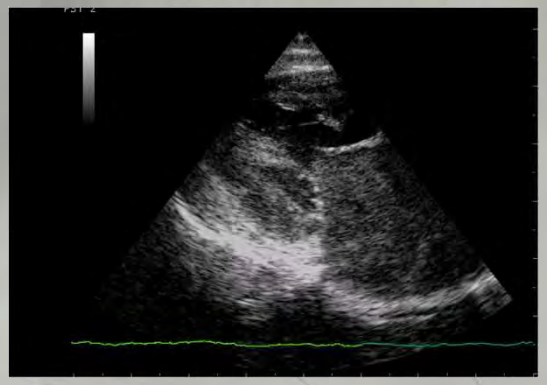


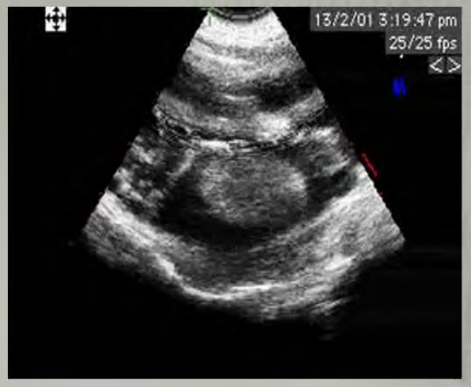


HCM Echocardiografie

- Predispositie voor thrombusformatie
  - Atriale dilatatie > 16 mm RPLA inflow view
  - FS LA < 12 %
  - FS LV < 30 %
  - Hypertrofie LV > 9 mm in diastole
  - MV E/A restrictief patroon
  - Spontaan echocontrast
  - Auriculaire snelheid < 0,25 m/s

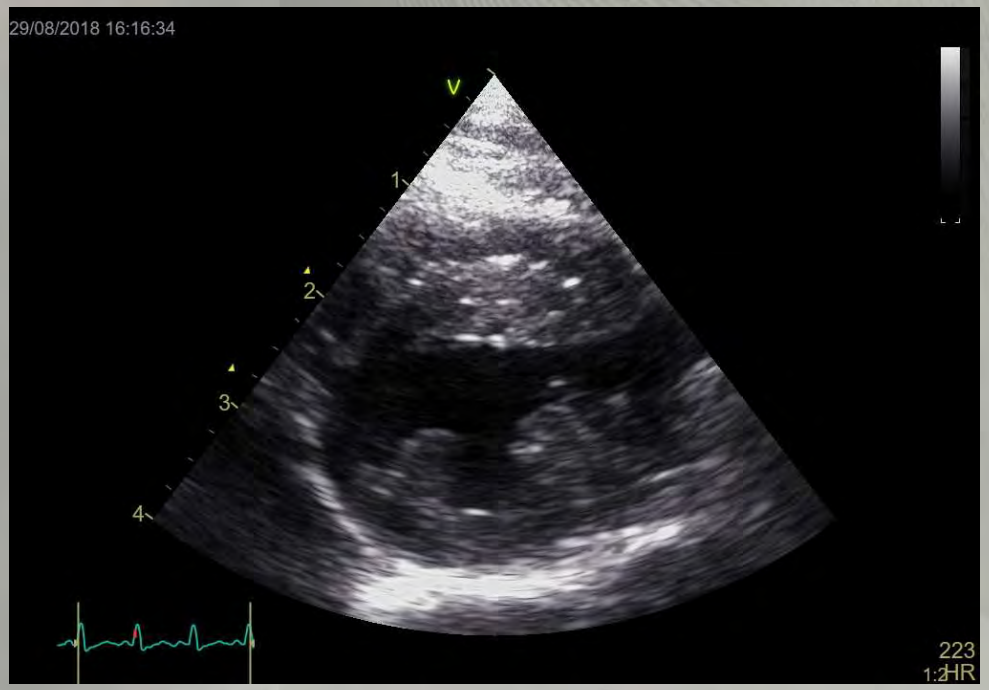


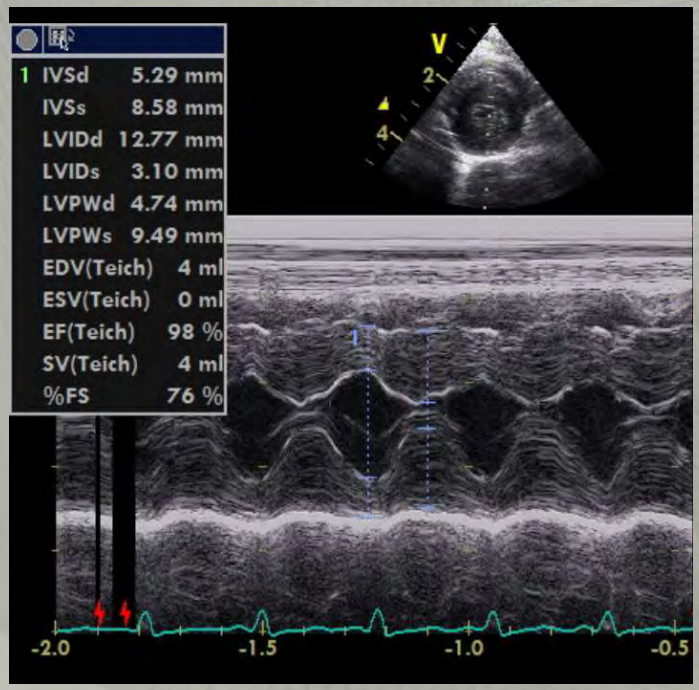




HCM Echocardiografie

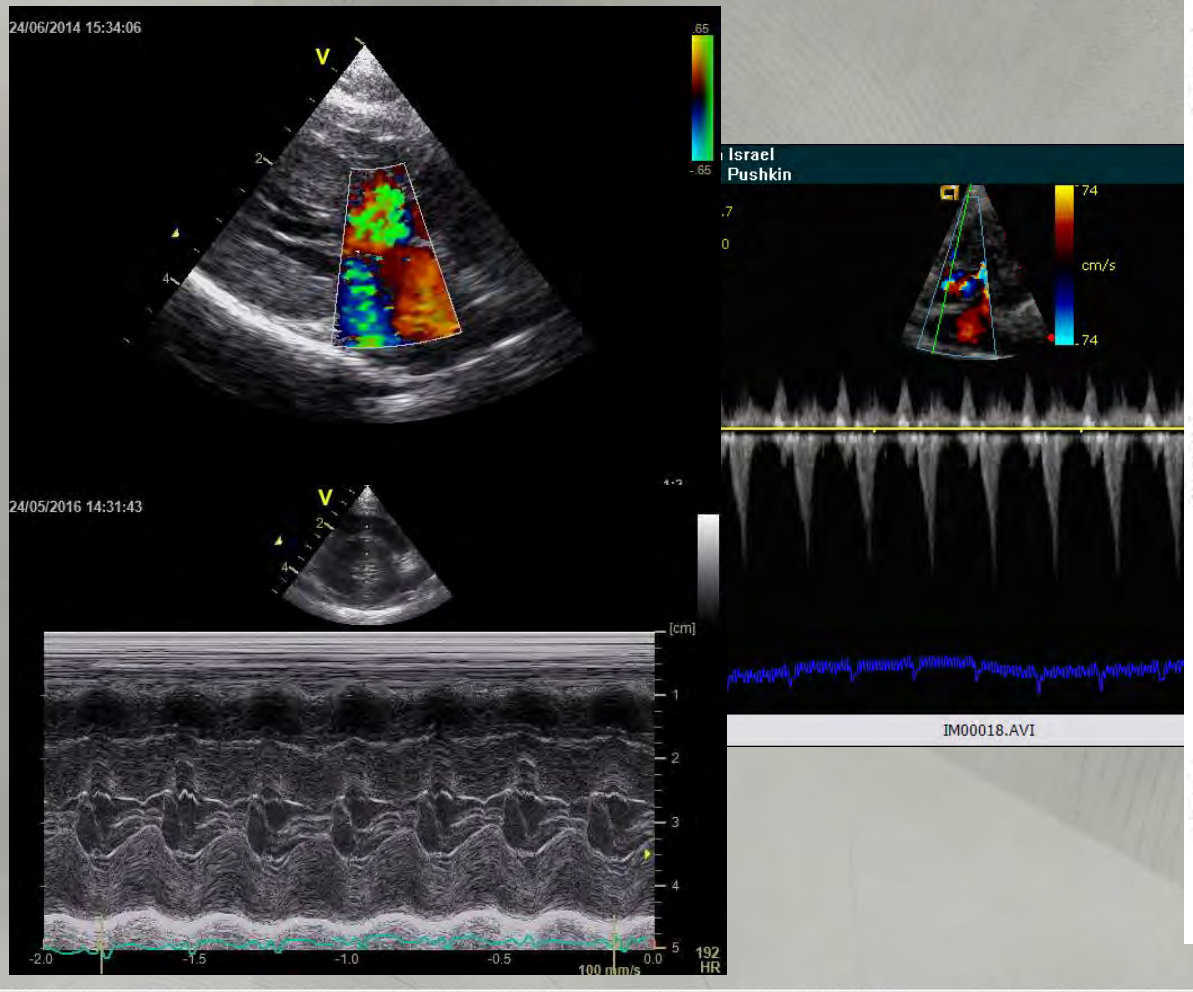
- Wanddikte
  - Korte as 2D of M-mode

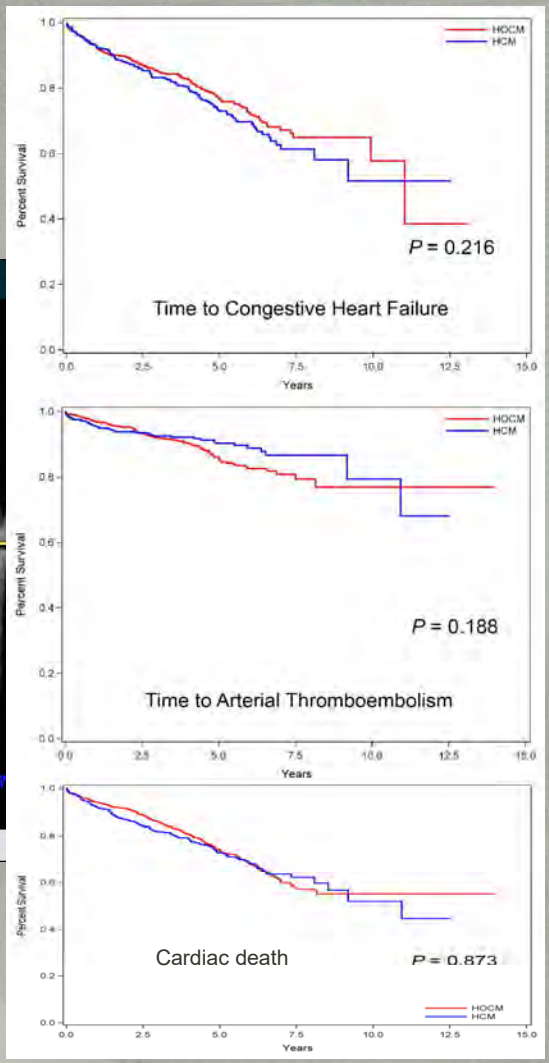




HCM Echocardiografie

- Dynamische obstructie



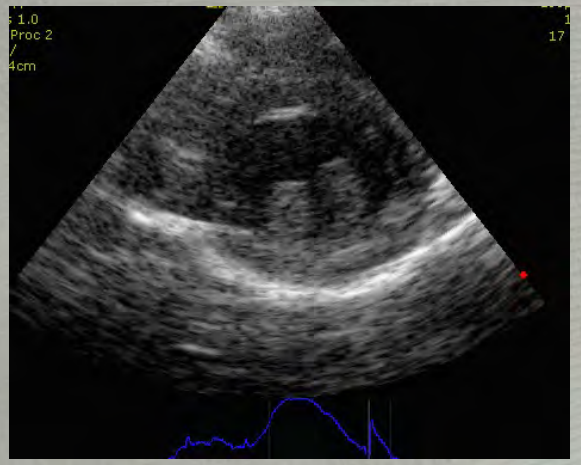


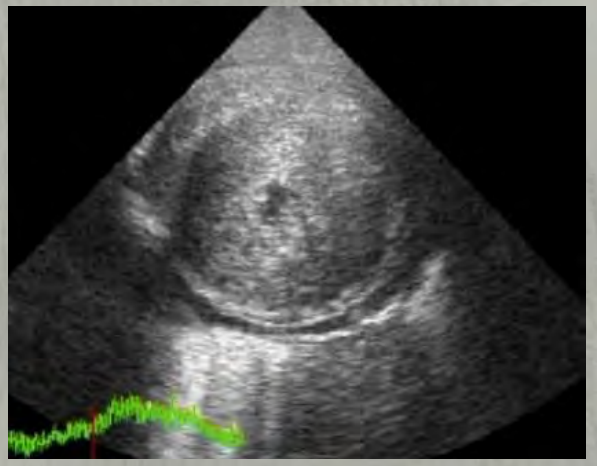
HCM Echocardiografie

- Diastolische en systolische functie
  - Normal diastolic function allows adequate filling of the ventricles during rest and exercise without abnormal increase in diastolic pressures
  - LV diastolic function can be assessed non-invasively by
    - Transmitral flow
    - Isovolumetric relaxation time
    - Pulmonary venous flow
    - CMM velocity propagation

Echo screening

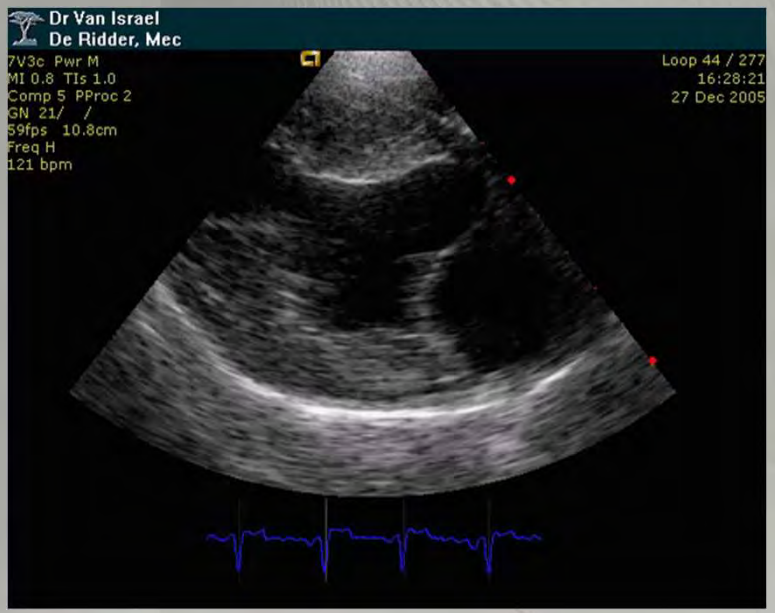
- No international guidelines as yet
- LA < 16 mm 2D
- Discussion LV wall
  diastole 5.5/6 mm ?
- Breed dependant
- Weight dependant
- Discussion SAM
- Papillary muscle
  enlargement
- LV obliteration
- Equivocal/Mild/Severe
- Many UCM

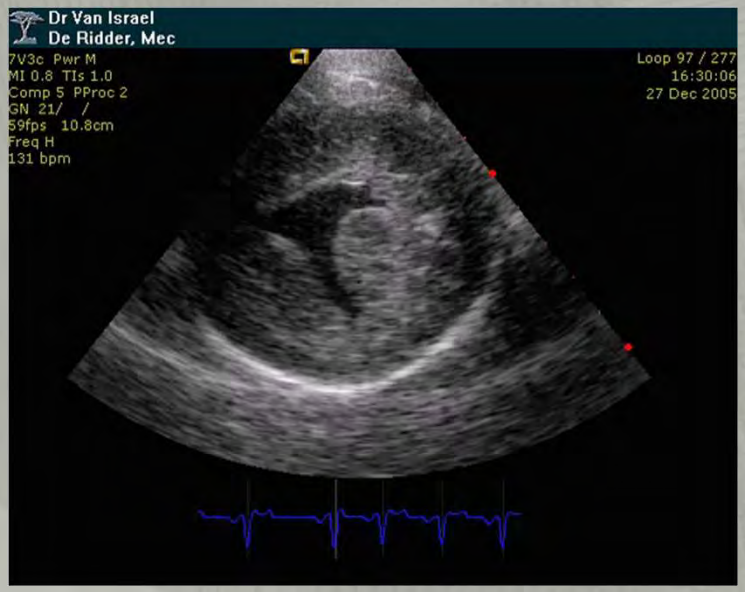




HCM Echocardiografie

- Pseudohypertrofie
  - Deshydratatie (CKD)
  - Bloedverlies





HCM Prognose

Cardiovascular morbidity and mortality in study populations

Study Population Groups								
	Control n=722		HCM n=430		HOCM n=578		HCM/HOCM n=1008	
Cardiovascular Morbidity	No. Events	% Normal	No. Events	% HCM	No. Events	% HOCM	No. Events	% HCM/HOCM
CHF	6	0.83	106	24.7	138	23.9	244	24.2
ATE	5	0.69	41	9.5	76	13.2	117	11.6
Cardiovascular Death								
SD	0	0	9	2.1	13	2.2	22	2.2
Cardiac Death	7	0.96	115	26.7	166	28.7	281	27.9

Slide 49

WU1 Windows User; 21-09-18

WU2 Windows User; 21-09-18

HCM Prognose

Risk	CHF		ATE		Sudden Death		All-Cardiac Death	
	% Population Remaining at-Risk	% Population Affected	% Population Remaining at-Risk	% Population Affected	% Population Remaining at-Risk	% Population Affected	% Population Remaining at-Risk	% Population Affected
1-year post diagnosis								
Control	100	0.00	100	0.00	100	0.00	100	0.00
HCM	93.3	6.7	95.8	4.2	99.3	0.7	92.3	7.7
HOCM	92.7	7.3	97.1	2.9	99.1	0.9	94.1	5.9
HCM/HOCM	93.0	7.0	96.5	3.5	99.2	0.8	93.3	6.7
5-years post diagnosis								
Control	99.6	0.4	99.6	0.4	100	0	99.3	0.7
HCM	79.5	20.5	92.3	7.7	98.1	1.9	77.7	22.3
HOCM	80.4	19.6	88.7	11.3	96.7	3.3	76.8	23.2
HCM/HOCM	80.1	19.9	90.3	9.7	97.3	2.7	77.2	22.8
10-years post diagnosis								
Control	99.2	0.8	99.3	0.7	100	0	99.0	1.0
HCM	75.6	24.4	91.2	8.8	97.4	2.6	73.3	26.7
HOCM	76.5	23.5	86.8	13.2	96.0	4.0	70.6	29.4
HCM/HOCM	76.1	23.9	88.7	11.3	96.6	3.4	71.7	28.3

HCM Prognose

- REVEAL
  - 30,5 % katten ontwikkelen CHF/ATE
  - Ze overleefden gemiddeld 1,3 ±1,7 jr
  - 27,9 % sterft cardiovasculaire oorzaak
  - Geen verschil tussen HCM/HOCM groep
  - 10 % vd katten worden 9-15 jr

REVEAL 2018

HCM Behandeling

- Doelstellingen
  - Congestief hartfalen voorkomen/controleren
  - Neurohumorale regulatie
  - Hemodynamische verbetering
  - Cardio-embolie vermijden
  - Plotse dood vermijden
- Classificatie
  - A: genetische predispositie
  - B1: HCM tekenen met normaal LA
  - B2: HCM met vergroot LA maar geen CHF
  - C1: HCM in acuut CHF
  - C2: HCM in chronisch CHF
  - D: HCM met refractair CHF

Adapted ACVIM MVE guidelines

HCM Behandeling A

- Geen
- Screening DNA/ Echo

HCM Behandeling B1

- Asymptomatisch
  - GEEN
- Symptomatisch
  - β-Blokkers: enkel controle van de klinische tekenen, geen overlevingsvoordeel

HCM Behandeling B2

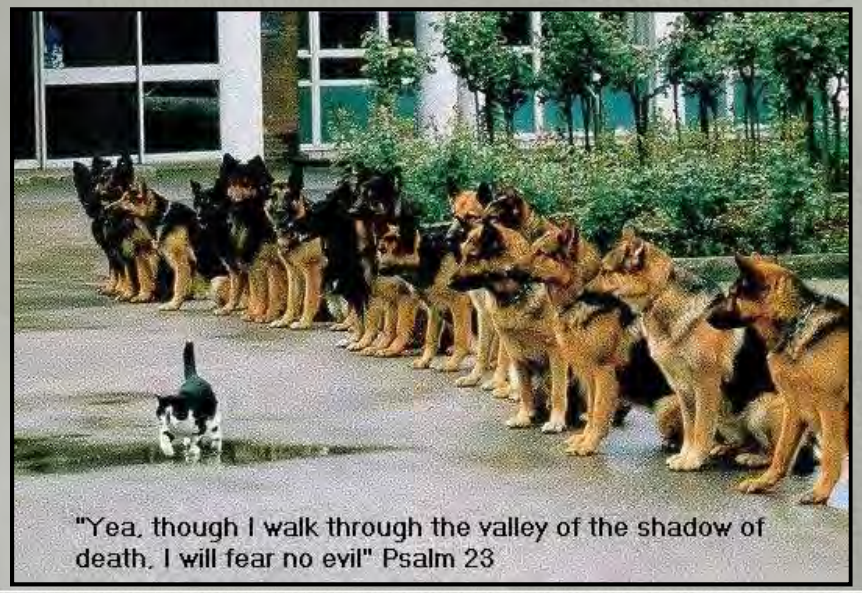
- LA dilatatie
  - ATE preventie
    - Clopidogrel 18,75 mg SID
    - Aspirine 5 mg PO q 72 hrs
    - (Rivaroxaban)
    - (Fondaparinux)

HCM Behandeling C1

- Zuurstofkooi
- Thoracocentese
- Furosemide IV/SC 1-2 mg/kg q 2-4 hrs max 6 mg/kg 24 hrs
- Nitroglycerine oorflap
- Sedatie butorphanol 0,1-0,4 mg/kg IM
- Geen ACEI in dit stadium!
- Indien **geen** dynamische obstructie en low cardiac output (BD<90 mm Hg):
  - Dobutamine CRI 1-4 mcg/kg/min
  - Pimobendan IV

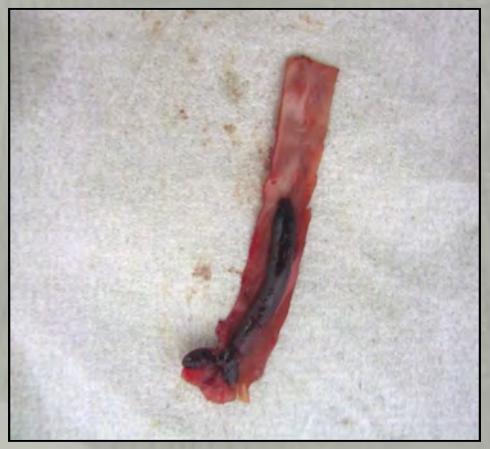
ATE Behandeling NVI

- Pijncontrole: buprenorphine
- Heparinisatie 300 IU/kg, gevolgd door 100 IU/KG q 8 hrs, spenen over 1 week
- Clopidogrel hoge dosis 75 mg1ste dag
- Cyproheptadine 1 mg PO hyperacuut
- CHF
- Shock
- Hyperkaliemie



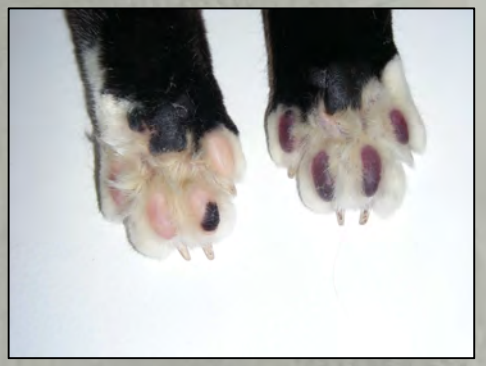
Relative good prognosis

- Control heart failure
- Absence of thrombi in the heart or echo "smoke"
- Good appetite
- Normal urea/creatinine/electrolytes
- Return of normal motor function
- Return of femoral pulse and pink pads/nail bed
- Absence of self mutilation
- Motivated owner



Poor prognosis

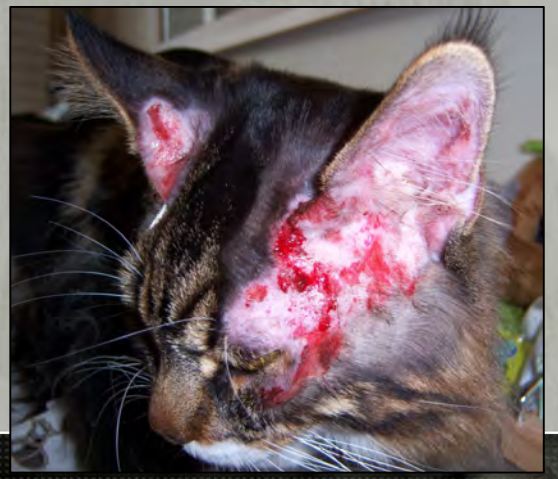
- Refractory heart failure/arrhytmia
- Acute hyperkalemia
- Muscle impaction 48-72 hr post-embolisation
- Multi-organ embolisation
- Recurrence
- Presence of a thrombus or “smoke”
- Increased urea/creatinine/electrolytes
- DIC
- Self mutilation
- Persistent hypothermia (< 37°2: 50 % survival)
- Enlarged LA and myocardial failure
- Bradycardia



Luis-Fuentes 2012, Payne et al 2015

HCM Behandeling C2

- Pulmonair oedeem controleren
  - Furosemide
- ATE preventie
- Neurohumorale modulatie ???
  - RAAS-inhibitoren
    - Spironolactone, ACEI ?, ARB ?
  - Betablokkers:
    - Dosis halveren indien inname, zeker nu niet opstarten



HCM Behandeling D

- Furosemide SC inspuiten
- Furosemide vervangen door torasemide
- Spironolactone aan diuretische dosis
- ATE preventive volhouden/optimaliseren
- RAAS-inhibitoren combineren (CRS!)
- Ritmestoornissen controleren
  - AF: diltiazem
  - Vtach: sotalol
- Pimobendan indien geen LVOTO !!!
  DUS GEEN BIJGERUIS

Reina 2014, ICVS 2016, Oldach 2019

HCM Behandeling