

The Murmur

Feline Hyperthyroidism: A Cardiovascular Review, Treatment Implications and the When, Where, and Y of Hill's Y/D.

Hyperthyroidism is the most commonly recognized endocrinopathy in cats as well as one of the most commonly diagnosed diseases in small animal practice. Hyperthyroidism most often affects middle age to older cats, with the average age of diagnosis being around 12 years, though cats as young as four have been uncommonly reported. It is a multisystemic disorder usually associated with functional adenomatous hyperplasia of either one (30%) or both (70%) thyroid glands, with only 1-2 % cases occurring secondary to thyroid carcinoma.

Signs and Pathophysiology

As veterinarians, we are very astute at recognizing the common clinical manifestations of hyperthyroidism. These signs may be mild to severe and are the result of hormonal effects on oxygen demand, heat production, protein, lipid and carbohydrate metabolism, and sympathetic tone. It is a hypermetabolic disease, resulting in polyphagia, weight loss, and polydipsia. Gastrointestinal signs are common, including vomiting secondary to rapid overeating and directed effects on the CRTZ, and diarrhea secondary to malabsorption. Cardiovascular signs, however, are frequently the most significant finding on physical exam.

The cardiovascular manifestations of thyrotoxicosis may be due to both the direct and indirect effects of thyroid hormones at the cellular level, to their interactions with the sympathetic nervous system, or to alterations of peripheral circulation. Tachycardia and systolic murmurs are noted on physical exam in 30-40% of cats while 10% of cases present with a gallop or arrhythmia. Sinus tachycardia is the most common rhythm disturbance occurring because of direct actions on the SA node. Atrial and ventricular arrhythmias secondary to altered calcium handling and changes in adrenergic tone occur less commonly and fortunately respond favorably to beta blockade. Mild systemic systolic hypertension can also be noted, though more severe hypertension can be seen in cats with concurrent renal disease. Counterintuitively, hyperthyroidism results in decreased peripheral vascular resistance due to its direct effect on vascular smooth muscle cells. Instead, the increase in systolic arterial pressure is likely secondary to increased cardiac output (increased heart rate, blood volume, and contractility). Mild hypertension usually resolves after effective thyroid control while more significant hypertension may require concurrent Amlodipine and/or Atenolol therapy.

Myocardial hypertrophy is a prominent feature of feline hyperthyroidism. It is related to the direct action of thyroid hormones on protein synthesis (mitochondrial and contractile), as well as the indirect effects of chronic volume overload, systemic hypertension, and increased sympathetic tone. Chronic tachycardia, increased myocardial oxygen demand, diastolic and eventual systolic dysfunction can result in congestive heart failure in cats with long standing unrecognized hyperthyroidism or in those with preexisting cardiac disease.

Tachypnea, panting, and dyspnea are often associated with CHF, however, these presenting complaints are also seen in cats without overt cardiac disease. These respiratory signs can be easily brought on by the stress of travel and veterinary visits and are thought to be secondary to respiratory muscle weakness, increased oxygen demand, and decreased lung compliance. When possible, patients diagnosed with hyperthyroidism should undergo complete cardiac evaluation, including echocardiography. This is even more important in cats presenting with murmurs, arrhythmias, respiratory signs, or in those undergoing surgery or I-131 treatment.

Treatment Options

Treatment of hyperthyroidism is aimed at removing or destroying abnormally functioning thyroid tissue, pharmacological inhibition of thyroid hormone synthesis, and decreasing the effects of excessive thyroid hormone on peripheral tissues. Each treatment method has its own advantages and disadvantages and should be selected on an individual basis.

Surgical Treatment

Surgical thyroidectomy is a potentially curative and relatively simple procedure which can be done in routine practice. Cats should be treated medically for 6-8 weeks prior to the procedure to make them better anesthetic candidates, however, cats with thyrotoxic cardiomyopathy will remain at increased risk for anesthetic complications. As 70% of cats will have bilateral thyroid nodules, most patients will require bilateral thyroidectomy, increasing the risks for potential side effects (Horner's, iatrogenic hypoparathyroidism, and hypothyroidism).

Methimazole Therapy

Methimazole (Tapazole® or Felimazole®), either oral or transdermal, prevents the conversion of T3 into T4, but has no effect on the underlying disease pathology. There is no particular contraindication for starting Methimazole and it remains an inexpensive treatment choice, at least in the short term. Please note that transdermal Methimazole may have mixed efficacy in the cat and oral dosing is the preferred route. Most adverse reactions usually occur within the first 3 months of starting treatment. Vomiting and anorexia are the most common signs, occurring in up to 15% of cats, but may be self limiting. A mild leukopenia can be seen without complication, however about 5% of cats will develop more severe hematologic abnormalities including agranulocytosis, thrombocytopenia, or immune mediated hemolytic anemia. These cats, along with those developing facial pruritis or hepatotoxic changes, will require withdrawal of the medication and another form of treatment. Methimazole remains the treatment of choice in patients with concurrent renal disease or those with significant cardiomyopathy, where having a T4 within the low to even normal range could result in clinical azotemia or CHF secondary to worsening systolic dysfunction.

I-131 Considerations

Radioactive iodine (I^{131}) is curative within three months in 95% of cats after a single injection and is considered the treatment of choice for most cats with hyperthyroidism. However, significant caution is recommended in cats undergoing I^{131} therapy that may have underlying renal disease or moderate to advanced cardiac changes. In many renal and/or cardiac patients, I^{131} treatment is likely contraindicated. Studies have shown 80% of cats will remain euthyroid four years after treatment, avoiding thyrotoxic changes associated with inadvertent inadequate T4 control. The cellular uptake of I^{131} occurs within the follicles of

hyperplastic or neoplastic tissue, resulting in local destruction, but sparing the surrounding atrophic normal thyroid tissue. Initial treatment cost is more expensive than other options, however, when taking into account the years of medication and monitoring, the difference is less significant. Extended hospitalization with minimal human interaction can be difficult in geriatric patients with concurrent diseases, as well as emotionally taxing for owners. Unfortunately, about 2-6% will go on to develop clinical hypothyroidism, once again requiring owners to medicate.

Hill's Y/D

Hill's has recently offered a new treatment option for feline hyperthyroidism. Hill's Y/D is a severely iodine restricted diet advertised to restore "thyroid health" in 3 weeks. The basis for using a severely restricted iodine diet to treat hyperthyroid cats is that iodine is an essential component of both T4 and T3. With severe dietary iodine deficiency, the thyroid cannot produce adequate amounts of thyroid hormone. The data provided by Hill's of the 150 colony cats trialed on the diet suggests that about 75% of hyperthyroid cats exclusively eating Y/D will have normal serum total T4 concentrations after four weeks. By eight weeks, 90% of cats have a normal serum T4 level and by 12 weeks, almost all cats should have normal T4 values. Further evaluation of the data reveals that the diet worked best in patients with mild to moderate T4 elevations and resulted in post-diet T4's within the high normal range. Studies of normal healthy senior cats have shown that normal T4 values fall within the low normal range, raising the concern that thyrotoxic changes may still be occurring in geriatric cats with mean T4's running 3.1-3.5 ug/dl. This could, however, be beneficial in cases of elderly cats that are intolerant to oral medications and/or require higher T4 levels due to concurrent illness.

Another potential concern raised regarding Y/D is the nutritional composition. As discussed earlier, hyperthyroidism results in a hypermetabolic state leading to increased protein requirements in a population of cats already predisposed to muscle wasting. These cats also show evidence of insulin resistance and hyperglycemia, suggesting a prediabetic state. This would imply that the best diet for a non-complicated hyperthyroid cat would be a higher protein, lower carbohydrate diet. Y/D is best described as high carbohydrate, moderately restricted protein diet with little animal source protein. In order for the diet to be effective, no other foods or treats can be given, making this treatment option more difficult in multicat households.

The choice of treatment should be individualized, taking into account the cat's overall condition, concurrent illnesses, and the owner's ability to comply with the recommended treatment plan. It would seem reasonable that radioactive iodine, a curative treatment, should remain the gold standard for most uncomplicated hyperthyroid cats. Hill's has provided veterinarians with a new treatment option, however, we should bear in mind that dietary management of hyperthyroidism has potential shortcomings and that long term management data is currently lacking.

Dr. Gina Pasioka, DVM, DACVIM (Cardiology), sees cases primarily out of our Leesburg and Vienna, VA locations.



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