

FERRET CARDIOMYOPATHY

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While acquired cardiac disease is relatively common in older ferrets, congenital cardiac disease has yet to be documented in the species. Dilated cardiomyopathy is the most commonly reported form, although the hypertrophic form also occurs. Both primary (idiopathic) cardiomyopathy and cardiomyopathy secondary to another disease process, such as lymphosarcoma or intestinal bloat with myocardial ischemia, occur in ferrets. Cardiomyopathy usually progresses to congestive heart failure in this species.

Clinicians should become familiar with the clinical signs of cardiac disease in ferrets as well as methods available to evaluate cardiac health in older ferrets (e.g., as part of a preanesthesia evaluation). Multiple references that characterize echocardiography, electrocardiography, and radiography for both normal and sick ferrets are available. When performing a physical examination, practitioners should be aware that the normal heart rate for ferrets is 180 to 250 beats/min and the normal respiratory rate is 33 to 36 breaths/min. A pronounced sinus arrhythmia resulting in a dramatic decrease in heart rate during auscultation may also be normal in ferrets.

DIAGNOSTIC CRITERIA

Historical Information

Gender/Breed Predisposition

- None known.

Age Predisposition

- Middle-aged to older ferrets (≥ 3 years).

Owner Observations

- Coughing, dyspnea.
- Anorexia, weight loss.
- Exercise intolerance, lethargy, weakness, hindlimb paresis, syncope.
- Owners may not observe insidious, nonspecific clinical signs in cases of mild, compensated cardiac disease.

Other Historical Considerations/Predispositions

- Heartworm status or history of heartworm prophylaxis.
- Exposure to other ferrets.
- Exposure to influenza virus.

Physical Examination Findings

Similar to findings in other mammals with cardiac insufficiency:

- Weakness, posterior paresis, lethargy, syncope.
- Cyanotic or pale mucous membranes, prolonged (>2 seconds) capillary refill time.
- Tachypnea, pulmonary crackles, increased bronchovesicular sounds, dyspnea with increased inspiratory effort.
- Muffled heart sounds, gallop rhythms, tachycardia or bradycardia, holosystolic murmur at the seventh to eighth intercostal space.
- Weak, irregular, or thready femoral pulses, bounding pulses, jugular pulses.
- Ascites, hepatomegaly, splenomegaly.

Laboratory Findings

Laboratory diagnostics should be pursued to confirm or exclude other important diseases that may occur concurrently with cardiomyopathy in middle-aged ferrets, such as adrenal neoplasia, lymphoma, dirofilariasis, *Helicobacter* infection, and insulinoma. Test results also provide a baseline for reference before initiating fluid and/or drug therapy in cardiac compromised patients. Normal reference ranges for ferrets are listed in Table 1; these values vary slightly depending on the gender and coloration of the individual ferret.

Complete Blood Count

Although no changes diagnostic of cardiomyopathy are found in the complete blood count, decreased leukocytes, total protein, hemoglobin, and hematocrit are present in many ferrets with cardiomyopathy.

Biochemical Profile

- Abnormalities in the biochemical profile for ferrets with cardiomyopathy are similar to those in cats with cardiomyopathy.
- Hypokalemia and elevated concentrations of creatinine and blood urea nitrogen have been documented in ferrets with cardiomyopathy.
- Thrombosis and associated elevations in alkaline phosphatase, aspartate amino transferase, and creatinine kinase activities have not been reported in ferrets secondary to cardiomyopathy.

Feline Antigen Heartworm Test §

- Negative.
- The sensitivity and specificity of this test in ferrets are unproven; however, I have had several patients with positive test results that also were positive for heartworms at necropsy.

Thoracentesis or Abdominocentesis of Pleural Effusion or Ascites §

- Fluid not normally obtained from the thorax or abdomen.
- Although nonspecific, a transudate is usually present with cardiomyopathy.

Other Diagnostic Findings

Radiography §

- Pulmonary venous congestion.
- Pulmonary edema: Patchy interstitial or alveolar pattern.
- Pleural effusion.
- Hepatomegaly, splenomegaly, ascites.
- Dorsal elevation of the trachea.
- Cardiac abnormalities:
 - Enlarged globoid cardiac silhouette.
 - Lateral view: Increased cardiac sternal contact.
 - Ventrodorsal view: Elongation and widening of the heart.

Electrocardiography §

- Most common finding: Sinus tachycardia.
- Less common findings: Ventricular premature complexes, atrial premature complexes, tall R waves, QRS prolongation, ST depression.

Echocardiography §§

- Increased left ventricular end-diastolic dimension (normal internal diameter, 0.88 [±0.15] cm).
- Increased left ventricular end-systolic dimensions (normal, 0.59 [±0.15] cm).
- Decreased fractional shortening (normal, 33% [±14%]).
- Enlarged left atrium (normal diameter, 0.71 [±0.18] cm).
- Right ventricular enlargement (normal internal diameter, 0.38 [±0.10] cm).

Doppler Echocardiography §§

- Reduced right ventricular systolic motion.
- Mitral regurgitation.
- Tricuspid regurgitation.

Summary of Diagnostic Criteria

- **Signalment:** 3 years of age or older.
- **History:** Exercise intolerance, lethargy, hindlimb paresis.

TABLE 1
Normal Reference
Ranges for Ferrets

| Parameter | Range |
|--|------------|
| Complete blood count | |
| Hematocrit (%) | 36–53 |
| Hemoglobin (g/dl) | 15.2–18.2 |
| Erythrocytes ($\times 10^6/\mu\text{l}$) | 6.77–12.18 |
| Leukocytes ($\times 10^3/\mu\text{l}$) | 2–10 |
| Total protein (g/dl) | 5.1–7.4 |
| Biochemical profile | |
| Total protein (g/dl) | 5.1–7.4 |
| Blood urea nitrogen (mg/dl) | 0.6–45.2 |
| Creatinine (mg/dl) | 0.1–1.2 |
| Potassium (mmol/L) | 4.5–7.7 |
| Creatinine kinase (U/L) | 98–564 |

- **Physical examination:** Cyanosis, abnormal auscultation, dyspnea, hindlimb weakness.
- **Electrocardiography:** Sinus tachycardia.
- **Thoracic radiography:** Increased cardiac size, increased cardiac sternal contact, dorsal elevation of the trachea, pleural effusion, pulmonary venous congestion, pulmonary edema.
- **Echocardiography:** Cardiac enlargement, decreased fractional shortening.

Diagnostic Differentials

- **Dirofilariasis:** Negative feline heartworm antigen testing and echocardiography that fails to detect or visualize parasites exclude dirofilariasis.
- **Insulinoma:** Blood glucose below 70 mg/dl excludes insulinoma in fasted ferrets.
- **Primary lung disease** (e.g., canine distemper virus, influenza, bacterial pneumonia, pulmonary mycoses, trauma, pulmonary neoplasia):
 - History, complete blood count, presence of radiographic pulmonary patterns, cytologic analysis of pleural effusion obtained via thoracentesis, endoscopy, bronchoalveolar lavage, and aspiration of lung masses may be necessary to differentiate primary lung disease from cardiomyopathy with secondary pleural effusion, pulmonary edema, or pulmonary venous congestion.
 - Lack of peripheral lymph node enlargement does not rule out lymphoma affecting the lungs. Systemic lymphoma can be excluded via biopsy or aspirate of lymph nodes.
- **Anterior mediastinal mass** (typically lymphoma): Excluded via radiography and ultrasonography.

TREATMENT RECOMMENDATIONS

Initial Treatment

Drug therapy is based on drug regimens for cardiomyopathy in dogs and cats. Controlled clinical or pharmacokinetic trials have not been performed with these drugs in ferrets.

- **Supplemental oxygen:** 40% to 60% oxygen-enriched inspired gas should be administered via facemask or oxygen cage until patient is stable. \$\$
- **Furosemide:** 1–4 mg/kg PO, SC, IM, or IV q8–12h for diuresis. The endpoint of diuretic therapy is the relief of such clinical signs as pulmonary edema, pleural effusion, ascites, and dyspnea. \$
- **Nitroglycerin 2% ointment:** Initial adjunctive venodilator for cardiomyopathy and cardiogenic edema. Reduces pulmonary edema in the acute management of congestive heart failure. The ointment can be applied to a shaved inner thigh, the pinna, or any hairless region of skin at a dose of $\frac{1}{6}$ to $\frac{1}{8}$ inch/ferret q12–24h. \$
- **Thoracentesis** (if pleural effusion is present): Performed in a manner similar to that used in cats, except that the entry point should be farther caudal (i.e., at the ninth to 10th intercostal space) to avoid the more caudally located ferret heart. \$

Alternative/Optional Treatments/Therapy

Treatment is based on the type of cardiomyopathy and can be initiated once the patient is stabilized. Combinations of an angiotensin-converting enzyme inhibitor with furosemide and other drugs based on the type of cardiomyopathy are generally used.

- **Calcium channel blocker** for long-term therapy of hypertrophic cardiomyopathy. \$
 - Diltiazem: 1.5–7.5 mg/kg PO q12h.
 - Enhances diastolic performance, increases ventricular filling, reduces heart rate and blood pressure, and reduces myocardial oxygen consumption.
 - May cause vomiting.
- **Angiotensin-converting enzyme inhibitor** for hypertrophic or dilated cardiomyopathy. \$
 - Enalapril: 0.25–0.5 mg/kg PO q24–48h or q24h for long-term therapy.
 - Balanced vasodilator.
 - May increase survival in cases of myocardial infarction.
 - Can cause lethargy.
 - May limit progressive myocardial dilation.
 - Not for use in animals with concurrent renal disease.

RESOURCE LIST

Nitroglycerin 2% ointment \$

- Apply to shaved inner thigh, pinna, or any hairless region of skin at a dose of $\frac{1}{6}$ – $\frac{1}{8}$ inch/ferret q12–24h for first 24–36 hours of therapy
- Alternate 12 hours with and 12 hours without ointment to reduce drug tolerance
- Initial vasodilator and preload reducer for cardiomyopathy; reduces pulmonary edema in the acute management of congestive heart failure

Furosemide \$

- Substantially reduces congestive state
- 1–2 mg/kg SC, IM, or IV (preferred) q1–2h as needed
- 1–4 mg/kg PO q8–12h
- For long-term therapy, dosage is reduced to q6–8h once pulmonary edema has been reduced and then to the lowest effective oral dosage (q12–24h or even q48h)

Butorphanol (Torbugesic or Torbutrol, Fort Dodge Animal Health) \$

- 0.05–0.4 mg/kg IM or SC as needed (usually <48 hours) for pain control and sedation

Digoxin \$

- 0.005–0.01 mg/kg PO q12–24h for long-term therapy
- Base dosage on lean body weight, usually 70% of body weight
- Monitor serum concentrations 10–14 days after initiating therapy
- Therapeutic concentrations of 1–2 ng/ml should be obtained 10–12 hours after oral administration
- Anorexia and depression are early signs of toxicity
- Draw blood samples for therapeutic monitoring if signs of toxicity are present
- Draw blood samples for therapeutic monitoring 10–14 days after start of therapy and immediately before oral dosing for the trough concentration and 6–8 hours after oral administration for peak concentrations

Enalapril (Enacard, Merial) \$

- 0.25–0.05 mg/kg PO q24–48h or q24h for long-term therapy

Propranolol \$

- 0.2–2 mg/kg PO q8–12h for long-term therapy

Atenolol \$

- 6.25 mg/ferret PO q24h for long-term therapy

Diltiazem \$

- 1.5–7.5 mg/kg PO q12h for long-term therapy

ON THE NEWS FRONT

In ferrets, serum cardiac troponin T is a sensitive and specific biomarker for cardiac disease or injury due to doxorubicin toxicosis, traumatic injury, ischemia, and cardiac puncture. This biomarker is more cardiospecific than creatinine kinase or lactate dehydrogenase isoenzyme activities in ferrets and mice.

- **β -blocker** for hypertrophic cardiomyopathy. **§**
 - Propranolol: 0.2–2 mg/kg PO q8–12h for long-term therapy.
 - Atenolol: 6.25 mg/ferret PO q24h for long-term therapy.
 - Prolongs filling; decreases myocardial ischemia.
 - May cause lethargy, anorexia, or hypotension.
- **Digoxin** **§**
 - 0.005–0.01 mg/kg PO q12–24h for long-term therapy.
 - Positive inotrope.
 - Although no therapeutic or toxic window has been established for ferrets, they seem to respond well clinically to digoxin therapy.
 - Digoxin is usually reserved for patients with unresponsive right-sided congestive heart failure, atrial fibrillation, supraventricular tachyarrhythmia, or myocardial failure/dilated cardiomyopathy.
 - Serum drug concentrations should be monitored.

Supportive Treatment

- **Fluid therapy** as indicated based on assessment of hydration and pulmonary status. Vascular access may be obtained by an IV catheter placed in the cephalic or jugular vein or an intraosseous catheter and a 20- or 22-gauge spinal needle placed in the femoral, tibial, or humeral marrow cavity. **§**
 - The recommended maintenance rate in ferrets is 70–100 ml/kg/24 hr; however, this rate may need to be substantially reduced (i.e., by 50% to 75%) depending on the patient's hydration, perfusion, and pulmonary congestion status. Fluids may be given by slow drip or syringe pump over 24 hours.
 - Recommended fluids include 2.5% dextrose in 0.45% sodium chloride solution or 5% dextrose in water (D5W).

- **Supplemental potassium** may be given to hypokalemic patients in fluids or orally. Supplementation rates should follow guidelines used in cats and dogs.
- **Sedation and pain control** may be indicated for ferrets that seem stressed or that refuse to allow a patent IV fluid line to be maintained. Low-dose butorphanol is an excellent sedative in ferrets
- **Nutritional support** with a low-sodium, high-protein, highly palatable force-fed diet is indicated in sick ferrets to establish a positive energy balance. Options include:
 - Chicken baby food without added onion or garlic is usually well accepted.
 - Standard veterinary force-fed diets (e.g., Hill's Prescription Diet Canine/Feline a/d or Eukanuba Veterinary Diets Maximum-Calorie).
- Many ill ferrets suffer from extreme hypothermia, and **thermal support** in the form of warmed fluids, forced heaters, or heating pads is indicated. The body temperature should be carefully monitored.

Patient Monitoring

- Respiratory rate and work of breathing should be monitored until they normalize and lung crackles resolve.
- Thoracic radiography is indicated to monitor alveolar infiltrates, which should clear within 24 to 72 hours of initiating therapy, and resolution of pulmonary effusion or edema.
- Plasma blood urea nitrogen, creatinine, and electrolyte concentrations should be checked:
 - The endpoint of diuretic therapy is relief of clinical signs and progressive increase in blood urea nitrogen and/or creatinine concentration.
 - Hypokalemia and dehydration can result from excessive diuresis.
- Serum digoxin concentrations should be monitored.
- Echocardiography should be performed every 3 months to recheck fractional shortening and other cardiac dimensions.

Home Management

- Exercise should be restricted, which may be difficult with ferrets.
- A low-salt diet may be beneficial but difficult to institute because no such commercially available ferret diet is available.
- Owners should be instructed to observe the animal for a recurrence of clinical signs, including but not limited to coughing, decreases in activity, lethargy, anorexia, and syncope.

Milestones/Recovery Time Frames

- The initial response to therapeutic management should be monitored via observation of respiratory rate and effort as well as auscultation of lung sounds.
- Other milestones and recovery time frames have not been reported; long-term clinical case management has not been reported retrospectively in ferrets.
- Recommendations for recheck physical examinations and diagnostics are similar to those for management of congestive heart failure in other species:
 - Electrocardiography, thoracic radiography, blood electrolytes, and renal indicators should be rechecked 7 to 10 days after initiating therapy.
 - Ultrasonography to check cardiac size measurements, output, and contractility is indicated every 3 months.

Treatment Contraindications

- Although anesthesia may be necessary for diagnostics and thoracentesis in ferrets with cardiomyopathy, any anesthetic event should be closely monitored.
- Prednisone therapy may be necessary in patients with insulinoma but may rarely result in fluid and salt retention, making management of cardiac insufficiency more difficult.
- Electrolytes should be carefully monitored in these patients; furosemide may result in hypokalemia, which is a contraindication for use of digoxin.
- Digoxin should be used with caution in ferrets with renal disease. Digoxin is principally eliminated by the kidneys, and patients with renal insufficiency must have their levels carefully monitored. Ferrets with renal disease seldom have elevated creatinine values, although increased phosphorous and blood urea nitrogen concentrations are markers of renal disease in this species. Practitioners should be aware of how digoxin interacts with cimetidine, metoclopramide, and antacids before using these agents in ferrets with concurrent gastric ulcers and cardiac disease. Use of diuretics such as furosemide may predispose patients to digoxin toxicity. Use of steroids may deplete body potassium and thus may also predispose patients to digoxin toxicity.
- Additional contraindications are listed for each drug separately under Alternative/Optional Treatments/Therapy.

PROGNOSIS

Too few cases of cardiomyopathy in ferrets with long-term follow up have been reported to accurately assess the prognosis of ferrets with this disease. However, ferrets with more severe disease based on clinical signs and diagnostic testing seem to respond more favorably than dogs and cats with similar findings and medication regimens.

Favorable Criteria

- Normalization of clinical signs (mucous membrane color and capillary refill time, cardiac rate and rhythm, pulse, respiratory rate and sounds) after initial treatment.
- Additional diagnostics fail to reveal concurrent endocrine, neoplastic, or heartworm disease.

Unfavorable Criteria

- Concurrent disease, such as lymphoma or insulinoma.
- Prednisone therapy for lymphoma or insulinoma in ferrets that also have cardiomyopathy may result in salt and fluid retention, making management of cardiac insufficiency more difficult.
- Concurrent *Helicobacter* infection (gastric ulcer disease) should be closely monitored.
- In contrast to the situation in cats, thromboembolic disease does not appear to be a common component of cardiovascular disease in ferrets. However, ferrets with petechia or ecchymoses carry a guarded prognosis and should be investigated for dirofilariasis and adrenal or other neoplasia.

RECOMMENDED READING

- Atkinson RM: Case reports on cardiomyopathy in the domestic ferret, *Mustela putorius furo*. *J Small Exotic Anim Med* 2(2):75–78, 1992.
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