Cardiac Disease in Rabbits

Introduction

• Rabbits can suffer from both congenital and acquired heart disease, this is increasingly recognized as the population ages

• Clinical signs can include dyspnea, exercise intolerance, weight loss and anorexia. There may however be NO noticeable clinical signs.

• Diagnostic evaluation should include a full physical examination, auscultation, ECG, chest radiography and echocardiography.

• Treatment recommendations follow those for other species. Once a diagnosis is made, use of the ‘Cascade’ allows suitable medical treatment.

• In an emergency decompensation situation, oxygenation, and application of 5mm of nitroglycerine gel to the inside of the pinna can be life-saving.

Disease Conditions

Most recorded information about cardiac diseases relates to infectious, toxin-induced or diet-related diseases of laboratory rabbits. Heart disease also occurs in pet rabbits and more information has become available as rabbits live longer and more diagnostic and therapeutic procedures are adopted for the individual animal. Congenital abnormalities such as ventricular septal defects occur as do age related cardiac problems such as valvular disease. Commonly noted clinical signs include exercise intolerance and dyspnea, however they may be very non-specific such as anorexia or weight-loss. On examination it may be possible to detect cyanosis of the mucus membranes, or appreciate a heart murmur or arrhythmia. Diagnosis and treatment follow the same lines as for dogs and cats. Clinical examination,
auscultation, electrocardiography, chest radiography should form part of the minimum
database. Many cases can be positively diagnosed by echocardiography. Most cardiac disease
is diagnosed in pet rabbits over the age of four years, and the larger breeds such as New
Zealand Whites and French Lops are over-represented.
Cardiomyopathy occurs in pet rabbits. Giant breeds appear most susceptible, but the
aetiology is unknown at the present time. Hypertrophic, restrictive and dilated forms have all
been reported. Histopathological findings indicate the presence of myocardial fibrosis.

The rabbit myocardium can be affected by several diseases. Vitamin E deficiency,
coronavirus infection and some bacterial infections such as salmonellosis and pasteurellosis
have been recorded as causes of cardiomyopathy in laboratory rabbits. Tyzzer’s disease not
only causes intestinal and hepatic lesions but can also cause a myocarditis resulting in
myocardial fibrosis in those animals that survive. *Encephalitozoon cuniculi* has been reported
as a cause of myocarditis in rabbits. Stress and catecholamines are proven causes of
cardiomyopathy. Myocardial necrosis and fibrosis have been recorded in rabbits
anaesthetized with ketamine/xylazine combinations by continuous infusion. It has been
postulated that hypoxaemia and coronary vasoconstriction result in cell death and necrosis.
The rabbit has limited collateral coronary circulation and is therefore predisposed to
ischaemia induced by coronary vasoconstriction. The authors draw an analogy with rabbits
used as models of catecholamine-induced cardiomyopathy in which alpha-adrenergic
mediated coronary vasoconstriction occurs. Hypotension and hypoxaemia are further
contributory factors.

Arteriosclerosis is a thickening and hardening of the arteriolar walls resulting from
proliferative or degenerative changes. Aortic arteriosclerosis occurs in rabbits and can cause
seizures or vague symptoms such as inactivity and weight loss. Mineralization of the aorta
occurs in hypercalcaemic rabbits, usually in association with renal disease that impairs calcium excretion. Mineralization of the aorta is seen radiologically and may be a significant but incidental finding. Calcification of the aorta is often associated with calcification of the kidney. Calcification of soft tissues can be caused by excessive intestinal absorption of calcium, such as in cases of vitamin D toxicity.

Coronavirus infection in rabbits can result in cardiomyopathy and pleural effusion. Experimentally, coronavirus infected rabbits are used as laboratory models to study virus induced cardiomyopathy. An analogy has been made between rabbit coronavirus and feline infectious peritonitis. Clinical signs vary, but infected rabbits are generally pyrexic and many die within 5 days of infection. Pulmonary oedema, pleural effusion and dilation of the right ventricle are found at post-mortem. As in feline infectious peritonitis, hypergammaglobulinaemia is a feature of chronic infection that can be manifested by myocardial degeneration, ascites and uveitis. An enteric form has also been described. At the present time, coronavirus induced pleural effusion and cardiomyopathy have only been reported in experimentally inoculated rabbits. It has not been described in pet rabbits.

**Cardiac Diagnostics**

1. A thorough history is essential and should include information regarding the diet, animals in contact, neutering and exposure to potentially toxic substances. Remember that cardiac disease may be subtle, and rabbits as a prey animal may conceal relevant clinical signs. Unexplained weight loss, exercise intolerance and anorexia are all potentially significant.

2. Physical examination: this should include a thorough general examination, paying attention to the respiratory rate, heart rate, presence or absence of murmur and pulse deficits. Remember that at heart rates above 300bpm murmurs, arrhythmias and deficits can be difficult to detect. It is also important to evaluate the lung fields...
thoroughly to determine the likely origin of any adventitious sounds. Any concurrent diseases found during the physical examination should be fully evaluated.

3. ECG: this diagnostic method is easy to adapt for use in rabbits. The leads are applied as for other species, and a reading can usually be made without the need for sedation. Normal measurements are available.

4. Blood pressure monitoring: with the correct cuff this can be easy to achieve in general practice. Normal values are available.

5. Radiography: most thoracic radiography will require sedation. In my experience both Hypnorm (the licensed sedative) and alpha-2 agonists (commonly used as part of the ‘triple combination’ for sedation) can have negative effects on cardiac function. It is also not ethical to consider use of inhalant gases alone because rabbits will commonly breath-hold particularly if isofluorane is used. Possible alternatives include the use of midazolam alone or in combination with ketamine or an opiate. NB the advantages of sedation may be outweighed by the risks of not having an intubated patient, and considerations of the risks and benefits of both options should be discussed with the owner.

   Chest x-rays should ideally be taken at the point of maximal inspiration, and two perpendicular views are required. Normal measurements for cardiac size are available.

6. Echocardiography: this can often be performed without sedation, depending on the temperament of the patient. Echocardiography will give the best determination of the structural and haemodynamic issues occurring within the heart. Normal measurements for rabbits are available.

**Treating cardiac arrhythmias**

Cardiac arrhythmias should be characterized using electrocardiography and heart structure
and function assessed echocardiographically.

- **Tachyarrhythmias**: Prolonged rapid heartbeat over a period of weeks to months can lead to congestive heart failure. Short episodes may contribute to syncope.
  1. Supraventricular tachycardias: these can be treated using digoxin (0.005 mg/kg SID-BID); however, there is a significant risk of toxicity with this drug. Ideally blood digoxin levels should be monitored after the first few days of treatment. The levels are usually checked 6–7 h post-dosing. Alternatively the rabbit can be watched carefully and the drug dose reduced/stopped if signs of anorexia or gastrointestinal stasis occur. Diltiazem, a calcium channel-blocker, can also be used to treat tachycardia by slowing atrioventricular conduction (0.5–1 mg/kg SID-TID). The downside to this medication is that it reduces myocardial contractility and may cause a drop in blood pressure.
  2. In emergency situations rapid ventricular tachycardias may respond to boluses of intravenous lidocaine (1–2 mg/kg IV PRN).
  3. Solatol and mexiletine have also been used anecdotally in rabbits at dog doses.

- **Bradyarrhythmias**: Severe bradycardia may lead to episodic weakness or syncope.
  1. Bradycardia during anaesthesia (not in the case of α2-agonists) should be treated with glycopyrrolate (0.01 mg/kg).
  2. Severe atrioventricular block may respond to oral theophylline (10–20 mg/kg); however, mechanical pacing may be required.

**Emergency treatment of congestive heart failure.**

- Oxygen
- Percutaneous nitroglycerine 1cm on the internal pinna
• Furosemide 1–2 mg/kg intravenously
• ACE-inhibitors: enalopril 0.25–0.5 mg/kg once daily
• Pimobendan: 0.1–0.3 mg/kg SID-BID

**Treating Chronic Cardiac Disease**

**Diuretics**

- **Furosemide**
Furosemide is a loop diuretic that exerts its effect on the ascending limb of the Loop of Henle. It increases excretion of calcium, magnesium and hydrogen as well as renal blood flow and glomerular filtration rate. This drug is commonly used in the management of congestive heart failure, often in combination with ACE inhibitors or pimobendan. There have been many studies on the cellular effects of furosemide on the rabbit kidney, demonstrating that despite the rabbit's relative inability to excrete $\text{H}^+$ ions through the kidney, furosemide is still effective in this species.

**ACE inhibitors**

- **Enalapril**
Enalapril inhibits the conversion of angiotensin I to angiotensin II, resulting in decreased pre- and after-load from venous and arteriodilation. It also decreases salt and water retention by reducing aldosterone production. It is often used in combination with loop diuretics in the treatment of congestive heart failure. ACE inhibitors may exacerbate pre-renal azotaemia in animals that are hypotensive or that have poor renal blood flow. They are of benefit in cases of hypertension and some cases of chronic renal failure.

- **Benazepril**
Benazepril exerts its effects in a similar manner to enalapril. It is commonly used in association with loop diuretics in the treatment of congestive heart failure. Benazepril is also useful in the treatment of hypertension and chronic renal insufficiency. Benazepril has significant hepatic metabolism to the active form benazeprilat. In rabbits regular monitoring of blood pressure, serum creatinine, urea and electrolytes is recommended, and hypotension, hyperkalaemia and azotaemia would be indications to re-evaluate the therapeutic plan.

- Pimobendan

Pimobendan is both a positive inotrope and a vasodilator (inodilator). The advantage associated with pimobendan is that it exerts positive inotropic effects without causing an increase in myocardial oxygen demand. This is achieved by sensitization of the myocardial contractile apparatus to intracellular calcium and by phosphodiesterase III inhibition. It is used in the management of congestive heart failure in dogs due to dilated cardiomyopathy (DCM) or valvular insufficiency. It is contraindicated where augmentation of the cardiac output through the mechanism of increased contractility is impossible, for example in cases of hypertrophic cardiomyopathy. The bioavailability of this drug is significantly reduced in the presence of food, meaning that its efficacy may be limited in rabbits compared with that in dogs, however this may be mitigated by use of the new injectable formulation, particularly in emergency situations.

**Further Reading:**


Fontes-Sousa, AP et al (2009) Echocardiographic evaluation including tissue Doppler imaging in New Zealand white rabbits sedated with midazolam and ketamine. Veterinary Journal 181(3) 326-331

Meredith, A., Lord B., (2014-Pending) BSAVA Manual of Rabbit Medicine, BSAVA.
