Cardiovascular Effects of Thyroid Disease

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Abstract: Thyroid hormones have many effects on cardiovascular function, and deficiency or excess of thyroid hormones can result in cardiac dysfunction. Abnormalities of the cardiovascular system are often identified during examination of hyperthyroid and hypothyroid patients. This article addresses the effects of thyroid hormones on the cardiovascular system and the clinical relevance of the cardiovascular response to thyroid dysfunction. In addition, treatment recommendations are presented.

Thyroid hormones have an integral role in cardiovascular homeostasis, affecting myocardial function, systemic vascular resistance, endothelial function, and response to catecholamines. Clinical evidence of the influence of thyroid hormones on the cardiovascular system is most apparent in hyperthyroidism, in which tachycardia and abnormal heart sounds are frequent findings on physical examination. The cardiovascular effects of hypothyroidism are typically more subtle, but they may be clinically important in some situations. This review addresses the effects of thyroid hormones on the cardiovascular system, the clinical consequences of hyperthyroidism and hypothyroidism, and the management of these disorders.

Cardiovascular Effects of Thyroid Hormone

Thyroid hormones alter cardiovascular function directly, through effects on the heart, and indirectly, through effects on the peripheral vasculature (BOX 1). Myocardial contractility and relaxation are enhanced by the genomic actions of 3,5,3’-triiodothyronine (T₃). Specifically, T₃ increases the expression of genes that encode ion transporters, β₁-adrenergic receptors, and contractile proteins. These effects increase calcium release and reuptake from the sarcoplasmic reticulum. The resultant increase in cytosolic calcium increases contractility, and the more rapid calcium reuptake enhances diastolic relaxation.

Nongenomic effects of T₃ on cardiac myocytes include stimulation of sarco/endoplasmic reticulum calcium ATPase (SERCA) activity, an increase in the activity of sodium-potassium pumps, recruitment of slowly inactivating membrane sodium channels, and an increase in membrane permeability to sodium ions. In hyperthyroidism, these effects may enhance myocardial function but may also predispose the patient to cardiac arrhythmias.

In addition to direct effects on cardiac function, thyroid hormones induce important changes in the peripheral circulation (BOX 1). T₃ has been shown to rapidly and directly cause relaxation of vascular smooth muscle cells, leading to decreased systemic vascular resistance. Generation of nitric oxide by endothelial cells is enhanced by thyroid hormones, contributing to arteriolar vasodilation in hyperthyroidism. In addition, thyroid hormones increase metabolic rate and oxygen demands of the peripheral tissues, resulting in locally mediated vasodilation. The renin-angiotensin-aldosterone system (RAAS) is activated in response to the decrease in resistance, thereby increasing plasma volume through sodium retention. Thyroid hormone also stimulates erythropoietin secretion, resulting in increased red blood cell mass.

Box 1. Effects of Thyroid Hormone on the Heart

- Increased myocardial contractility
  - Increased expression of contractile proteins
  - Increased numbers of β-adrenergic receptors
  - Increased calcium release from sarcoplasmic reticulum
  - Increased sodium-potassium pump activity
  - Increased membrane permeability to sodium ions
- Enhanced myocardial relaxation via increased calcium reuptake by sarcoplasmic reticulum
- Increased preload
  - Stimulation of erythropoietin, increasing red cell mass
  - Activation of the renin-angiotensin-aldosterone system, increasing plasma volume
- Decreased afterload
  - Relaxation of vascular smooth muscle
  - Increased generation of nitric oxide
  - Increased locally mediated vasodilation secondary to increased metabolic rate of peripheral tissues
Figure 1. This electrocardiogram was recorded from a 13-year-old castrated domestic shorthaired cat with hyperthyroidism (paper speed = 50 mm/sec, sensitivity = 10 mm/mV). The heart rate is 230 bpm and the cardiac rhythm is sinus. There is an intraventricular conduction disturbance characterized by leftward deviation of the mean electrical axis associated with normal QRS duration. S waves are evident in leads I, II, III, and aVf; the terminal deflections of leads I and II are slurred. There are limited published data that provide pathologic validation of abnormal feline QRS configurations. However, this electrocardiogram has features of the left axis deviation, sometimes described as a left anterior fascicular block, together with incomplete right bundle branch block.

Hyperthyroidism

First described in 1980, feline hyperthyroidism has become increasingly recognized and is currently the most frequently diagnosed feline endocrinopathy, with a prevalence of 2% across cats of all ages.10,11 Because of increased awareness of hyperthyroidism and routine screening of serum thyroxine (T4) concentrations in older cats, modern clinical manifestations of feline hyperthyroidism are often mild compared with early descriptions of the disease. In cats, hyperthyroidism is caused by adenomatous hyperplasia of the thyroid gland or, rarely (1% to 3% of cases), by thyroid carcinoma.11 Hyperthyroidism in dogs is much less common and is either iatrogenic13 or the result of a functional thyroid follicular carcinoma.12 Hyperthyroidism is caused by adenomatous hyperplasia of the thyroid gland or, rarely (1% to 3% of cases), by thyroid carcinoma.11 Hyperthyroidism in dogs is much less common and is either iatrogenic13 or the result of a functional thyroid follicular carcinoma or adenocarcinoma.14 Only 10% to 20% of thyroid tumors in dogs are functional, and unlike those affecting cats, most thyroid tumors of dogs are malignant.15

Cardiovascular Effects of Hyperthyroidism

The direct cardiac effects of excess thyroid hormone include enhanced contractility and diastolic function that contribute to an increase in stroke volume. Cardiac output is increased further by positive chronotropic effects that result from heightened responsiveness to sympathetic stimulation, conferred by an increase in the number of β1-adrenergic receptors, enhanced rate of spontaneous depolarization of sinoatrial node cells,16 and reduced influence of the parasympathetic nervous system.17 –19 The reduced systemic vascular resistance induced by peripheral vasodilation and increased blood flow induced by hyperthyroidism further increase cardiac output. The resulting hemodynamic burden and altered myocardial dynamics can lead to cardiac dysfunction.

Whereas diastolic and mean arterial blood pressures are decreased and systolic pressure is increased in people with hyperthyroidism, systolic, diastolic, and mean systemic arterial pressures were all elevated in cats with experimentally induced hyperthyroidism of 2 weeks’ duration.20 These findings suggest an increase, rather than a decrease, in vascular resistance, but it is unclear if similar changes are present in cats with naturally occurring hyperthyroidism. Hypertension likely results from the marked increase in cardiac output combined with expanded plasma volume caused by activation of the RAAS and expanded red cell mass caused by stimulation of erythropoietin release.21 –22 However, the role of the RAAS in cats with hypertension associated with hyperthyroidism is unclear.21 Important clinical manifestations of hyperthyroidism-induced cardiac dysfunction in veterinary patients include arrhythmias, intolerance of aggressive fluid therapy or stress, hypertension, and congestive heart failure (CHF).3,16

Clinical Findings

The cardiovascular effects of hyperthyroidism are responsible for some of the most prevalent clinical findings in affected patients. Heart murmurs or gallop sounds are auscultated in 35% to 50% of affected cats, and tachycardia is found in a slightly higher proportion.24 Cardiomegaly is noted radiographically in approximately 26% to 40% of hyperthyroid cats.25 –27 Increased R-wave amplitude in hyperthyroid cats is sinus tachycardia, detected in 34% of cases. Other ECG abnormalities include increased R-wave amplitude consistent with left ventricular enlargement (8% of patients) and left anterior fascicular block pattern (FIGURE 1) or right bundle branch block (6% to 10% of cases). In addition, arrhythmias—including atrial and ventricular premature contractions and, less frequently, atrioventricular block, atrial tachycardia, and ventricular tachycardia—may be identified.25,29 –31 Increased R-wave amplitude correlates poorly with echocardiographic evidence of left ventricular enlargement.32 While not well documented, arrhythmias are expected to resolve after successful treatment of hyperthyroidism.

Abnormal echocardiographic findings are common, although usually mild, in hyperthyroid cats.33 The most common echocardiographic abnormality in hyperthyroid cats is hypertrophy of the left ventricular posterior wall, identified in approximately 72% of affected cats.34 Other echocardiographic abnormalities of hyperthyroidism include left atrial enlargement in 50% of cats, increased left ventricular end-diastolic diameter in 47%, septal
hypertrophy in 40%, and increased fractional shortening in 22%. Enhanced left ventricular systolic function with normal diastolic function has been documented using Doppler tissue imaging in hyperthyroid cats. Severe ventricular dilation with myocardial hypocontractility has also been reported. Eccentric hypertrophy (an increase in myocardial mass associated with an increase in ventricular volume) is expected secondary to the increase in preload and decrease in systemic vascular resistance. However, as has been reported in some human patients, concentric hypertrophy also occurs, possibly reflecting an increase in systolic wall stress. The influence of concurrent disease, such as renal dysfuncation or systemic hypertension, on myocardial remodeling is unknown but could contribute to development of concentric hypertrophy in hyperthyroid cats.

It is unclear from investigations of hyperthyroid cats if eccentric or concentric hypertrophy predominates. This likely reflects the paucity of reports and the complex pathogenesis of myocardial changes, both direct and indirect, in hyperthyroidism. There is echocardiographic evidence that hyperthyroid-induced cardiac changes resolve with treatment in many cats, but they may persist in others. However, published echocardiographic data obtained after treatment of hyperthyroidism are limited, and factors that might affect resolution of cardiac changes have received little attention. There is considerable overlap in echocardiographic findings between cats with hyperthyroidism-related concentric hypertrophy and those with hypertrophic cardiomyopathy. In addition, hypertension can cause left ventricular posterior wall and/or septal hypertrophy similar to changes induced by hyperthyroidism. Although the prevalence of asymmetric hypertrophy and perhaps systolic anterior motion of the mitral valve may be greater in patients with primary myocardial disease, echocardiography cannot reliably differentiate these conditions; therefore, thyroid function and blood pressure should be evaluated in middle-aged and older cats with cardiac abnormalities.

The prevalence of CHF in hyperthyroid cats is approximately 2%. Cats in CHF show clinical signs typical of that condition, such as dyspnea, anorexia, cyanosis, and potentially weak femoral pulses. Pleural effusion secondary to CHF can obscure the cardiac silhouette on thoracic radiographs. Pulmonary venous engorgement and a patchy interstitial or alveolar pattern resulting from pulmonary edema may also be seen (FIGURE 2). As in people, heart failure in hyperthyroid cats would be expected to resolve after thyroid hormone levels are controlled. However, the response to treatment of heart failure in hyperthyroid cats with current primary myocardial disease is less certain.

The cardiac phenotype of hyperthyroid cats with CHF has been incompletely described; therefore, findings in people with hyperthyroidism may be relevant. Heart failure occurs in 6% of people with hyperthyroidism and is usually associated with the development of atrial fibrillation. Left ventricular dilation and decreased ejection fraction are found in about 50% of hyperthyroid humans with CHF. In people with hyperthyroidism and preserved left ventricular ejection fraction, CHF almost always resolves after a euthyroid state is established. Resolution of heart failure and left ventricular dysfunction after treatment of hyperthyroidism is less predictable in patients with reduced ejection fraction, although indices of systolic myocardial function return to normal in most cases.

In the most detailed report of CHF in hyperthyroid cats, Jacobs et al described four cases of CHF characterized by pleural effusion in hyperthyroid cats, two of which died of CHF. The echocardiographic abnormalities of these cats primarily reflected severe ventricular dilation and myocardial hypocontractility rather than the ventricular hyperkinesis observed in many cases of hyperthyroid heart disease. While the poor outcome of these cases may be unusual, this case series demonstrates that hyperthyroidism can contribute to, or directly cause, severe heart disease. Other, less detailed reports of hyperthyroid cats with heart failure include those with systolic dysfunction as well as normal contractility.

Because the cases with hypocontractility were reported when dilated cardiomyopathy (DCM) secondary to taurine deficiency was common, it is possible that some of these cats had concurrent hyperthyroidism and DCM. However, DCM has also been reported in people secondary to thyrotoxicosis.

It is likely that tachycardia and other effects of hyperthyroidism are detrimental in patients with underlying primary cardiomyopathy and could cause decompensation of a previously subclinical condition. Because 16% of apparently healthy cats were found to have subclinical cardiomyopathy in a 2009 study, hyperthyroidism and primary cardiomyopathy would be expected to coexist in a
substantial number of feline patients. However, cardiac changes in hyperthyroid heart disease may be similar to those resulting from primary hypertrophic cardiomyopathy, so it is unknown how frequently hyperthyroidism complicates preexisting heart disease. Serial echocardiograms after resolution of hyperthyroidism may be the most reliable method to determine if primary cardiomyopathy is present. However, diagnosis of primary cardiomyopathy before treatment of hyperthyroidism is problematic.

The cardiac biomarker N-terminal-pro-B-type natriuretic peptide (NT-pro-BNP) has proven useful in the diagnosis of CHF in cats and has been shown to differentiate normal cats from those with occult cardiomyopathy.69 Hyperthyroidism induces an increase in NT-pro-BNP in humans70 and has been shown in a preliminary report to result in modest elevations in hyperthyroid cats.50 Cardiac troponin I, an indicator of myocardial cellular damage, was elevated in some cats with hyperthyroidism in one study.51 Until these biomarkers are compared in cats with hyperthyroidism and cats with primary cardiac disease, it is not clear if they will prove useful in differentiating these disorders.

Hypertension is a common complication of hyperthyroidism in cats, and although the prevalence varies considerably depending on the population studied, it is likely to be 10% to 20%.52–57 Hypertension has been shown to persist in at least the first 4 weeks of treatment with methimazole despite normalization of thyroid hormone concentrations,58 and some cats that are normotensive before treatment may become hypertensive when euthyroid.52 Concurrent renal disease may play a role in the latter finding; approximately 15% of cats become azotemic after treatment of hyperthyroidism59 as previously subclinical renal insufficiency is unmasked. However, in one study,60 only 35% of cats that became hypertensive after treatment for hyperthyroidism were azotemic, so renal disease is likely not the sole cause of posttreatment hypertension. Blood pressure should be measured at the time of diagnosis of hyperthyroidism and after the disease has been controlled.

The clinical findings in hyperthyroid dogs are similar to those in cats, with presenting signs including panting, polyphagia, weight loss, and polyuria/polydipsia.13,59,60 Cardiovascular manifestations of canine hyperthyroidism are also similar and include tachycardia, premature ventricular contractions, increased R-wave amplitude, and hypertension.13,59 These signs, accompanied by an elevated T4 concentration, should prompt a search for a functional thyroid tumor or oversupplementation of thyroid hormone. As in cats, treatment of the hyperthyroidism resolves the cardiovascular signs.

Treatment
Feline hyperthyroidism can be controlled with oral antithyroid agents, a low-iodine diet, thyroidectomy, or radioactive iodine. Medical management with methimazole is recommended as the initial strategy for any cat with significant cardiovascular complications. Definitive treatments can be considered after heart disease has been stabilized and hyperthyroidism controlled for several weeks. Monitoring of cats treated for hyperthyroidism should include, at minimum, evaluation of physical examination findings, blood urea nitrogen, serum creatinine and T4 concentrations, urine specific gravity, and blood pressure at 1, 3, and 6 months after treatment is initiated.

Specific treatment for cardiac abnormalities is unnecessary in most hyperthyroid cats that do not have clinical signs of CHF. Treatment of hyperthyroidism resolves the abnormal heart sounds in many, but not all, cats. In our experience, and as reported by others, persistence of a heart murmur after control of hyperthyroidism is not consistently associated with the presence of clinically significant heart disease.51 Arrhythmias and left ventricular hypertrophy are expected to improve or resolve when euthyroidism is established.54 However, hyperthyroid cats with severe cardiac manifestations need to be stabilized before surgery to minimize anesthetic risk, or before receiving radioactive iodine therapy. To achieve this stabilization, β-adrenergic antagonists may be administered to reduce the detrimental effects of tachycardia. These agents are the mainstay of treatment of hyperthyroid-induced heart disease, although, as discussed below, their use when heart failure is present requires careful consideration. Propranolol (0.5 to 1.0 mg/kg PO q8h) or atenolol (1 to 2 mg/kg PO q12h) ameliorates some of the cardiovascular complications of hyperthyroidism, particularly sinus tachycardia and supraventricular arrhythmias. Propranolol has the additional potential benefit of reducing the conversion of T4 to T3 and has been demonstrated to reduce heart rate in hyperthyroid cats.61,62 However, as a non-selective β-blocker, propranolol may exacerbate bronchoconstriction in cats with chronic lower airway disease. Atenolol, a selective β1 blocker, less likely to be associated with bronchoconstriction, so it is preferred to propranolol in cats with concurrent bronchial disease.63 Other potential adverse effects of β blockers include bradycardia, lethargy and/or depression, and hypotension.

The general therapeutic principles of managing heart failure in euthyroid patients are likely valid in the setting of hyperthyroidism, although, of course, the additional need for specific treatment of...
the endocrinopathy exists. On an emergency basis, supplemental oxygen should be provided immediately. Furosemide (0.5 to 2 mg/kg IV or IM) is administered every 1 to 4 hours until dyspnea starts to resolve; the dosage interval is then increased to 6 to 12 hours. Thoracocentesis should be performed if pleural effusion is responsible for dyspnea. Diuretic doses and dosage intervals are determined most appropriately by clinical response; the lowest dose that relieves congestive signs is considered to be optimal. For chronic therapy, the use of furosemide (0.5 to 2 mg/kg PO q12–24h) and an angiotensin-converting enzyme (ACE) inhibitor (enalapril at 0.25 to 0.5 mg/kg q12–24h or benazepril at 0.25 to 0.5 mg/kg q24h) is reasonable, but specific therapy might be best guided by echocardiographic findings when available.

The use of pimobendan in cats with primary myocardial disease has been reported, but systematic evaluation of its efficacy in the management of feline cardiac disease has not. Pimobendan may be useful in feline patients with hyperthyroidism, heart failure, and echocardiographically documented systolic myocardial dysfunction. Serial chemistry panels should be evaluated 2 weeks after each dosage change or every 3 months to monitor renal function and electrolytes. While there may be a role for gradual up-titration of β-blockers in the long-term management of systolic myocardial dysfunction, the acute hemodynamic effects of these drugs are likely to be deleterious. Therefore, it is probably best to avoid β-blockers in patients with clinical signs caused by congestion unless echocardiography demonstrates hyperdynamic ventricular performance associated with tachycardia.

The prognosis of hyperthyroid cats with CHF that do not have concurrent primary myocardial disease is probably good. However, some cats with hyperthyroidism and CHF respond poorly to treatment. It is unclear if these cats have concurrent primary myocardial disease that has been exacerbated by hyperthyroidism or if the hyperthyroid-induced heart disease is irreversible for unknown reasons. Some hyperthyroid cats that have responded poorly to treatment for CHF had impaired contractility that was identified on echocardiography, but the significance of this is unclear. Mere cardiac structural changes, tachycardia, and arrhythmias have not been shown to increase risk of death.

If hypertension is of sufficient magnitude (systolic blood pressure persistently >180 mm Hg) to carry a risk of target organ damage, or if clinical signs or examination findings secondary to hypertension (tortuous retinal vessels, retinal edema or hemorrhage, severe proteinuria, or neurologic abnormalities) are present at any time during management of hyperthyroidism, treatment of hypertension should be initiated concurrently with that for hyperthyroidism. Because the efficacy of antihypertensive agents in hyperthyroid cats has not been systematically evaluated, the recommended treatment is similar to that for euthyroid hypertensive cats. The calcium channel blocker amlodipine (0.625 mg, or one-quarter of a 2.5-mg tablet per cat PO q24h) is the drug of choice for initial treatment. The dosage can be increased to 0.625 mg PO q12h if the systolic blood pressure still exceeds 160 mm Hg after 1 to 2 weeks of treatment. An ACE inhibitor (enalapril 0.25 to 0.5 mg/kg q12–24h or benazepril 0.25 to 0.5 mg/kg q24h) may be used in addition to amlodipine if hypertension persists. Administration of atenolol to hypertensive hyperthyroid cats is insufficient to control blood pressure in most cases, so β-blockade might be most effective when combined with other agents. Evidence is conflicting on whether hypertension affects survival in hyperthyroid cats, and the effects of treatment of hypertension on survival have not been studied.

Hypothyroidism
Hypothyroidism is the most commonly diagnosed endocrinopathy in dogs. Because thyroid hormones affect all organ systems, deficiency results in a wide variety of clinical signs. Classic clinical signs are obesity, lethargy, and alopecia. The diagnosis can be complicated by the suppressive effects of nonthyroidal illness, such as CHF, on thyroid function tests. Naturally occurring feline hypothyroidism is rare, but iatrogenic hypothyroidism as a consequence of treatment of hyperthyroidism is relatively common.

Cardiovascular Effects of Hypothyroidism
The cardiovascular manifestations of hypothyroidism tend to be less dramatic than those of hyperthyroidism, but important abnormalities have been seen in some patients. Hypothyroidism has direct negative inotropic effects caused by a shift from the predominant myosin isoenzyme to the low-ATPase myosin heavy chain β in some species, although this is likely of limited importance in dogs and cats. Diastolic relaxation is prolonged and heart rate is reduced by reductions in SERCA activity and numbers of β adrenergic receptors, respectively. Cardiac function can be impaired further by fibrosis and accumulation of mucopolysaccharides in the myocardial interstitium, increasing cardiac mass and wall stiffness. Severe, experimentally induced hypothyroidism has been shown to result in impaired myocardial blood flow caused by a loss of arterioles as well as progressive systolic dysfunction, limiting compensatory responses for decreased myocardial mechanical work efficiency. Thyroid hormone deficiency increases peripheral vascular resistance, contributing to increased cardiac afterload. These abnormalities result in a decrease in cardiac output and may contribute to the clinical abnormalities common in hypothyroid dogs.

In addition to effects on myocardial function, hypothyroidism in humans also results in alterations of the peripheral vasculature. Lack of adequate thyroid hormone increases peripheral vascular resistance and arterial wall stiffness and thus contributes to increased cardiac afterload and systemic hypertension in humans, although this has not been documented in dogs. Reduced responsiveness to vasodilators has been demonstrated in hypothyroid rats and likely further contributes to increased peripheral vascular resistance. Impaired free water excretion, documented in hypothyroid humans and rats, can contribute to fluid retention, hyponatremia, and edema formation. The importance of these changes in hypothyroid dogs and cats is unclear.

Clinical Findings
Common physical examination findings in hypothyroid dogs include a slower than expected heart rate, weak pulses, muffled
heart sounds, and a weak apex beat. Bradycardia (<70 bpm) is present in 5% to 22% of cases. ECG abnormalities may include decreased amplitude of the R wave (present in up to 58% of dogs examined), sinus bradycardia, and first- or, rarely, second-degree atrioventricular block. Bradycardia and atrioventricular block resolve within 9 to 19 weeks of treatment in most affected dogs. Echocardiographic findings are indicative of decreased left ventricular systolic function. Median fractional shortening was 26% in 10 hypothyroid dogs in one study and 29% in another study of 11 dogs. After treatment for a mean of 9 and 19 weeks, fractional shortening increased by 15% and 28%, respectively, compared with pretreatment results. The thickness of the left ventricular posterior wall and interventricular septum is decreased in some hypothyroid dogs; this change resolves with treatment.

Although the cardiovascular effects of hypothyroidism are usually insufficient to cause clinical signs, they can cause decompensation in patients with preexisting cardiac diseases, such as DCM. It is also possible that prolonged anesthesia or aggressive fluid therapy may compound preexisting circulatory dysfunction and lead to congestion or edema. Myocardial failure resulting in CHF in the apparent absence of primary cardiomyopathy has been documented in a small number of hypothyroid dogs. Clinical signs included lethargy, inappetence, cough, tachypnea, and, in some dogs, ascites. Atrial fibrillation was present in most cases. Echocardiograms revealed markedly decreased fractional shortening and enlarged left atria and ventricles. Heart failure was controlled after levothyroxine supplementation with concurrent treatment consisting of some combination of digoxin, furosemide, diltiazem, and an ACE inhibitor (lisinopril or benazepril).

While the atrial fibrillation persisted in all cases, myocardial function improved substantially within 4 to 6 weeks of initiating levothyroxine supplementation. Some of these dogs may have had underlying, subclinical breed-related DCM made clinical by hypothyroidism. Clinical suspicion for hypothyroidism should be high for an obese dog with apparent DCM, particularly if myxedema, alopecia, or hypercholesterolemia is present.

Atherosclerosis is a known complication of the hypercholesterolemia and lipid abnormalities induced by hypothyroidism in people and has been reported to be a rare but serious complication of hypothyroidism in dogs. When coronary arteries are affected (Figure 3), atherosclerosis can result in myocardial ischemia and impaired cardiac function. In people with hypothyroidism, atherosclerosis has been attributed to hypercholesterolemia, hypertension, and impaired endothelial function. Hypothyroid dogs with atherosclerosis have consistently been markedly hypercholesterolemic. Atherosclerosis predisposes dogs to thrombosis and multiorgan disease, with clinical manifestations varying with the affected body system. CHF has been found in some dogs with atherosclerosis and hypothyroidism; however, other signs, including those compatible with thrombosis of the central nervous system, aorta, or other organs, are more common. Treatment is palliative and centers around levothyroxine supplementation and, if necessary, a low-fat diet.

**Treatment**

As in feline hyperthyroidism, treatment of cardiac dysfunction associated with hypothyroidism is best accomplished by resolving the underlying thyroid dysfunction. Only in cases with CHF or concurrent cardiac disease is it necessary to provide cardiovascular-specific treatment. The cardiac changes induced by hypothyroidism are reversible; decreased fractional shortening and decreased R-wave amplitude in hypothyroid dogs improve with supplementation with levothyroxine. Recheck echocardiography is recommended 4 to 8 weeks after initiation of levothyroxine if hypothyroidism is thought to be contributing to decreased contractility.

In hypothyroid dogs with CHF or significant cardiac arrhythmias, the initial dose of levothyroxine should be less than the typical dosage. This recommendation is based on the cardiac decompensation that sometimes follows the sudden increase in oxygen demand in peripheral tissues and the myocardium when the hypothyroid state is reversed rapidly in humans. Therefore, levothyroxine should be initiated at 0.005 mg/kg PO q24h. The dosage may be increased gradually by 0.005 mg/kg every 2 weeks, with the patient being evaluated for improvement in cardiovascular status and measurement of serum T4 concentration before dosage adjustment. Hypothyroid dogs without important cardiovascular complications should receive levothyroxine at a starting dose of 0.02 mg/kg PO q24h. When present, CHF should be managed as in other dogs with heart failure caused by systolic dysfunction. In emergent situations, supplemental oxygen should

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**Figure 3.** A canine heart demonstrating marked atherosclerosis. The coronary arteries are prominent and are lined with pale atherosclerotic plaques (arrows). (Photograph courtesy of Dr. Roger Panciera)
be provided immediately and furosemide administered (2.2 to 4.4 mg/kg IV or IM q30–60min) until dyspnea starts to resolve.46 Chronic therapy for canine heart failure caused by systolic dysfunction generally consists of furosemide (1 to 2 mg/kg PO q12h; adjusted to lowest dose that eliminates congestive signs), an ACE inhibitor (enalapril 0.5 mg/kg PO q12h or benazepril 0.5 mg/kg PO q12h), and pimobendan (0.25 mg/kg PO q12h).

Use of Thyroid Hormone in Primary Cardiac Disease

Cardiac disease may induce a state referred to as "myotrophic illness in dogs" and humans,91 wherein plasma thyroid hormone concentrations are decreased in the absence of thyroid gland dysfunction. In people, the decrease in serum $T_3$ concentrations is proportional to the severity of heart failure.92 Compared with many other tissues, the myocardium is relatively deficient in deiodinases necessary for conversion of $T_4$ to the metabolically active $T_3$ in quantities sufficient to maintain a normal intracellular concentration of $T_3$ when the plasma concentration of $T_3$ is reduced. This finding, along with the positive inotropic, chronotropic, and lusitropic effects of thyroid hormones, has led many researchers to postulate that supplemental administration of thyroid hormone or a thyroid mimetic may be helpful in treating severe cardiac disease. Considerable research with experimental heart failure supports potential benefits of $T_3$ in improving cardiac function.93 Initial studies in humans have been promising, with improvement in left ventricular function and neurohormonal status after supplementation with $T_3$ or $T_4$ in patients with DCM and CHF.94-97 Unacceptable adverse effects were seen in a large-scale study of administration of a thyroid analog, but this could reflect overdosage rather than an unavoidable effect.98 In the single published veterinary study, 19 dogs in CHF from DCM were given a standard treatment of digoxin and furosemide or the standard treatment plus propranolol and levotheroxine. The difference in survival times between the groups was not statistically significant,99 although because sample size was small and variability in survival times was large, it is possible that the study was not sufficiently powered to detect clinically relevant differences. There is no indication for use of thyroid hormone in euthyroid dogs with CHF until further research is conducted.

Conclusion

Thyroid hormones enhance myocardial contractility and diastolic function. They also influence the peripheral vasculature, resulting in abnormal heart sounds, arrhythmias, altered left ventricular function, and hypertension in patients with hyperthyroidism. Hypothyroidism generally results in opposing changes, including a reduction in heart rate and myocardial contractility. Both hyper- and hypothyroidism can contribute to or cause CHF. Most of the changes are reversible when the endocrinopathy is controlled, but more severely affected animals may require specific treatment for heart failure or hypertension.

References

1. Rohrer D, Dillmann WH. Thyroid hormone markedly increases the mRNA coding for sarcoplasmic reticulum Ca$^{2+}$-ATPase in the rat heart. J Biol Chem 1988;263:6941-6944.


85. Ishchi T. Thyroid hormone and atherosclerosis. Vasc Pharmacol 2010;52:151-156.
1. Which of the following is not a cardiovascular effect of thyroid hormone?
   a. increased responsiveness to sympathetic stimulation
   b. increased contractility
   c. increased myocardial oxygen consumption
   d. arteriolar vasoconstriction

2. Which of the following would be a highly unlikely finding during auscultation of a hyperthyroid cat?
   a. atrial fibrillation
   b. gallop rhythm
   c. tachycardia
   d. heart murmur

3. Which is the most common echocardiographic change in hyperthyroid cats?
   a. decreased fractional shortening
   b. left ventricular posterior wall hypertrophy
   c. right atrial enlargement
   d. septal hypertrophy

4. How should the initial dose of levothyroxine be adjusted for a hypothyroid dog in congestive heart failure (CHF)?
   a. No dose adjustment is necessary.
   b. Approximately double the standard initial dose of levothyroxine should be administered.
   c. Approximately 25% of a standard initial dose of levothyroxine should be administered as an initial dose.
   d. A dog in CHF should never receive supplemental levothyroxine.

5. Which of the following would be the most appropriate therapy for ameliorating excessive tachycardia secondary to hyperthyroidism before anesthesia for thyroidectomy?
   a. atenolol
   b. benazepril
   c. furosemide
   d. amlodipine

6. Which of the following is the recommended initial treatment for severe hypertension in a hyperthyroid cat showing evidence of target organ damage?
   a. atenolol
   b. benazepril
   c. furosemide
   d. amlodipine

7. __________ is not a potential cardiovascular effect of hypothyroidism.
   a. Myocardial fibrosis
   b. Decreased myocardial contractility
   c. Enhanced diastolic ventricular function
   d. Increased peripheral vascular resistance

8. A(n) __________ is the most common ECG change in hypothyroid dogs.
   a. prolonged Q-T interval
   b. increased T-wave amplitude
   c. decreased R-wave amplitude
   d. absent P wave

9. Which of the following would be the most reasonable palliative treatment for atherosclerosis in a hypothyroid dog?
   a. levothyroxine supplementation and a low-fat diet
   b. furosemide and an angiotensin-converting enzyme inhibitor
   c. amlodipine and a β blocker
   d. levothyroxine supplementation and a novel-protein diet

10. In dogs, CHF secondary to hypothyroidism is consistently associated with _____________.
    a. atrioventricular block.
    b. atrial fibrillation.
    c. systemic arterial hypertension.
    d. jugular venous distention.