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# Cardiovascular Disease

*Connie J. Orcutt, DVM, Diplomate ABVP (Exotic Companion Mammal)* and *Rebecca L. Malakoff, DVM, Diplomate ACVIM (Cardiology, Internal Medicine)* 

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Cardiac disease has become increasingly recognized in pet rabbits, presumably because pet rabbits are living longer and increasingly sophisticated diagnostic and therapeutic modalities are used for their care. However, despite their frequent use as laboratory models for cardiac disease in people, reports of spontaneous heart disease in rabbits are sporadic, and case numbers are often low. As a result, relatively little is known about the pathogenesis and treatment of naturally occurring heart disease in pet rabbits.

# NORMAL CARDIOVASCULAR STRUCTURE AND RELATED ANATOMY

The rabbit heart is unique in several ways: the tricuspid valve is composed of two rather than three cusps, the aortic nerve is not associated with chemoreceptors but only with baroreceptors, the pulmonary artery and its branches are heavily muscular, and a persistent left cranial vena cava is normally present and drains into the coronary sinus.<sup>4,15,17</sup> In addition, the right and left auricles are relatively large compared with the rest of the atria, and the ostium of the coronary sinus is quite large.<sup>15,27</sup> Important clinically is the fact that the rabbit's myocardium has limited collateral circulation and is therefore predisposed to ischemia mediated by coronary vasoconstriction.<sup>22</sup>

The rabbit's thoracic cavity is extremely small compared to the rest of its body, and its heart occupies more of the thoracic area relative to other animals.<sup>25</sup> The mediastinum and pericardium of the rabbit normally contain fat, which can mimic cardiomegaly in obese animals.<sup>26,27</sup>

# EXAMINATION OF THE RABBIT WITH CARDIOVASCULAR DISEASE

#### History

A thorough general history, including husbandry, diet, and past or present illnesses, should be obtained for rabbits suspected of having cardiac disease. Tachypnea, dyspnea, syncope, anorexia, weight loss, and malaise may be signs of heart disease in rabbits.<sup>26</sup>

# **Physical Examination**

Take care to minimize the handling of a rabbit in cardiac distress; a complete physical examination and further diagnostic testing must sometimes be delayed until the rabbit is clinically stable. Stress can be minimized by examining the rabbit in a quiet room and moving slowly. Rabbits are a prey species and therefore very sensitive to external stimuli. If necessary, the rabbit may be sedated to minimize the risk of self-injury. Sedation can be achieved with midazolam (0.5-1 mg/kg intramuscularly [IM] or intravenously [IV]) (see also Chapter 37).<sup>26,27,29</sup> Provide flow-by oxygen as needed if the rabbit is dyspneic or becomes tachypneic with handling. In rabbits suspected of having cardiac disease or respiratory distress, focus the initial examination on observing the respiratory rate and pattern, obtaining the heart rate and rhythm, auscultating the thorax, examining the mucous membranes, and palpating the pulses. The normal heart rate is 200-300 beats/min, and the normal respiratory rate is 30-60 breaths/min<sup>26,27</sup>; however, the respiratory rate can approximate the heart rate in stressed animals. Rabbits are obligate nasal breathers; therefore, do not occlude the nares during restraint. Peripheral pulses can often be palpated at the central artery of the ear and should be strong and synchronous with the heartbeat.<sup>27</sup> Two heart sounds ( $S_1$  and  $S_2$ ) are normally ausculted.<sup>27</sup> Referred upper airway sounds often overlie heart sounds and can mimic a murmur; therefore perform auscultation until the respiratory and heart sounds can be resolved.<sup>26</sup> Auscultation of any murmur should be followed by echocardiography.<sup>27</sup>

Rabbits with heart disease may have cyanotic or pale mucous membranes, arrhythmias, or heart murmurs. Rabbits in congestive heart failure often have tachycardia, tachypnea, and labored breathing; however, coughing is uncommon in the authors' experience. Pulses may be irregular or weak. The entire thorax should be auscultated to localize heart murmurs and detect extra heart sounds (gallop sounds), arrhythmias, and abnormal lung sounds. A pediatric stethoscope allows better localization of heart sounds in rabbits and is preferred for cardiac auscultation, whereas a stethoscope with a larger diaphragm enhances auscultation of the lungs. Auscultatory findings vary among rabbits with congestive heart failure, and these findings are not pathognomonic. The clinician may hear muffled heart and lung sounds with pleural effusion and increased bronchial sounds or crackles with pulmonary edema. However, the absence of crackles should not be used to rule out pulmonary edema in this species. Most rabbits in congestive heart failure have an increased, superficial respiratory pattern. In addition, although heart and lung sounds can be muffled in rabbits with pleural effusion, similar findings can be detected in obese rabbits with significant subcutaneous and intrathoracic fat deposits.<sup>27</sup>

## **DIAGNOSTIC METHODS**

Diagnosis of cardiovascular disease is based on a complete history and physical examination, as well as findings of diagnostic tests. Thoracic radiographs, electrocardiography, echocardiography, and routine blood tests are useful in reaching a definitive diagnosis and developing a treatment plan.

#### Radiography

Thoracic radiography provides critical information in the patient with cardiopulmonary disease—namely, cardiac shape and size, pulmonary pattern, vascular pattern, and other thoracic lesions. The vertebral heart score has been determined for New Zealand white rabbits (n = 50), and for cross, lop, and dwarf breeds (n = 27) by using the method described by Buchanan et al. for dogs.<sup>2,9,25</sup> However, this measurement in rabbits is not commonly used in clinical practice in the United States.

Congestive heart failure and respiratory disease can be differentiated by evaluating thoracic radiographs. Radiographic findings supporting a diagnosis of cardiac disease are similar to those in other species: cardiac enlargement, pulmonary vascular enlargement, a pulmonary interstitial and alveolar pattern of pulmonary edema, and pleural effusion. However, in the normal rabbit, the cranial heart border is usually difficult to distinguish from the cranial mediastinum.<sup>9</sup> Figs. 19.1 and 19.2 show thoracic radiographs of a normal adult rabbit and a rabbit with congestive heart failure, respectively.

## Electrocardiography

Electrocardiography is a simple and practical diagnostic test in rabbits with suspected or confirmed cardiac disease. An electrocardiogram (ECG) is critical to diagnosing and managing arrhythmias or syncope. The ECG may also be a helpful addition to the cardiac database. However, one should not use an ECG to assess or detect chamber enlargement or hypertrophy. In most rabbits, the ECG can be recorded with the rabbit awake and under only minimal restraint.9 Record the ECG with the rabbit in sternal recumbency. Use toothless alligator-style electrodes to minimize skin trauma; then place medical-grade alcohol or electrode gel on the clips to enhance conduction. Record tracings with a vertical calibration of 2 cm/mV and a horizontal paper speed of 50 mm/s. Normal rabbit rhythm is sinus and does not include respiratory sinus arrhythmia.<sup>26</sup> Spontaneous changes in the QRS complex have been observed in normal rabbits in serial ECG recordings.



Fig. 19.1 Normal thoracic radiographs of a 6-year-old rabbit. (A) Right lateral projection. (B) Ventrodorsal projection.

Normal ECG values for a variety of pet rabbit breeds have been reported.<sup>20,27</sup> Reference ranges for ECGs are summarized in Table 19.1.

### Echocardiography

Echocardiography provides a sensitive, accurate, noninvasive means of assessing cardiac structure and function. Most rabbits tolerate echocardiography without sedation, making it a practical diagnostic tool. However, in rabbits that are tachypneic or dyspneic, administer oxygen by face mask during restraint. The echocardiographic exam may be performed with the rabbit in lateral or sternal recumbency. Standard views used to evaluate dogs and cats can also be obtained with the rabbit. Because of the rabbit's rapid heart rate and small size, optimal evaluation requires a high-frequency transducer (e.g., 7.5 MHz) and a high frame-rate ultrasound machine. Two-dimensional and M-mode echocardiography assess cardiac structure, chamber size, wall thickness, and motion as well as extracardiac structures, masses, and pleural effusion. Color-flow, spectral, and tissue Doppler echocardiography assess direction and velocity of blood flow, further defining cardiac conditions with more insight on systolic and diastolic function.



**Fig. 19.2** Severe generalized cardiomegaly with congestive heart failure in a 5-year-old male castrated Angora rabbit. (A) In the right lateral projection, the cardiac silhouette is generally enlarged. The carina is elevated owing to left atrial and ventricular enlargement. A marked bronchointerstitial pattern is present in the caudal dorsal lung lobes, which is compatible with pulmonary edema. The lung lobes are mildly retracted and the ventral border of the cardiac silhouette is obscured, indicating mild pleural effusion. (B) In the ventrodorsal projection, a markedly enlarged left auricle is present (*black arrowheads*). An enlarged right atrium is also present (*white arrowhead*). An increased bronchointerstitial pattern is evident in the caudal lung lobes, which is more pronounced on the right than the left. Retraction of the lung lobe indicates pleural effusion (*black arrows*).

#### TABLE 19.1 Electrocardiographic Values (Lead II) in Clinically Normal Rabbits

	New Zealand White Rabbits (awake) <sup>9</sup> (N = 100: 44 M; 56 F)		Client-Owned Fancy, Fur, and Cross Breeds (awake) <sup>20</sup> (N = 46: 24 M [8 intact]; 22 F [8 intact])	
Parameter	Mean ± SD	Range	Mean ± SD	Range
Age, mo	_	6 (all)	—	2–84
Body weight, kg	2.62 ± 0.20	2.1–3.0	_	1.1–7.9
Heart rate, beats/min	243 ± 34	154-330	264 ± 34	198–330
P wave amplitude, mV	$0.05 \pm 0.02$	0.01-0.13	0.08 ± 0.02	0.04-0.12
P wave duration, s	$0.032 \pm 0.004$	0.021-0.045	$0.03 \pm 0.01$	0.01-0.05
P-R interval, s	$0.050 \pm 0.006$	0.036-0.072	0.06 ± 0.01	0.04-0.08
R wave amplitude, mV	0.18 ± 0.09	0.04-0.42	0.21 ± 0.09	0.03-0.39
QRS duration, s	$0.056 \pm 0.004$	0.043-0.066	$0.04 \pm 0.01$	0.02-0.06
Q-T interval, s	0.143 ± 0.012	0.115-0.173	0.12 ± 0.02	0.08-0.16
T wave amplitude, mV	0.16 ± 0.07	0.01-0.51	0.11 ± 0.03	0.05-0.17
Mean electrical axis	_	–60° to 180°ª	19° ± 31°	-43° to 80°

aln 85% of the rabbits, the mean electrical axis was -30° to 90°.

Relative structural measurements are similar to those in other mammalian species—e.g., the diameter of the left atrium is 1 to 1.5 times that of the aorta, the left and right atria are similar in size, and the diameter of the aorta and the pulmonary artery are equivalent.<sup>27</sup> In addition, the thickness of the left ventricular free wall approximates that of the interventricular septum and is 2 to 3 times thicker than the right ventricular free wall.<sup>27</sup> The coronary sinus, which encircles the atrioventricular junction, is normally quite large in the rabbit and should not be inadvertently interpreted as a congenital anomaly or a structural sign of right heart failure.<sup>27</sup>

Note that sedative drugs used for restraint, especially alpha-2 agonists such as dexmedetomidine and xylazine, may affect cardiac measurements. Reduced percent fractional shortening, reversal of the E/A ratio (peak velocity blood flow from gravity in early diastole [E wave] to peak velocity flow in late diastole due to atrial contraction [A wave]), decreased heart rate, and other changes have been documented with ketamine at a dose of 50 mg/kg IM and xylazine at 4 mg/kg IM.<sup>34</sup> Sedation with ketamine (20 mg/kg) and midazolam (2 mg/kg) given subcutaneously has been shown to be less cardiodepressive.<sup>7</sup> Normal echocardiographic values have been published for several breeds of rabbits (Tables 19.2 and 19.3).

#### **Blood Pressure Measurement**

Hypotension is not uncommon in rabbits anesthetized with inhalant agents.<sup>11</sup> Doppler-measured arterial blood pressure reportedly correlates well with direct peripheral (auricular

artery) blood pressure measurement in the rabbit.<sup>11</sup> Using the technique described for a dog or a cat, place a 8.2-MHz frequency ultrasonic Doppler flow detector transducer over a branch of the radial artery on the medial aspect of the carpus, and use a pediatric blood pressure cuff with a width 40%–50% of the circumference of the limb.<sup>11</sup> The systolic blood pressure in the clinic is generally 120–180 mmHg.<sup>27</sup> Indirect blood pressure measurements <80 mmHg indicate hypotension.<sup>11</sup> Rabbits demonstrate circadian patterns in heart rate, as well as both systolic and diastolic blood pressure, with all three parameters being higher at night.<sup>31</sup>

#### DISEASES AND MANAGEMENT

Although the prevalence of cardiovascular disease in rabbits is unknown, the incidence generally increases with age—for example, over 4 years of age.<sup>27,38</sup> Large breeds, such as New Zealand white rabbits, may be overrepresented.<sup>38</sup>

To date, there are no cardiac drugs approved by the U.S. Food and Drug Administration for use in rabbits. Recommended dosages published in the literature are primarily based on extrapolation from dogs and cats, the authors' clinical experience, or both.<sup>27</sup> Drugs should always be dosed on a milligram-per-kilogram basis, and oral drugs should be given in liquid, not tablet, form.

#### **Congestive Heart Failure**

Congestive heart failure is the clinical condition in which pulmonary edema, pleural effusion, hepatomegaly, or all three

TABLE 19.2 **M-mode and 2-dimensional Echocardiographic Measurements in Clinically Normal New Zealand White Rabbits**<sup>a,b</sup>

	Awake	Sedated
Parameter	$(N = 100)^9$	$(N = 26)^{7}$
Body weight, kg	2.6 ± 0.2	$2.3 \pm 0.4$
Age, mo	6 (all)	4 - 5
Sex	44 M; 56 F	26 M; 0 F
Heart rate, beats/min	227 ± 36	263 ± 37 (Doppler)
IVSd, mm	2.74 ± 0.51	2.65 ± 0.31
IVSs, mm	4.01 ± 0.70	$3.63 \pm 0.34$
LVIDd, mm	13.28 ± 1.91	13.51 ± 1.05
LVIDs, mm	8.32 ± 1.47	$8.64 \pm 0.82$
LVFWd, mm	2.78 ± 0.54	2.25 ± 0.29
LVFWs, mm	3.56 ± 0.52	$3.15 \pm 0.38$
FS, %	37.17 ± 4.99	36.01 ± 4.31
EF, %	71.12 ± 6.32	69.58 ± 5.33
LA, mm	8.62 ± 1.02 (2D)	7.49 ± 1.14
Ao, mm	7.90 ± 0.77 (2D)	$6.57 \pm 0.46$
LA/Ao	1.09 ± 0.10 (2D)	1.15 ± 0.19
EPSS, mm	_	1.41 ± 0.25

 $^{a}$ Values are mean  $\pm$  standard deviation except for age and sex.

<sup>b</sup>All values are M-mode derived unless indicated otherwise (2D).

°Sedated with ketamine (20 mg/kg SC) and midazolam (2 mg/kg SC).

*Ao,* aorta diameter; *EF,* ejection fraction; *EPSS,* E-point to septal separation; *FS,* fractional shortening; *IM,* intramuscularly; *IVSd,* interventricular septum in diastole; *IVSs* interventricular septum in systole; *LA,* left atrial diameter; *LVIDd,* left ventricular internal diameter in diastole; *LVFWd,* left ventricular free wall in diastole; *LVFWd,* left ventricular free wall in diastole; *LVFWd,* left ventricular free wall in diastole; *LVFWs,* left ventricular free wall in systole; *SC,* subcutaneously.

# TABLE 19.3 Doppler Echocardiographic Measurements, Including Tissue Doppler Imaging (TDI) Derived Values, in Clinically Normal New Zealand White Rabbits

Parameter	Awake (N = 100) <sup>9</sup>	Awake (N = 20) <sup>34</sup>	Sedated <sup>7</sup> (N = 26)
Body weight, kg	2.62 ± 0.20	2.92	2.3 ± 0.4
Age, mos	6 (all)	4	4-5
Sex	44 M; 56 F	10 M; 10 F	26 M; 0 F
Heart rate, beats/min	227 ± 36	$234 \pm 26$	263 ± 37 (Doppler)
Ao <sub>max,</sub> m/s	0.75 ± 0.14	0.75 ± 0.20	0.86 ± 0.12
PA <sub>max,</sub> m/s	0.79 ± 0.16	—	0.78 ± 0.12
Mitral <i>E</i> -wave, m/s	0.64 ± 0.13	0.72 ± 0.14	0.78 ± 0.15
Mitral A-wave, m/s	0.52 ± 0.10	0.51 ± 0.15	0.55 ± 0.11
Mitral E/A	1.23 ± 0.25	1.44 ± 0.28	1.44 ± 0.16
IVRT, ms	36.29 ± 12.77	38 ± 5	31.42 ± 6.19
DT E, ms	64.95 ± 17.67	_	_
IVCT, ms	_	24 ± 11	25.00 ± 3.68
LVET, ms	_	126 ± 14	95.72 ± 10.21
Tei index	_	0.57 ± 0.20	0.60 ± 0.10
TDI Lat E', m/s	_	0.067 ± 0.019	0.16 ± 0.05
TDI Sep E', m/s	_	0.050 ± 0.017	0.11 ± 0.04
TDI Lat A', m/s	_	0.039 ± 0.007	$0.09 \pm 0.03$
TDI Sep A', m/s	_	0.032 ± 0.009	0.08 ± 0.02
TDI Lat S', m/s	_	0.055 ± 0.013	0.11 ± 0.02
TDI Sep S', m/s	_	0.053 ± 0.010	0.10 ± 0.02
TDI Lat E'/A'	_	—	1.83 ± 0.43
TDI Sep E'/A'			1.55 ± 0.44
Mitral E/TDI Lat E' (E/E' lateral)	_	_	5.24 ± 1.55
Mitral E/TDI Sep E' (E/E' septal)	—	-	$7.75 \pm 2.69$

<sup>a</sup>Values are mean  $\pm$  standard deviation except age and sex.

<sup>b</sup>Sedated with ketamine (20 mg/kg SC) and midazolam (2 mg/kg SC).

°Sedated with ketamine (2 mg/kg IM) and medetomidine (0.15 mg/kg IM).

Aomax, maximal aortic outflow velocity; *DT E*, E-wave deceleration time; *IM*, intramuscularly; *IVCT*, isovolumetric contraction time; *IVRT*, isovolumetric relaxation time; *LVET*, left ventricular ejection time; *Mitral A*, peak transmitral late diastolic (atrial contraction) velocity; *Mitral E*, peak transmitral early diastolic velocity; *PAmax*, maximal pulmonary artery outflow velocity; *SC*, subcutaneously; *TDI Lat A'*, peak late diastolic mitral annular velocity from lateral wall; *TDI Lat E'*, peak early diastolic mitral annular velocity from septal wall; *TDI Sep A'*, peak late diastolic mitral annular velocity from septal wall; *TDI Sep S'*, peak systolic mitral annular velocity from septal wall.

develop as a result of structural or functional cardiac disease. As a prey species, rabbits may hide signs of illness or debilitation; thus, rabbits with congestive heart failure may be presented after heart disease has become advanced.<sup>27</sup> Any rabbit with respiratory abnormalities, particularly in the absence of upper respiratory signs, should be evaluated for heart disease. In some instances, aggressive fluid therapy for treatment of ileus or other abnormalities may result in abnormal breathing and radiographic signs of congestive heart failure.<sup>26</sup>

The goal of therapy for congestive heart failure is to relieve congestion, control future retention of sodium and fluids, and improve cardiac performance. Various management strategies are used during the acute stage. A common initial treatment protocol is to place the patient in a quiet cage with supplemental oxygen and administer parenteral furosemide (1–4 mg/kg IV or IM every 4–12 hours); nitroglycerin 2% ointment (1/8 inch applied transdermally every 6–12 hours) can be applied to the

inner pinna for vasodilation to reduce preload. In a rabbit with pleural effusion, perform therapeutic pleurocentesis if the rabbit is dyspneic.

Long-term therapy of congestive heart failure should include a diuretic (furosemide 1–3 mg/kg by mouth [PO] every 8–24 hours) combined with treatment directed at the underlying precipitating cause.<sup>27</sup> Knowledge of the cardiac disease process is the basis of specific treatment of the underlying condition. An angiotensin-converting enzyme (ACE) inhibitor, such as enalapril maleate (0.25–0.5 mg/ kg PO every 24–48 hours, begun every 24 hours), is often added to furosemide for the treatment of rabbits with congestive heart failure. Pimobendan (0.1–0.3 mg/kg PO every 12–24 hours), which has both inotropic and vasodilatory properties as well as antiinflammatory effects, may also be used for treatment of systolic dysfunction and myocardial failure.<sup>27</sup> During acute and chronic management, it is critical that clinical and radiographic signs, hydration status, appetite, and body weight, as well as serum or plasma blood urea nitrogen, creatinine, and electrolyte concentrations be monitored.

#### **Congenital Heart Disease**

Congenital heart disease is rarely reported in rabbits. A ventricular septal defect in an unnamed breed and suspected cor triatriatum dexter in a dwarf lop were both diagnosed with echocardiography.<sup>28,38</sup> A ventricular septal defect, pulmonary hypertension, and a valvular cyst identified at necropsy have been described in a New Zealand white rabbit.<sup>18</sup>

#### Arrhythmias

Although relatively rare, arrhythmias such as atrial fibrillation and ventricular premature complexes have been identified in pet rabbits with underlying cardiomyopathies and congestive heart failure.<sup>21,26,27</sup> In a rabbit with a clinically relevant arrhythmia, the treatment protocol should be based on ECG findings and clinical signs.

For anesthesia-induced bradycardia, glycopyrrolate may be more effective than atropine sulfate in increasing heart rate, in large part because some rabbits produce atropinesterases.<sup>24,38</sup> For syncope associated with bradycardia, oral theophylline or pacemaker implantation may be indicated. Although wireless-powered microimplant pacemakers have been used experimentally in New Zealand white rabbits,<sup>13</sup> clinical use of a pacemaker has not yet been reported in a pet rabbit.

Supraventricular tachycardias may be treated with oral digoxin or diltiazem. If digoxin is used, monitor the rabbit's appetite as well as stool production and measure blood levels by ≤8 hours after the last dose.<sup>27</sup> The dose may need to be reduced or digoxin discontinued if the rabbit becomes anorexic or develops ileus.<sup>38</sup> Use of diltiazem can result in hypotension, so closely monitor rabbits treated with this agent. Ventricular tachyarrhythmias may respond to boluses of intravenous lidocaine.<sup>27,38</sup> Using dosages determined for dogs, sotalol and mexiletine have also been used anecdotally in rabbits.<sup>38</sup>

Empirical dosages are published for lidocaine, atropine, and glycopyrrolate (see the Appendix). Other antiarrhythmic drugs have been used at dosages published for cats or ferrets.

#### **Myocardial Disease**

Numerous myocardial diseases have been reported in rabbits, and cardiomyopathy is a common postmortem finding in older rabbits.<sup>28</sup> Giants breeds may be most susceptible.<sup>38</sup> Hypertrophic, restrictive, and dilated forms of cardiomyopathy have all been reported,<sup>38</sup> and anecdotally, dilated cardiomyopathy appears to be the form of cardiomyopathy diagnosed most frequently in rabbits.<sup>23,26</sup>

The primary causes of cardiomyopathy in rabbits are generally unknown.<sup>38</sup> Vitamin E deficiency produces a muscular dystrophy in which the myocardium may be affected.<sup>3</sup> Taurine deficiency has not been reported in rabbits.<sup>26</sup> However, in a study of 5-month-old albino rabbits with experimentally induced aortic regurgitation and subsequent congestive heart failure, daily supplementation with taurine dosed at 100 mg/kg significantly improved myocardial contractility and decreased mortality.<sup>35</sup> There are no published reports of pet rabbits being supplemented with taurine.<sup>26</sup>

Although infectious myocarditis is rare in pet rabbits, organisms reported to be associated with myocarditis in this species include *Pasteurella multocida*, *Salmonella* species, *Clostridium piliforme*, *Encephalitozoon cuniculi*, and coronavirus.<sup>1,5,6,16</sup>Although infection with a coronavirus is used to create a rabbit model of dilated cardiomyopathy, no naturally occurring cases have been reported.<sup>1,4</sup> In experimental studies, myocardial disease has also been induced by inoculation of *Trypanosoma cruzi*<sup>30</sup> and administration of doxorubicin.<sup>37</sup>

The alpha-agonist drug detomidine has been associated with myocardial necrosis and fibrosis in New Zealand white rabbits.<sup>14</sup> A similar ischemia-mediated process is suggested in association with ketamine/xylazine administration in Dutch belted rabbits.<sup>22</sup> Rabbits subjected to intermittent crowding developed an apparent stress-induced cardiomyopathy, which was fatal in 34 of 44 experimental animals.<sup>39</sup>

#### Valvular Disease

Mitral and tricuspid insufficiencies are not uncommon and have been identified in pet rabbits, particularly as animals age.<sup>23,25,38</sup> Valvular insufficiencies may be associated with primary valve degeneration, cardiomyopathy, or infection. Progression of the condition leads to volume overload and potential congestive heart failure. A focal murmur is the most common clinical finding. Valvular disease is diagnosed with two-dimensional and Doppler echocardiography (Fig. 19.3). Echocardiographic findings most often include thickening of one or both atrioventricular valves, dilation of cardiac chambers, and turbulent regurgitation of blood detected by Doppler scanning.

#### Dental Disease and Abscessation

Vegetative endocarditis due to *Haemophilus parainfluenzae was* diagnosed post mortem in a 4-year-old rabbit that had presented with a 2-week history of progressive lethargy and weight loss.<sup>22a</sup> A continuous IV/VI parasternal murmur and an arrhythmia had been ausculted on physical examination. The ECG findings revealed atrial fibrillation conducted with a left bundle branch morphology, and echocardiography showed vegetative and aortic endocarditis and a secondary aortocavitary fistula. Bacteremia was suspected secondary to severe dental disease.

#### Vascular Disease

Spontaneous arteriosclerosis of the aorta and other arteries has been observed in nearly all rabbit breeds, with historical incidence ranging from 13% in Dutch breeds to 40% or greater in Flemish giant, chinchilla, New Zealand white, and English spot breeds.<sup>8,19</sup> Arterial walls and other soft tissues mineralize; the aortic arch and descending thoracic aorta are most commonly affected. Radiopaque vessels, caused by calcification, may be visible on radiographs.<sup>19,32</sup> Clinical signs, if present, may include lethargy, anorexia, and weight loss. The cause is unknown; however, such variation of incidence by breed suggests a genetic predisposition.<sup>8,19</sup>





**Fig. 19.3** Standard echocardiographic views in rabbits with cardiac disease. (A) Right parasternal long-axis view of a rabbit with dilated cardiomyopathy and pericardial effusion, which is a manifestation of congestive heart failure. Note the dilated left atrium and left ventricle, and the thin left ventricular walls. (B) Right parasternal short-axis view at the level of the heart base in a rabbit with dilated cardiomyopathy. Note the dilated left atrium and auricle. (C) M-mode derived from a right parasternal short-axis view of a rabbit with dilated cardiomyopathy, showing aortic root and left atrial dimensions. *LV*, Left ventricle; *LA*, left atrium; *RV*, right ventricle; *RA*, right atrium; *Ao*, aorta; eff, pericardial effusion.

Hypervitaminosis D, resulting from errors in feed formulation, can result in excessive absorption of dietary calcium and subsequent calcification of blood vessel walls and other soft tissues.<sup>10,33</sup> It has also been suggested that aortic mineralization can occur in hypercalcemic rabbits secondary to renal disease and compromised calcium excretion.<sup>10</sup>

Pulmonary hypertension associated with high altitude has been reported in a rabbit.<sup>12</sup> Lesions included right ventricular hypertrophy and pulmonary artery proliferation from hypoxia. Based on research, rabbits with pulmonary hypertension may respond to phosphodiesterase type-5 inhibitors, particularly vardenafil.<sup>36</sup> Systemic hypertension is reportedly rare but may occur with renal failure.<sup>27</sup> Rabbits tolerate enalapril well; however, anecdotal reports suggest that they are particularly susceptible to the hypotensive effects of benazepril.<sup>29</sup>

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