Universität Bern | Universität Zürich
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ESK ENNETSeeKLINIK für Kleintiere

Pimobendan bei Katzen, Clopidogrel anstatt Aspirin?

Neue Therapieansätze bei Kardiomyopathien der Katze

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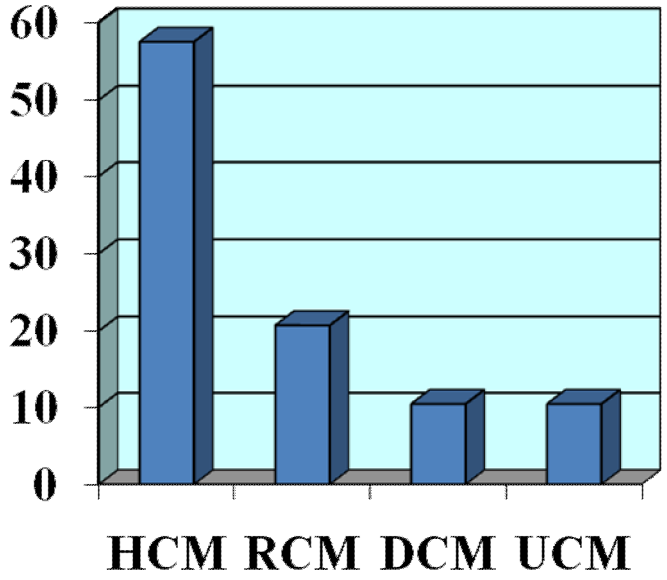
Klassifizierung der Herzmuskelerkrankungen der Katze

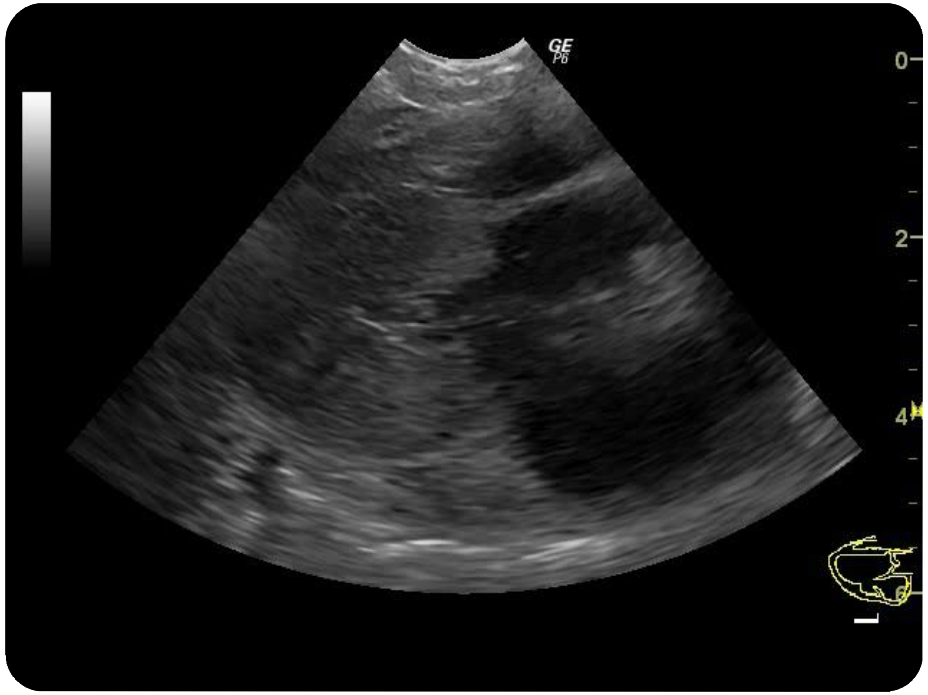
Hypertrophe Kardiomyopathie (HCM), restriktive Kardiomyopathie (RCM), dilatative Kardiomyopathie (DCM), unklassifizierte Kardiomyopathie (UCM), arrhythmogene rechtsventrikuläre Kardiomyopathie (ARVCM), spezifische Kardiomyopathie (Myokarditis)



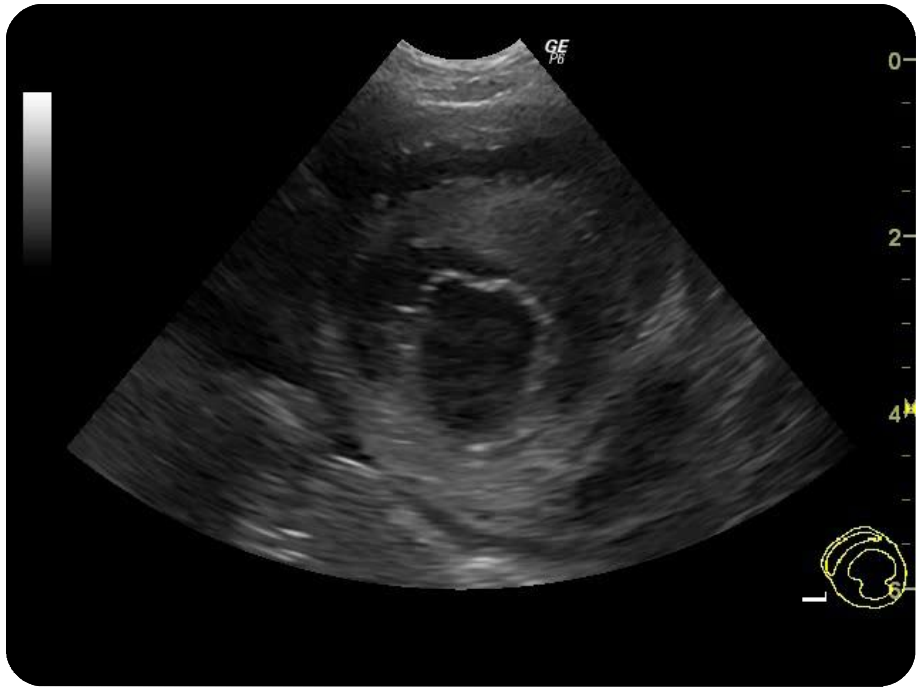
HCM: Ultraschall

Hochgradig verdickte Muskulatur der linken Kammerwand, Reduktion des linksventrikulären Kammerlumen

RP LAX



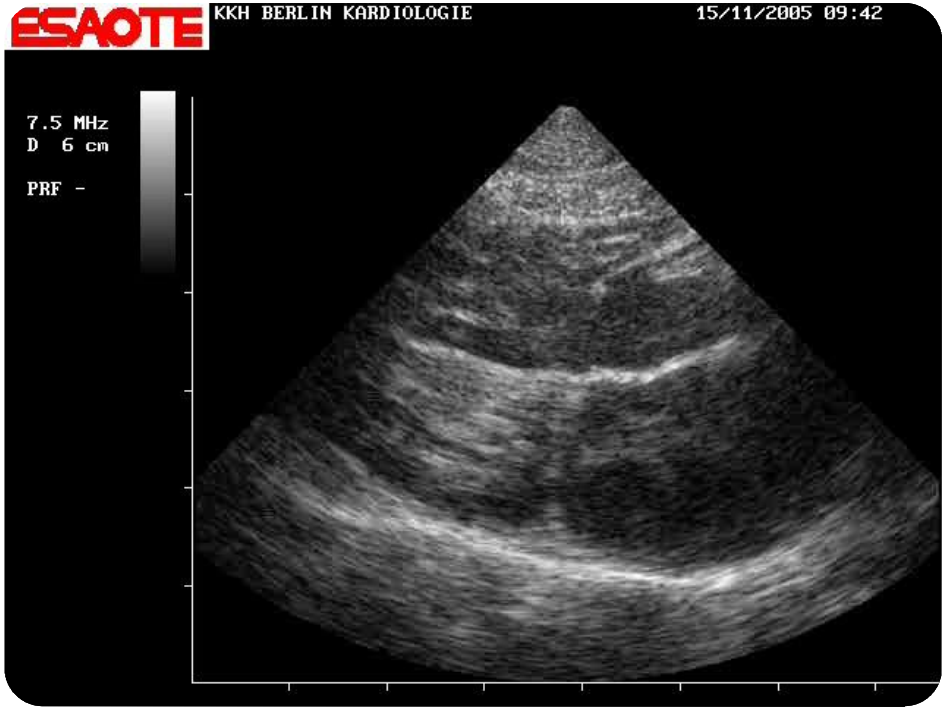
RP SAX



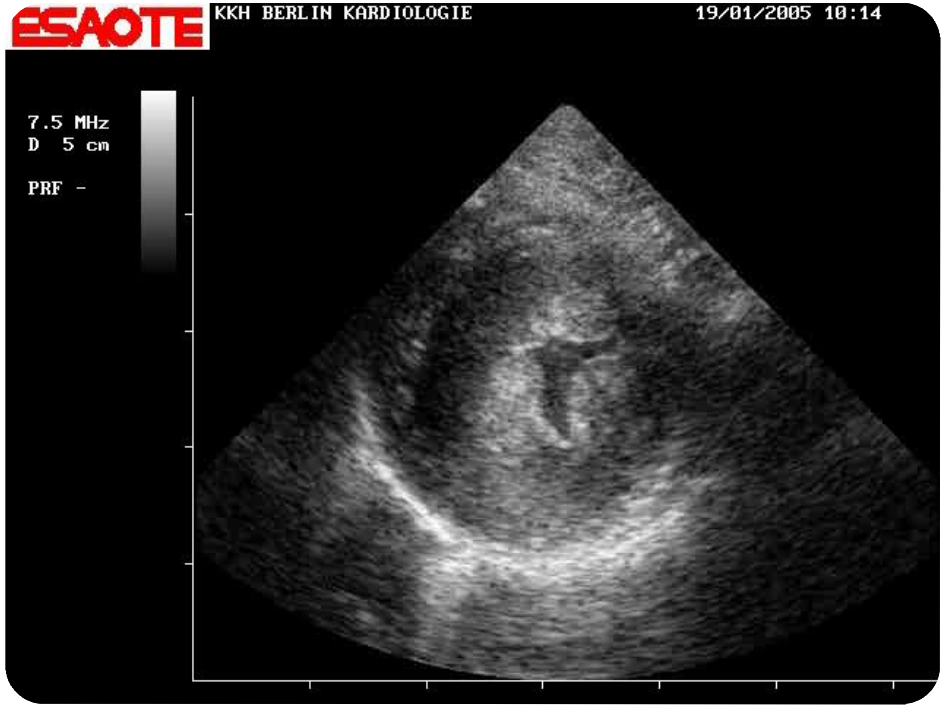
RCM: Ultraschall

Hyperechogenes Endokard und/oder Myokard

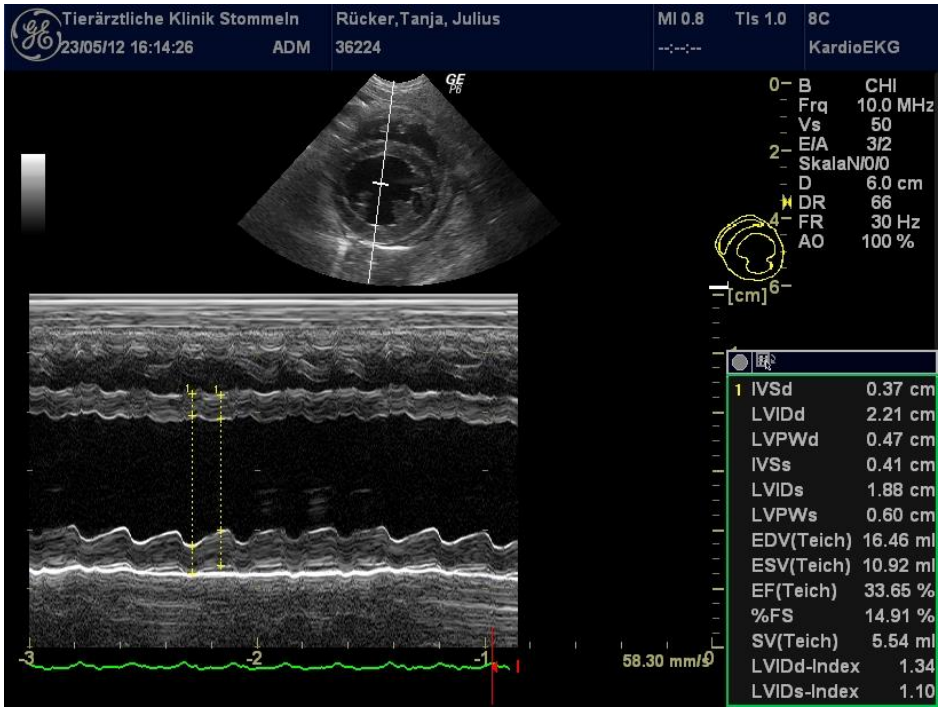
RP LAX RP

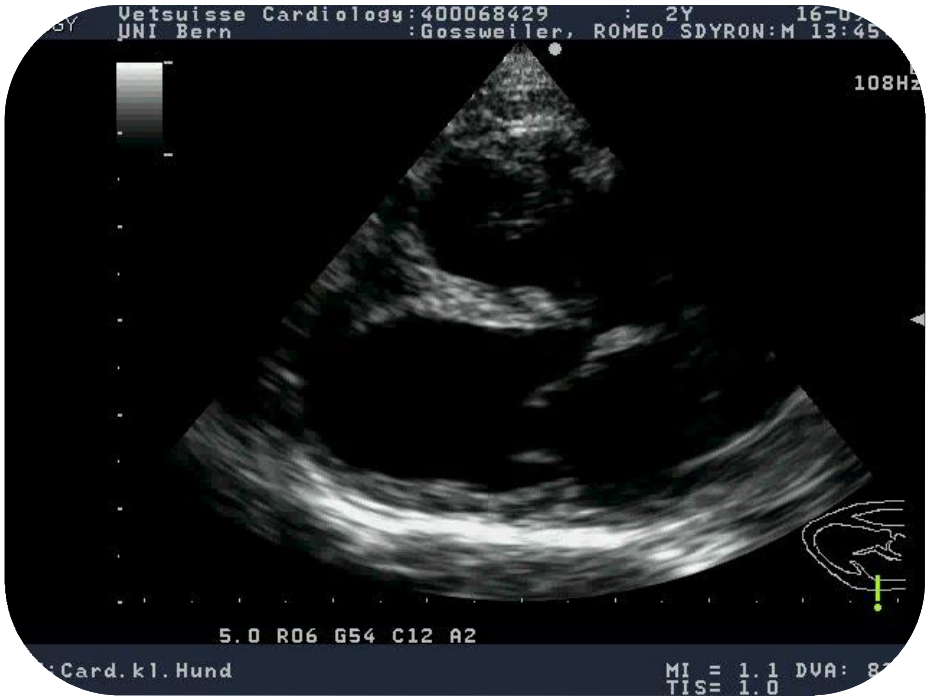


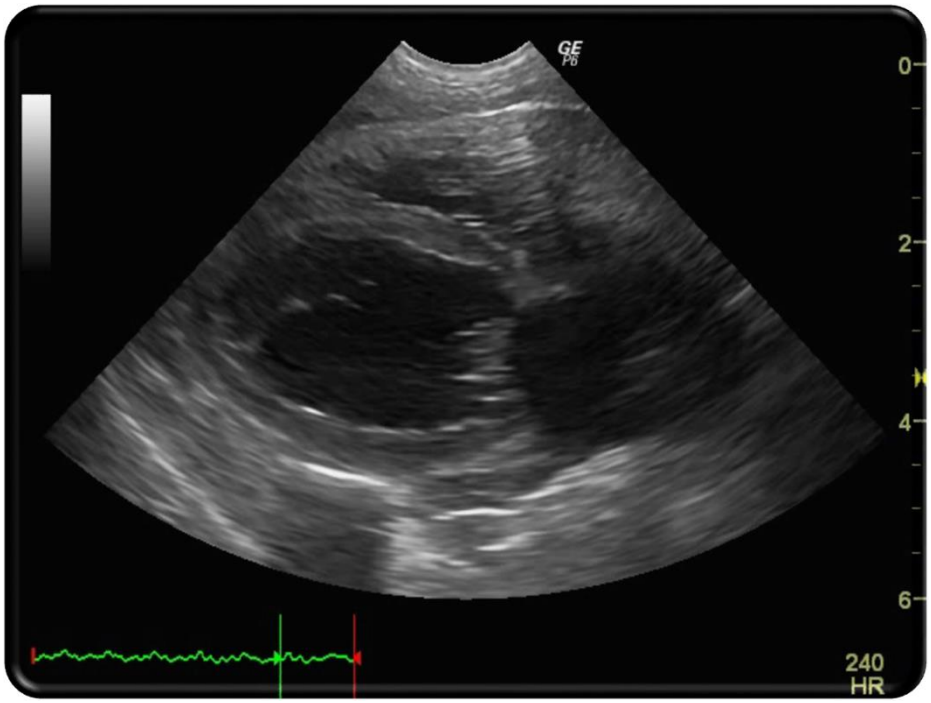
SAX LA/Ao



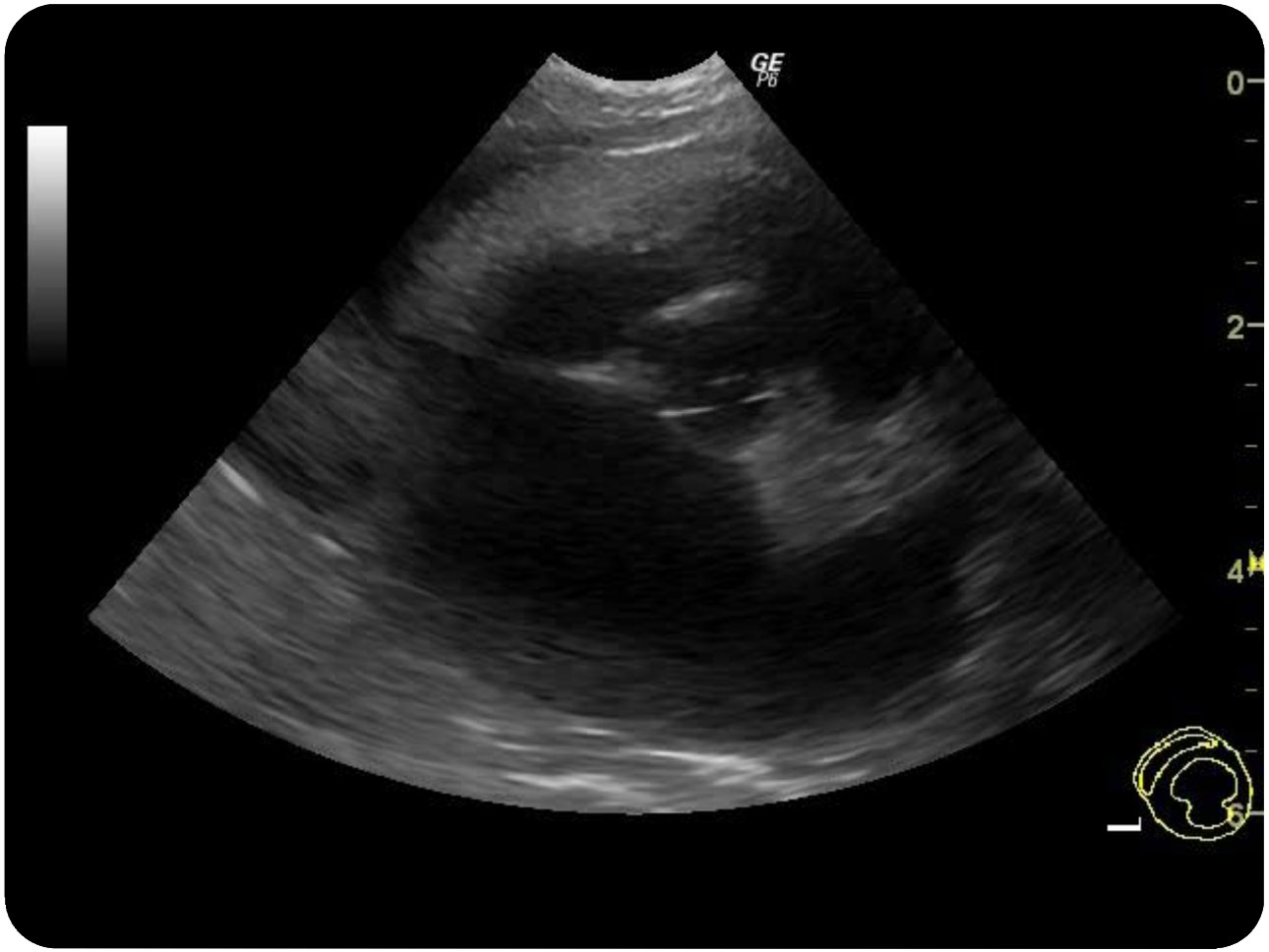
End stage CMP, dilatative CMP?



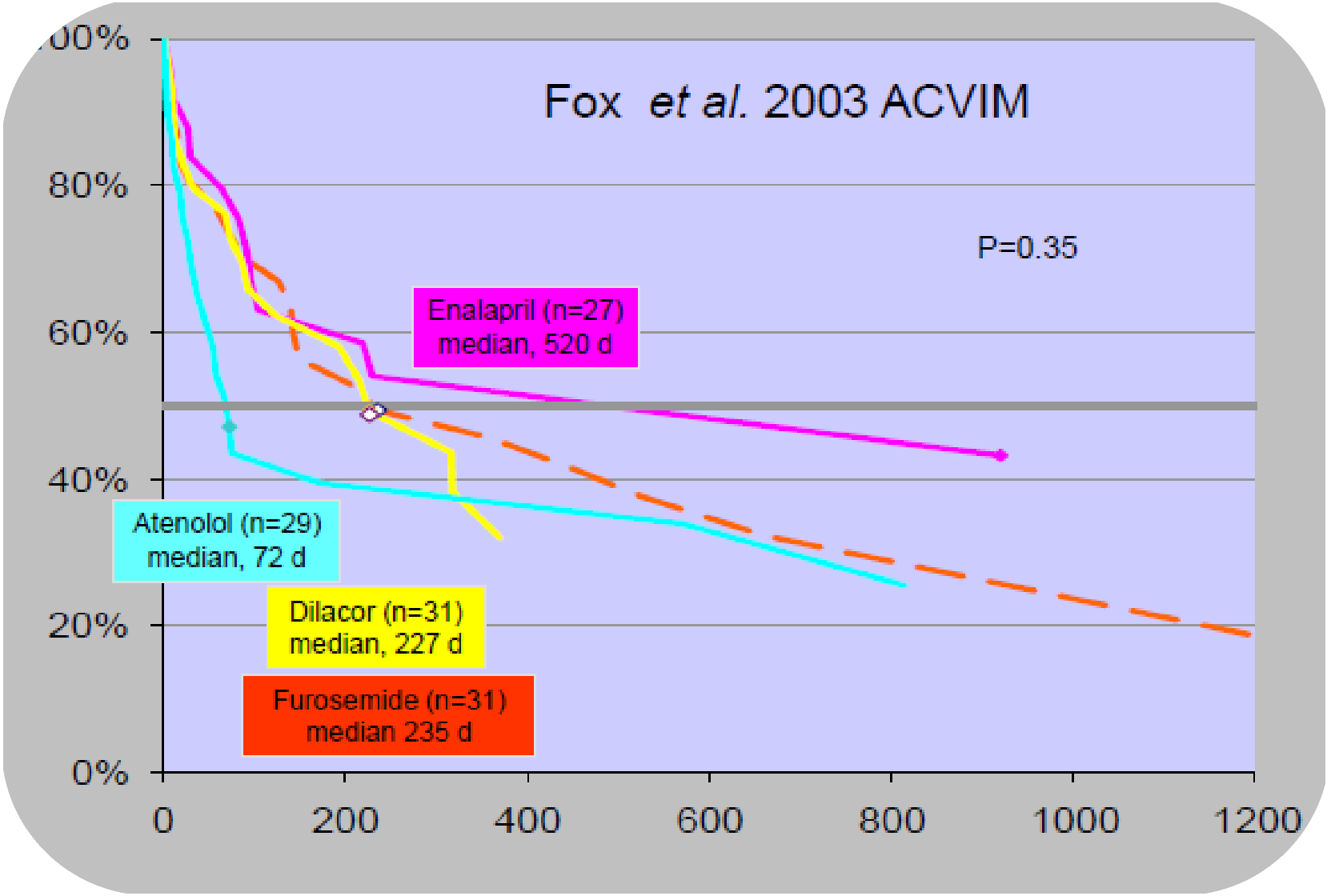




Hochgradig erweiterter linker Vorhof
SAX LA/Ao; LA/Ao = 2,5



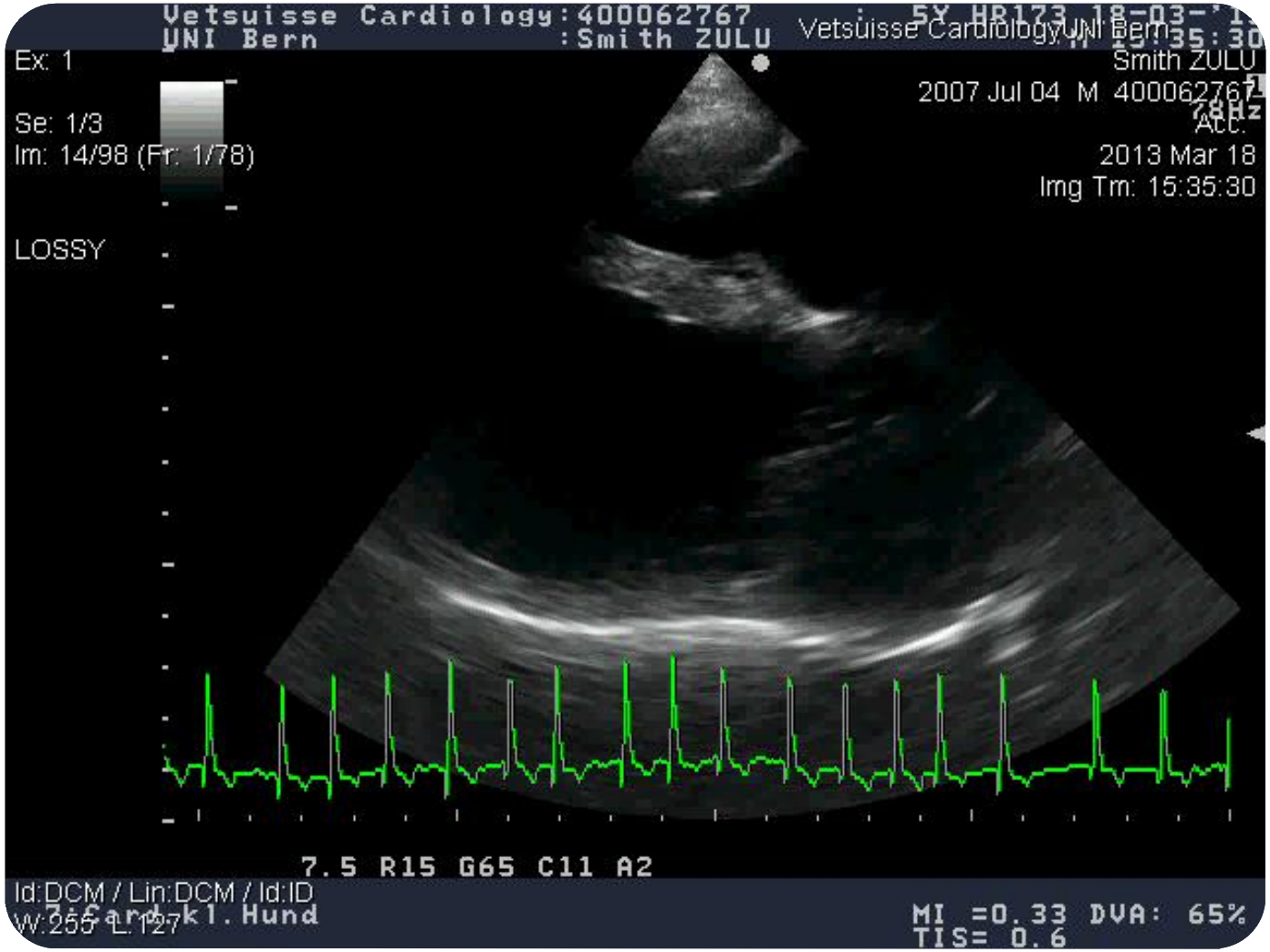
Therapie symptomatischer Katzen



Pimobendan

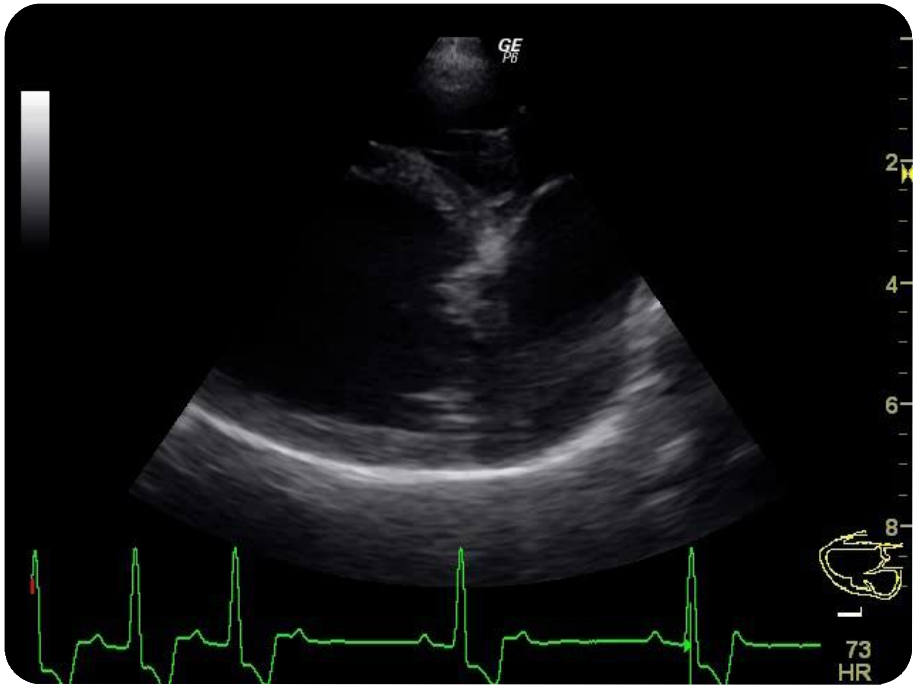
- Pimobendan ist ein positiv inotropes und vasodilatatives Mittel welches eine Erhöhung der Ca^{++} Sensitivität des Herzmuskel und der Gefässmuskulatur erzeugt
- Es ist zugelassen bei Hunden
- Die häufigste Indikation stellen DCMP und Mitralendokardiose
- Es soll nicht bei obstruktiven Erkrankungen eingesetzt werden

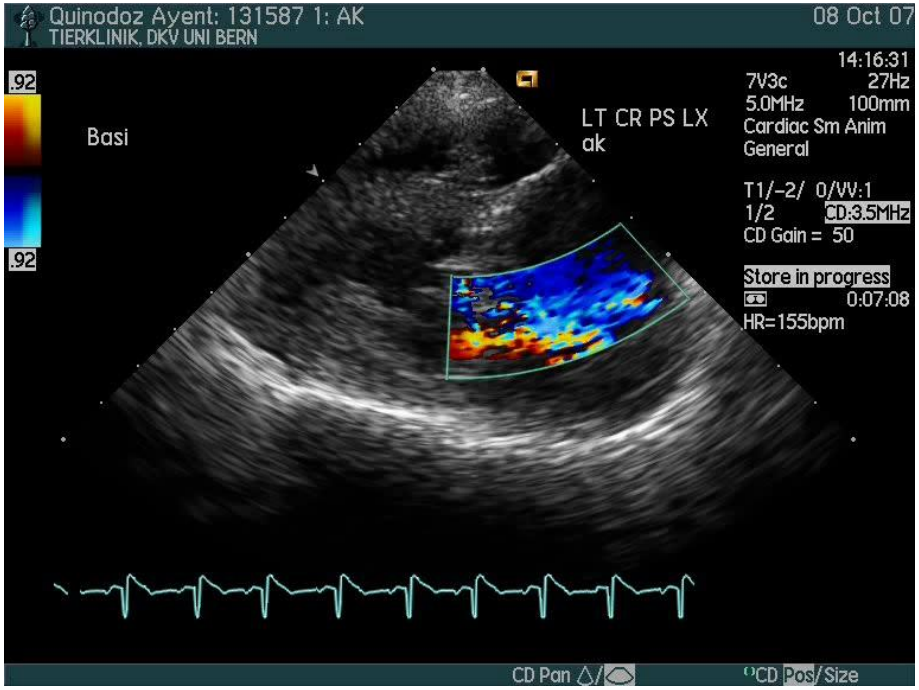
Indikation DCMP Hund



RP LAX

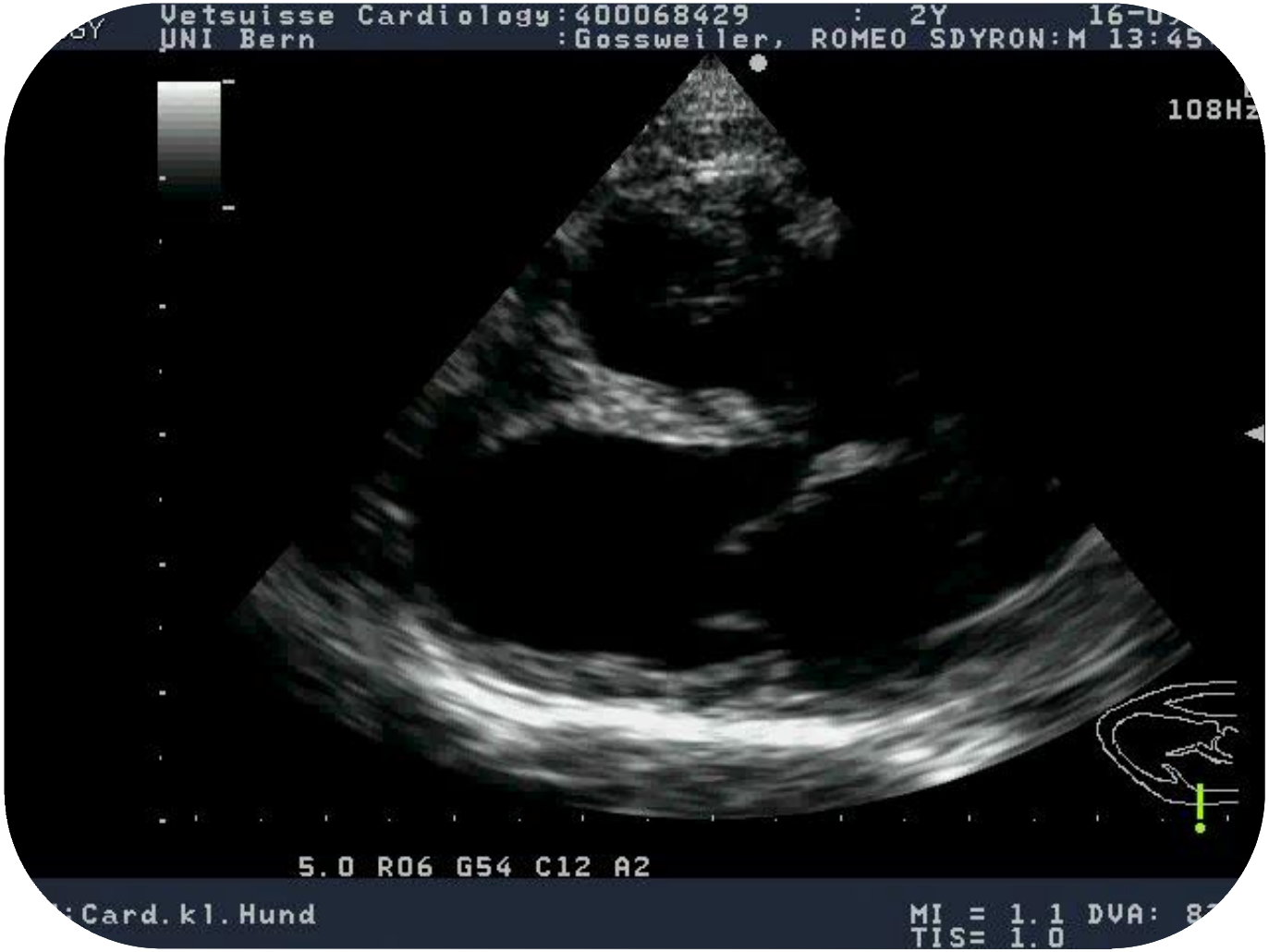
Indikation Mitralendokardiose Hund

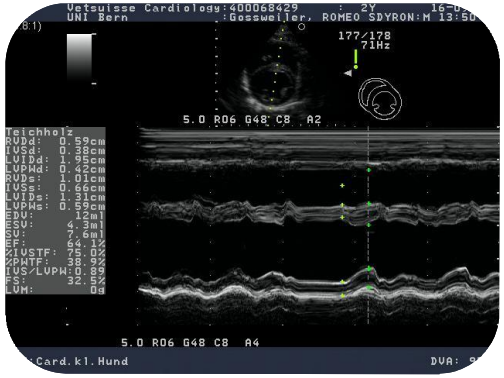




RP LAX

Indikation systolische Dysfunktion Katze?





Literaturangaben zu Pimobendan bei Katzen

Clinical Efficacy of Pimobendan in 11 Cats with Systolic Heart Failure

17TH ECVIM-CA CONGRESS, 2007

C.P. Sturgess[1]; L. Ferasin[2]

[1]Anderson Sturgess Veterinary Specialists, Winchester, Hampshire, UK; [2]University of Minnesota, College of Veterinary Medicine, St Paul, MN, USA

Pimobendan (Vetmedin®) is classified as an inodilator as it exhibits both positive inotropic and vasodilator activity. A limited number of studies have looked at its activity in cats both *in vivo* and *in vitro* and have consistently shown a positive inotropic effect. Hypotension was noted in one study supporting a vasodilator activity. In all *in vivo* studies, pimobendan was administered intravenously to anaesthetised cats. Whilst the majority of acquired feline heart disease is hypertrophic and hyperdynamic, it has been estimated that around 15-20% of cats might benefit from positive inotropy including a proportion of cats with hypertrophy that develop systolic failure in the later stages of disease. To date, digoxin has been widely prescribed in cats requiring inotropic support however it's narrow therapeutic index, slow onset of activity and the lack of evidence of clinical efficacy makes digoxin a questionable choice. Based on the experimental data, pimobendan represents a more logical choice for cats with cardiac disease requiring positive inotropic support.

In response to this lack of a proven alternative for cats, an open trial of pimobendan was undertaken. The clinical records from the 11 cats that had received pimobendan (1.25mg BID) as part of their therapeutic regime were reviewed retrospectively. All cats had evidence of systolic failure based on their echocardiographic examination and 10/11 cases had pulmonary oedema or pleural effusion with an associated tachypnoea. Mean heart rate at presentation was 216 bpm and mean systolic blood pressure was 124 mmHg. Based on a traditional classification, seven cats had dilated, three hypertrophic and one restrictive cardiomyopathy. Survival time was highly variable (range 9-585 days) but never shorter than the median survival time in a cohort of cats with similar diagnoses not given pimobendan. Maximum duration of therapy was 585 days. In those cases which survived beyond 2 weeks, the owners felt that there was a significant improvement in the demeanour and appetite of their cats. This was associated with improvements in clinical signs with resolution of the dyspnoea and pleural effusion in echocardiographic parameters where measured that were marked in some cases. Adverse side effects relatable to the use of the pimobendan were not noted. Whilst recognising that pimobendan was not given as a monotherapy, the authors feel that the data from these cases when compared to a cohort of cats not given pimobendan as part of their therapeutic regime strongly justifies further evaluation of the use of pimobendan in the management of systolic failure in cats.

Literaturangaben zu Pimobendan bei Katzen

Effect of pimobendan on the clinical outcome and survival of cats with non-taurine responsive dilated cardiomyopathy

Journal of Feline Medicine and Surgery
14(4) 233–239

DOI: 10.1177/1098612X11429645
jfms.com
SAGE

Lydia E Hambrook and Peter F Bennett

Abstract

This retrospective study was designed to assess the effect of pimobendan on the median survival time (MST) of cats with non-taurine responsive dilated cardiomyopathy (DCM). Thirty-two client-owned cats with a left ventricular internal dimension at end systole (LVIDs) >14 mm, a fractional shortening (FS) <28% and a lack of response to taurine therapy were included over a 9-year period (2001–2010). These cats were divided into pimobendan (n=16) and non-pimobendan (n=16) treatment groups. All cats received standard treatment with frusemide, taurine and benazepril or enalapril. Nine cats in the non-pimobendan group also received digoxin. The MST of the pimobendan group (49 days; range 1 to >502 days) was four times that of the non-pimobendan group (12 days; 1 to 244 days). The difference in survival between the two groups was statistically significant ($P = 0.048$). Hypothermia and FS <20% were associated with a poor prognosis. No adverse effects to pimobendan were noted.

Literaturangaben zu Pimobendan bei Katzen

Journal of Veterinary Cardiology (2011) 13, 251–260

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Journal of Veterinary Cardiology
ESVC

www.elsevier.com/locate/jvc

Use of pimobendan in 170 cats (2006–2010)☆

John M. MacGregor, DVM [a,b,*], John E. Rush, DVM, MS [c], Nancy J. Laste, DVM [d], Rebecca L. Malakoff, DVM [d], Suzanne M. Cunningham, DVM [c], Natalie Aronow, DVM [c,f], Daniel J. Hall, VMD [c], Justin Williams, DVM [d], Lori L. Price, DVM [e]

Literaturangaben zu Pimobendan bei Katzen

Abstract *Hypothesis/Objectives:* To describe the therapeutic use of pimobendan in cats, describe the patient population to which it was administered, document potential side effects and report the clinical course following administration of pimobendan in conjunction with standard heart failure therapy. It is hypothesized that cats with advanced heart disease including congestive heart failure from a variety of causes will tolerate pimobendan with a minimum of side effects when used in treatment in conjunction with a variety of other medications.
Animals, materials and methods: One hundred and seventy client owned cats with naturally occurring heart disease, one hundred and sixty four of which had congestive heart failure. Medical records were reviewed and owners and referring veterinarians were contacted for follow-up data. Data collected included pimobendan dose, other medications administered concurrently, data collected at physical examination, presence or absence of heart failure, adverse effects, classification of heart disease, echocardiographic data and survival time. The data were analyzed for significance between the initial visit and any follow-up visits.
Results: All cats were treated with pimobendan. The median pimobendan dose was 0.24 mg/kg q 12 h. Pimobendan was used in combination with multiple concurrent medications including angiotensin converting enzyme inhibitors, diuretics and antithrombotics. Five cats (3.0%) had potential side effects associated with pimobendan. One cat (0.6%) had presumed side effects severe enough to discontinue pimobendan use. Median survival time for 164 cats with congestive heart failure after initiation of pimobendan was 151 days (range 1–870).
Conclusion: Pimobendan appears to be well tolerated in cats with advanced heart disease when used with a variety of concurrent medications. Randomized controlled studies need to be performed to accurately assess whether it is efficacious for treatment of congestive heart failure in cats.

Case-control study of the effects of pimobendan on survival time in cats with hypertrophic cardiomyopathy and congestive heart failure

Yamir Reina-Doreste, DVM; Joshua A. Stern, DVM, PhD; Bruce W. Keene, DVM, MS; Sandra P. Tou, DVM; Clarke E. Atkins, DVM, MS; Teresa C. DeFrancesco, DVM; Marisa K. Ames, DVM; Timothy E. Hodge, DVM; Kathryn M. Meurs, DVM, PhD

Objective—To assess survival time and adverse events related to the administration of pimobendan to cats with congestive heart failure (CHF) secondary to hypertrophic cardiomyopathy (HCM) or hypertrophic obstructive cardiomyopathy (HOCM).

Design—Retrospective case-control study.

Animals—27 cats receiving treatment with pimobendan and 27 cats receiving treatment without pimobendan.

Procedures—Medical records between 2003 and 2013 were reviewed. All cats with HCM or HOCM treated with a regimen that included pimobendan (case cats) were identified. Control cats (cats with CHF treated during the same period with a regimen that did not include pimobendan) were selected by matching to case cats on the basis of age, sex, body weight, type of cardiomyopathy, and manifestation of CHF. Data collected included signalment, physical examination findings, echocardiographic data, serum biochemical values, and survival time from initial diagnosis of CHF. Kaplan-Meier survival curves were constructed and compared by means of a log rank test.

Results—Cats receiving pimobendan had a significant benefit in survival time. Median survival time of case cats receiving pimobendan was 626 days, whereas median survival time for control cats not receiving pimobendan was 103 days. No significant differences were detected for any other variable.

Conclusions and Clinical Relevance—The addition of pimobendan to traditional treatment for CHF may provide a substantial clinical benefit in survival time for HCM-affected cats with CHF and possibly HOCM-affected cats with CHF. (*J Am Vet Med Assoc* 2014;245:534–539)

Hypothese

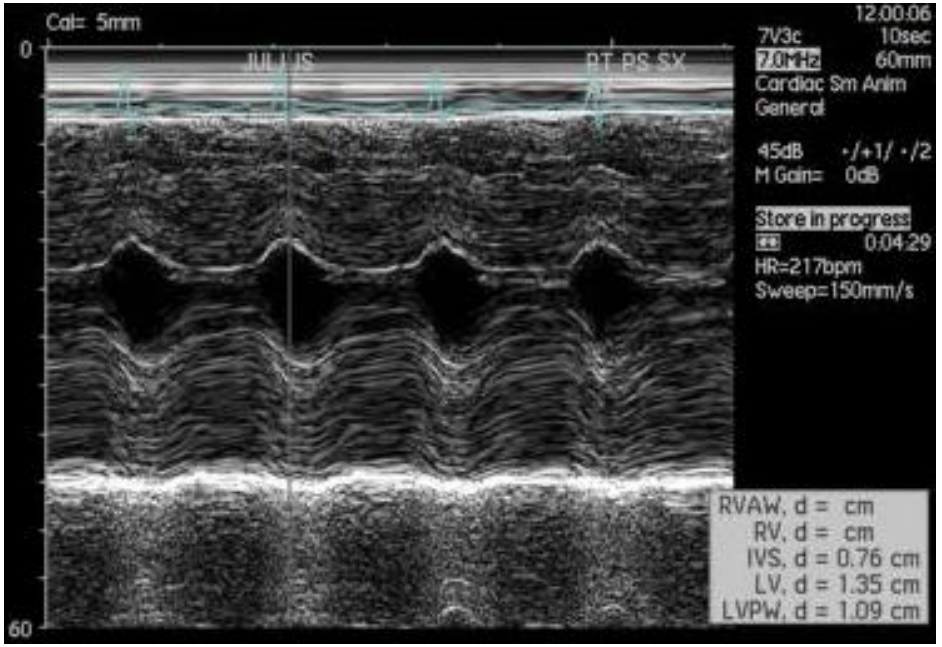
Der Zusatz von Pimobendan zu etablierten Therapie des kongestiven Herzversagen bei Katzen mit hypertropher Kardiomyopathie und obstruktiver hypertrophen Kardiomyopathie (Diuretika, Aspirin/Clopidogrel, ACE Hemmer und B- Blocker) führt zu längerer Überlebungszeit der Patienten.

Material und Methoden

Katzen mit diagnostizierten HCMP, oHCMP und radiologischer Bestätigung von kardiogenem Lungenödem

Ausschluss von Ursachen 2° HCMP wie Hypertension, SAS und Hyperthyreoidismus

Echodimensionen der Wände des linken Ventrikels in der Diastole > 6mm, Fraktionsverkürzung > 30% und LVOT Vmax >2m/s



Studienpopulation

Datenbasis von 164 Patienten

Es wurden 27 Pimokatzen festgestellt

Eine Kontrollgruppe wurde aufgebaut

Pimogruppe:

21 mk, 6 wk

Median KGw 5.1 kg (2.5-8.3)

Alter 9.0 (3.1-16.5)

22 HCM, 5 HOCM

Kontrollgruppe:

21 mk, 6 wk

Median KGw 5.3 kg (3.7-8.9)

Alter 8.8 (3.0-18)

22 HCM, 5 HOCM

Studienpopulation

Table 1—Drugs administered to cats with CHF secondary to HCM or HOCM treated with a regimen that included (case cats) and that did not include (control cats) pimobendan.

Drug	Case (n = 27)	Control (n = 27)
Pimobendan	27	0
Furosemide	27	27
Enalapril	21	24
Benazepril	2	0
Atenolol	3	9
Clopidogrel	13	4
Aspirin	1	4
Dalteparin	5	7
Clopidogrel and dalteparin	3	2
Clopidogrel and aspirin	1	0
Aspirin and dalteparin	2	2

Studienpopulation

Table 1—Drugs administered to cats with CHF secondary to HCM or HOCM treated with a regimen that included (case cats) and that did not include (control cats) pimobendan.

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Aspirin	1	4
Dalteparin	5	7
Clopidogrel and dalteparin	3	2
Clopidogrel and aspirin	1	0
Aspirin and dalteparin	2	2

Studienpopulation

Table 2—Complications at the time of CHF diagnosis or that developed subsequently in cats with CHF secondary to HCM or HOCM treated with a regimen that included (case cats) and that did not include (control cats) pimobendan.

	Case (n = 27)		Control (n = 27)	
Complication	**At CHF diagnosis**	**Developed subsequently**	**At CHF diagnosis**	**Developed subsequently**
Arterial thromboembolism	2	5	2	3
Left atrial thrombi	5	0	0	0
Ventricular ectopy	3	2	6	4
Supraventricular ectopy	2	2	2	2
Atrial fibrillation	3	4	0	1
Atrioventricular block	1	1	0	0

Studienpopulation

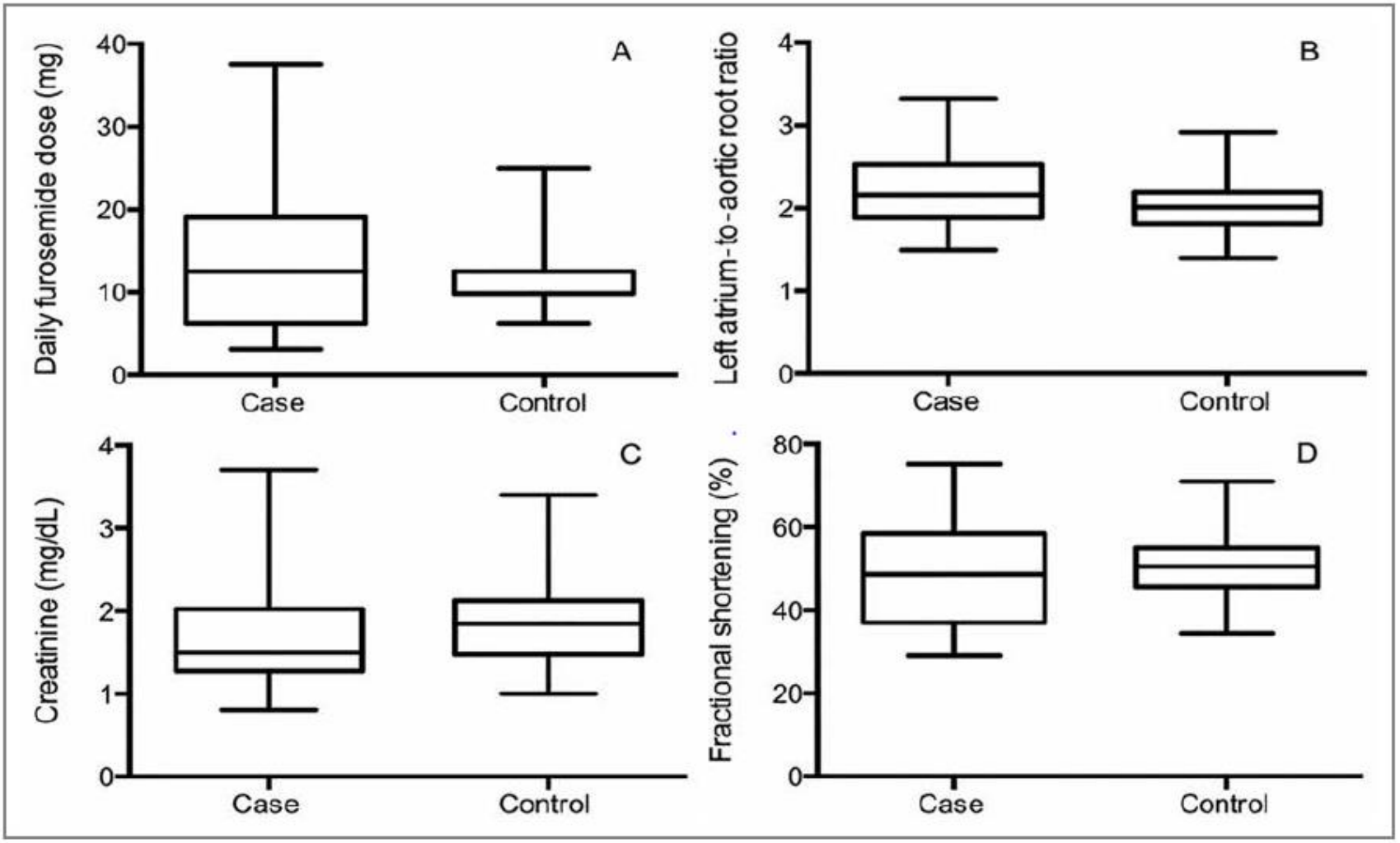


Figure 1—Box-and-whisker plots of the daily dose of furosemide (A), left atrium-to-aortic root ratio (B), serum creatinine concentration (C), and fractional shortening (D) at the time of CHF diagnosis in cats with CHF secondary to HCM or HOCM treated with a regimen that included (case cats; n = 27) and that did not include (control cats; 27) pimobendan. There were no significant ($P > 0.05$) differences between case and control cats for any of the variables. For each plot, the box represents the IQR, the horizontal line in each box represents the median, and the whiskers represent the minimum and maximum values.

Case-control study of the effects of pimobendan on survival time in cats with hypertrophic cardiomyopathy and congestive heart failure

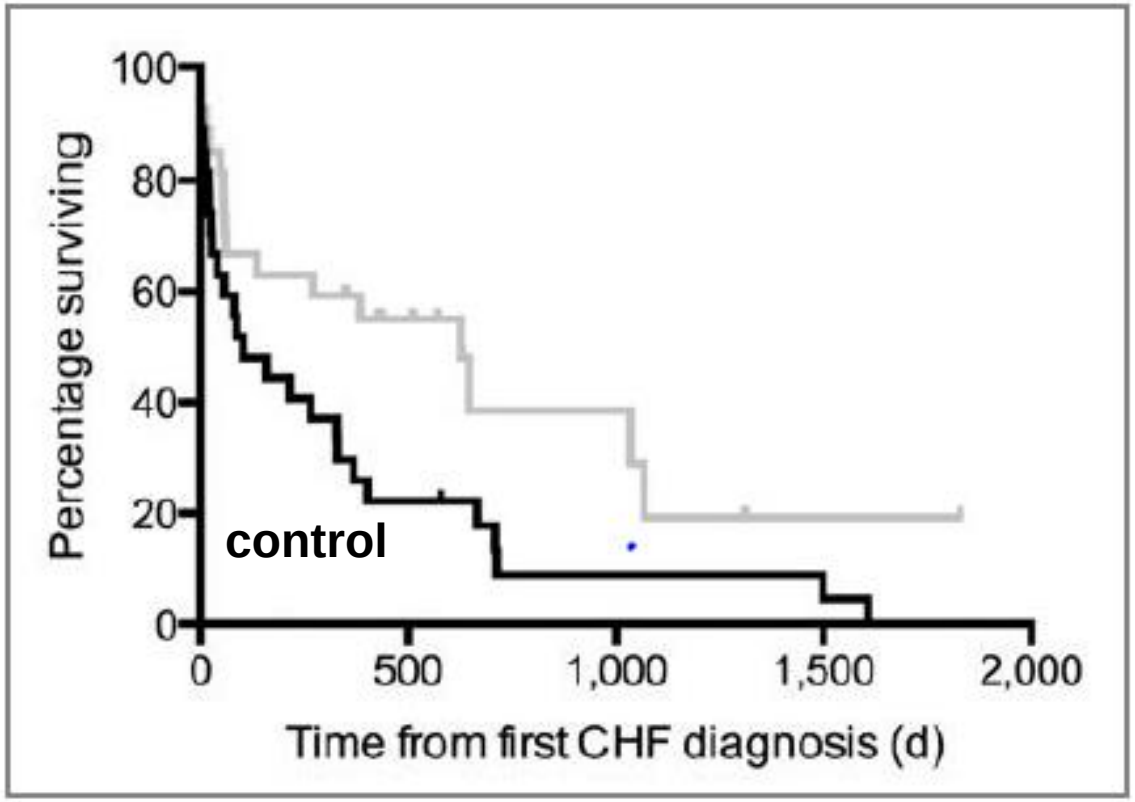


Figure 2—Kaplan-Meier survival curves for cats with CHF treated with a regimen that included (case cats; gray line) and that did not include (control cats; black line) pimobendan. The 2 curves differ significantly ($P = 0.024$) indicating a survival benefit in the pimobendan group.

Zusammenfassung

Case-control study of the effects of pimobendan on survival time in cats with hypertrophic cardiomyopathy and congestive heart failure

Results—Cats receiving pimobendan had a significant benefit in survival time. Median survival time of case cats receiving pimobendan was 626 days, whereas median survival time for control cats not receiving pimobendan was 103 days. No significant differences were detected for any other variable.

Conclusions and Clinical Relevance—The addition of pimobendan to traditional treatment for CHF may provide a substantial clinical benefit in survival time for HCM-affected cats with CHF and possibly HOCM-affected cats with CHF. (*J Am Vet Med Assoc* 2014;245:534–539)

Komplikation der Kardiomyopathien -FATE

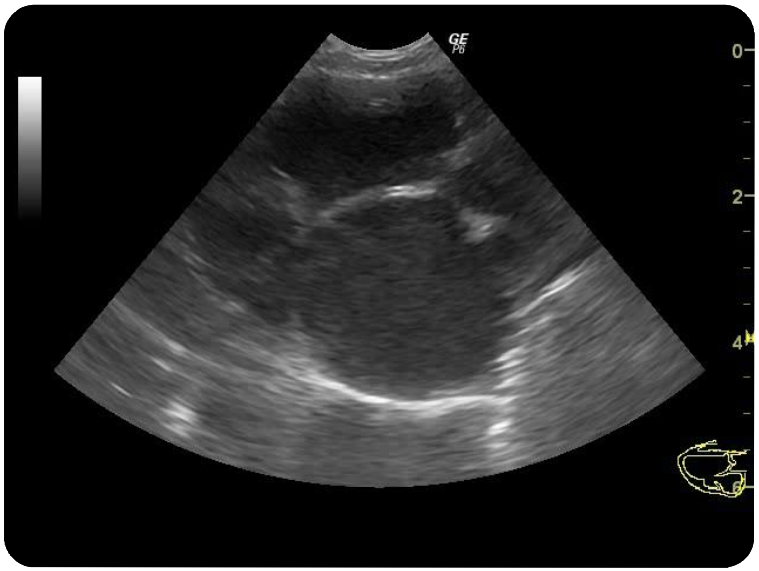
Akuter Verschluss der Aorta durch einen verschlepptes Gerinnsel. Komplikation einer Herzmuskelerkrankung Kardiomyopathie, Entzündungen, Infektionen, Tumoren sowie Überfunktion der Schilddrüse

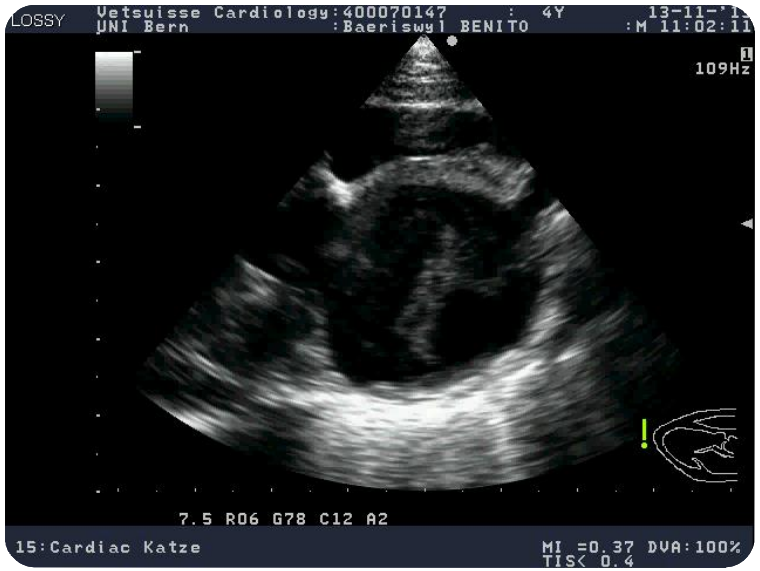
Häufigkeit im Patientengut ist bei 0,5%

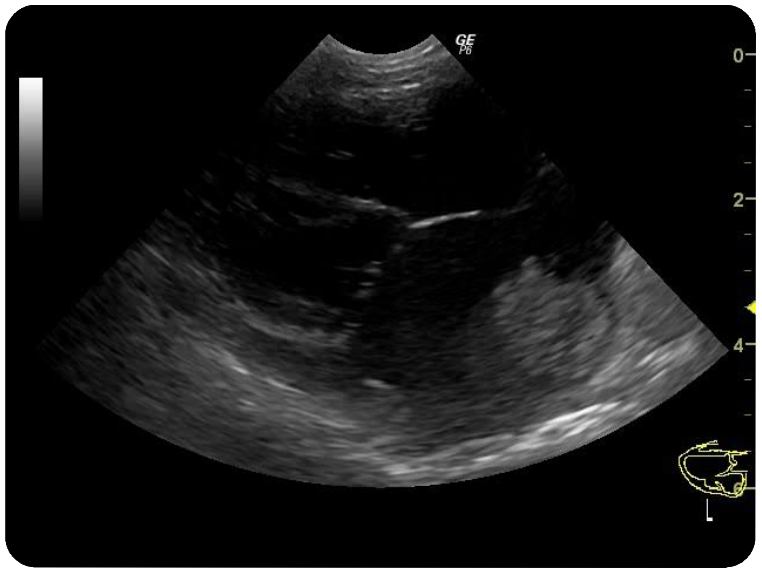
Es muss eine Virchowische Triade vorliegen: Strömungsverlangsamung, Hyperkoagulabilität, Schädigung des Endothels

Aufzweigung der abdominalen Aorta (*trifurcatio aortae*- Sattelthrombus). Ischämische Myo-/Neuropathie der Hintergliedmaßen

Progression der Gerinnselbildung

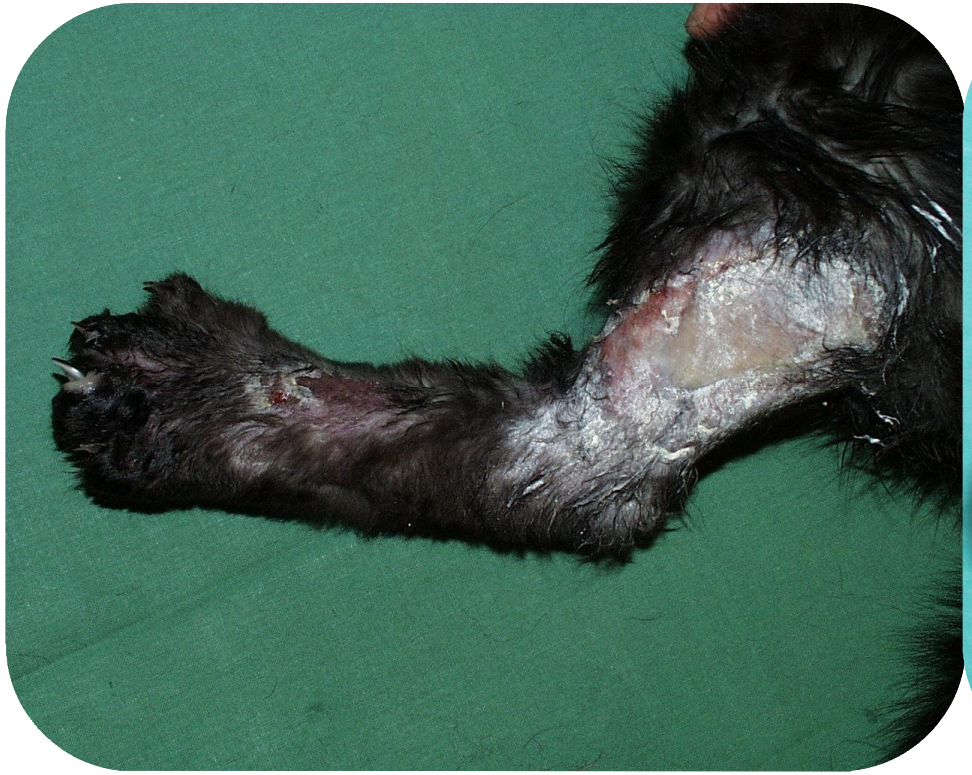


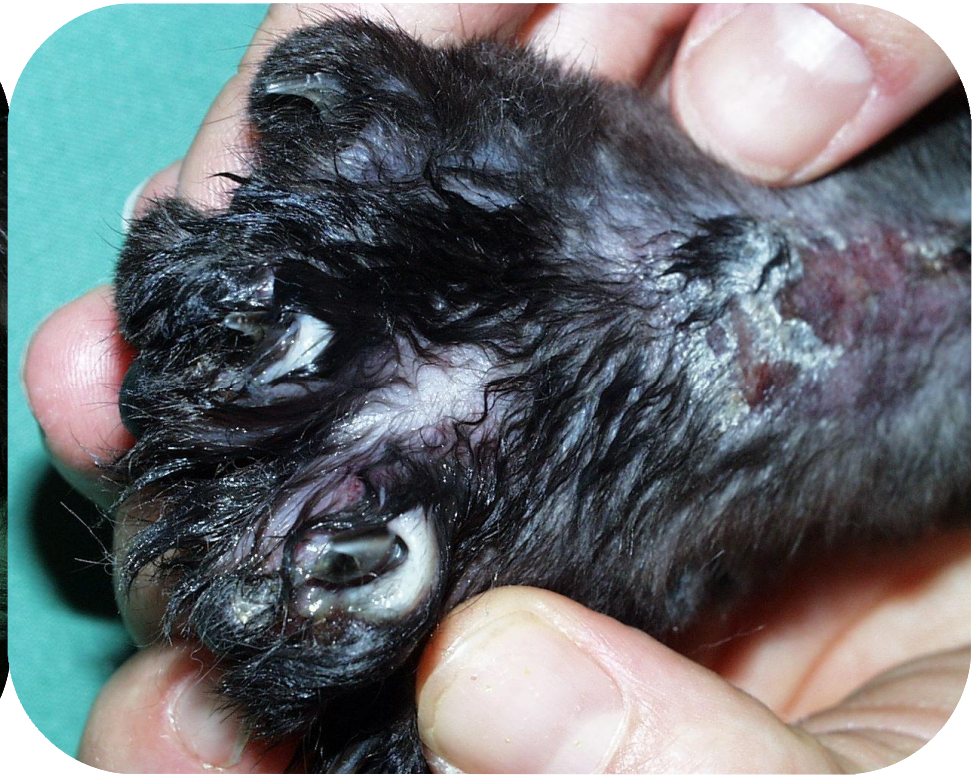




Feline Aortenthrombose FATE
Komplikationen

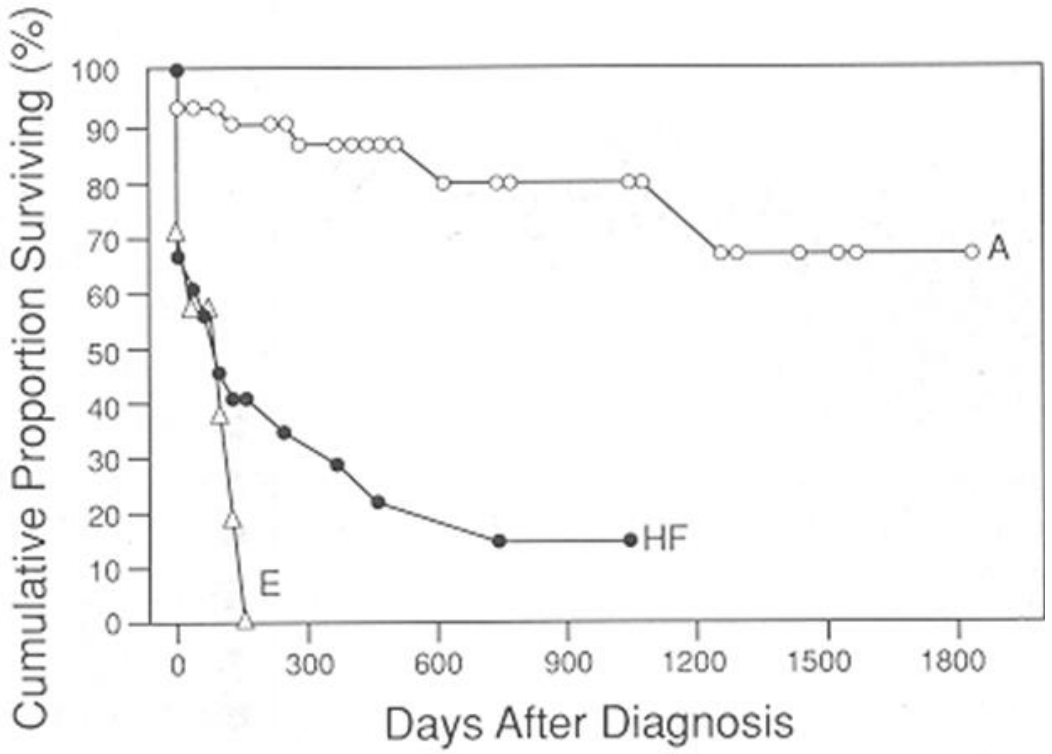
Nekrosen/Gangräne der Hinterbeine treten bei 5% der Patienten auf und sind eine Indikation zur Amputation



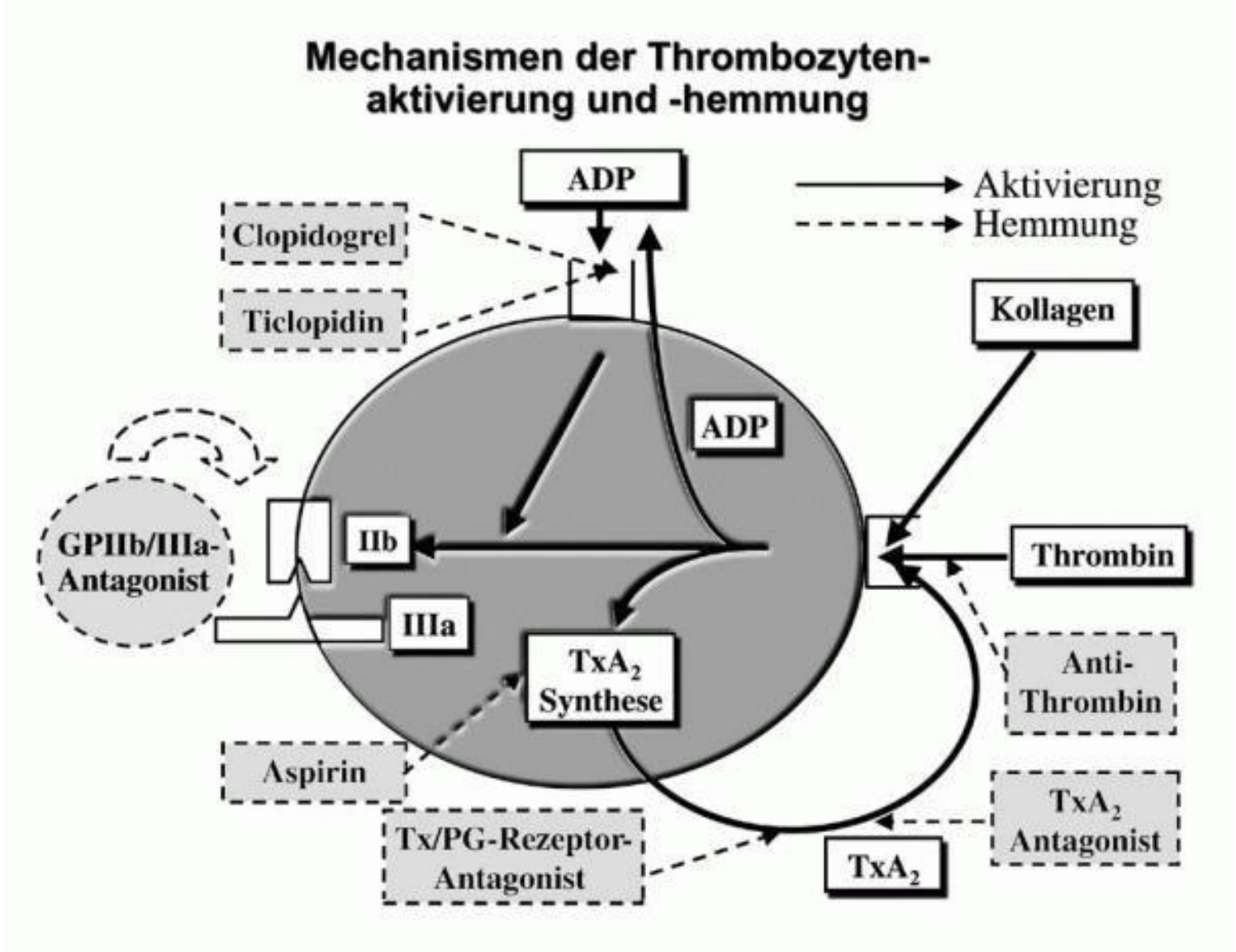


Die Prognose bei der Aortenthrombose

<u>Langzeitprognose</u> ist ungünstig: mediane Überlebungszeit in diversen Studien von 61, 117, 184 Tagen, 30 Monate



Atkins et al, JAVMA 1992



Huber K et al. Journal für Kardiologie 2003; 10 (12): 554-560 ©

Therapieprotokolle

Aspirin 5 mg 2x/Woche

Aspirin 25 mg 2x/Woche

Aspirin 81 mg 2x/Woche

Clopidogrel 18,75 mg SID

D. Hogan; P. Fox; K. Jacob; B. Keene; N. Laste; S. Rosenthal

Purdue University, West Lafayette, IN, USA; The Animal Medical Center, New York, NY, USA; Chesapeake Veterinary Cardiology Associates, Annapolis, MD, USA; North Carolina State University, Raleigh, NC, USA; Angell Memorial Animal Hospital, Boston, MA, USA

Analysis of the Feline Arterial Thromboembolism: Clopidogrel vs Aspirin Trial (Fat Cat). Proceedings, ACVIM 2013.

- Katzen mit vorgegangener Thrombembolie (1-3 Monate vor Studienbegin).
- Randomisiert Aspirin (81 mg PO q 3 d) oder Clopidogrel (18.75 mg PO SID).
- Primärer Endpunkt erneute Thombembolie.
- Sekundärer Endpunkt: Tod, inklusive Herztod, oder Nebeneffekte der Therapie.
- Geplante Studiendauer 1 Jahr

Insgesamt 72 Katzen, 36 Tiere pro Gruppe
Die Aufteilung der Gruppen bezüglich Alter, Gewicht, Geschlecht und grundliegender Herzerkrankung ergab 2 vergleichbare Gruppen. Prospektive, double-blinded, Multicenterstudie.

Resultate zur Studiendauer 1 Jahr

Je eine Katze pro Gruppe zeigte Probleme welche als Nebeneffekt der Therapie erklärt wurden und die Katzen wurde aus der Studie ausgeschlossen.

Primärer Endpunkt
Aspirin: mediane Überlebungszeit der 192 Tage
Clopidogrel: Medianwert nicht bestimmbar

Herztod
Aspirin: mediane Überlebungszeit 128 Tage
Clopidogrel: 346 Tage

Alle Todesursachen
Aspirin: 116 Tage
Clopidogrel: 248 Tage

Resultate zur Gesamtstudiendauer

Primärer Endpunkt
Aspirin: mediane Überlebungszeit der 192 Tage
Clopidogrel: 443 Tage

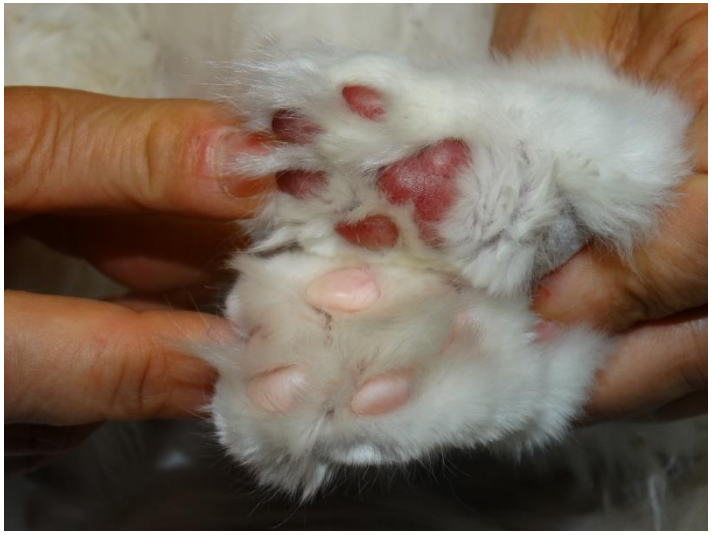
Herztod
Aspirin: mediane Überlebungszeit 128 Tage
Clopidogrel: 346 Tage

Alle Todesursachen
Aspirin: 116 Tage
Clopidogrel: 248 Tage

Zusammenfassung

Die Therapie mit Clopidogrel verlängert die mediane Überlebungszeit von Katze NACH einer Thrombembolie im Vergleich zu Aspirin

Über die prophylaktische Wirkung von Clopidogrel zur ersten Thrombose bei Herzkranken Katzen wurde NICHT berichtet



14.6.2016

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10.10.2016