Hyperthyroidism and Renal Disease: Is a methimazole trial necessary?

Hyperthyroidism and chronic kidney disease (CKD) are common disorders in older cats. The prevalence of concurrent renal disease in cats with hyperthyroidism is approximately 30 - 35%.

How does hyperthyroidism mask renal disease?

Hyperthyroidism can increase renal blood flow (RBF) and glomerular filtration rate (GFR). When GFR is increased in a hyperthyroid cat with underlying CKD, it can mask renal insufficiency; serum concentrations of urea nitrogen (BUN) and creatinine may be normal (due to increased clearance) despite mild to moderate kidney disease. Overlying this, decreased muscle mass contributes to lowered serum creatinine concentration.

Treating hyperthyroidism restores the serum T4 concentration to normal. In cats with CKD, GFR will fall to the low normal or subnormal levels expected with moderate renal dysfunction. This decrease in GFR can result in the apparent worsening of the serum kidney function tests or the apparent development of renal disease as creatinine levels normalize appropriate to the GFR.

It is important to remember that treating the hyperthyroidism itself does not cause CKD in these cats. The renal disease was already there but was masked by hyperthyroidism. This unmasking will occur regardless of the method being used to treat hyperthyroidism (drug therapy, surgery, or radioiodine).

How does hyperthyroidism contribute to renal disease?

Research provides evidence that untreated hyperthyroidism contributes to the development or progression of CKD in cats. Studies all suggest that leaving a hyperthyroid cat untreated or poorly regulated may be detrimental to long-term kidney function. With time, hyperthyroidism can lead to renal changes including glomerular hypertension, glomerulosclerosis, proteinuria, and hyperplasia and hypertrophy of renal tubules. Treating and curing hyperthyroidism may help to both reverse renal damage and preserve remaining kidney function.

Can we predict which hyperthyroid cats have underlying CKD?

About 20-25% of hyperthyroid cats without known CKD develop azotemia after successful treatment of hyperthyroidism irrespective of type of therapy. Predicting which cats will develop overt azotemia after treatment can be difficult to impossible. Routine pretreatment parameters such as BUN or creatinine concentrations and urine specific gravity are useful, but they cannot

consistently predict post treatment azotemia.

Should methimazole trials be performed in all hyperthyroid cats? (Spoiler alert - NO)

For years it has been accepted practice to perform a methimazole trial in newly diagnosed hyperthyroid cats to evaluate the impact of a euthyroid state on renal function. We now know that this approach in cats without pre-treatment azotemia (creatinine <176 umol/L) is questionable for several reasons:

1. The survival time of cats that develop azotemia is not shorter than those that do not develop azotemia after treatment of hyperthyroidism. In one study, the median survival time of cats that developed azotemia (595 days) was similar to cats that remained nonazotemic (584 days) after treatment.

2. In most cats that develop post-treatment azotemia, CKD is not severe or life threatening. It is also unusual to see an increase of more than one IRIS stage after treatment. In other words, hyperthyroid cats with IRIS Stage I-II may develop overt azotemia after treatment but one would not expect the CKD to advance to more than IRIS Stage II-III after treatment.

3. The decline in GFR after successful treatment of hyperthyroidism is not usually very progressive. The fall in the GFR is detectable within 1 month but generally remains stable at this level for months thereafter. This means that the rise in BUN and creatinine in cats with CKD follows the decrease in GFR such that the azotemia, if it occurs, would be expected to develop within 1 month of treatment but then remain relatively stable over many months.

Some more good reasons to think carefully before starting a methimazole trial: Unneeded methimazole trials will unnecessarily increase the client's cost of treating hyperthyroidism, can lead to stress in the client-cat bond, and up to 20% of cases result in side effects (some severe) resulting in sick kitties, even more client money spent to treat these side effects, and unhappy clients.

So, we now know that we can comfortably treat newly diagnosed, hyperthyroid, non-azotemic cats without a methimazole trial.

But what about newly diagnosed cats with pre-existing azotemia (creatinine > 176)?

In hyperthyroid cats with overt CKD, GFR is likely to fall once normal thyroid levels are restored. Therefore, it is generally advised to try medical management prior to definitive treatment in newly diagnosed cats with pre-existing CKD. Because the decline in GFR stabilizes after a month of successful resolution of hyperthyroidism, one can decide at that time whether the cat's renal function is stable or worsening.

If the renal function remains stable after a euthyroid state is established, a more definitive treatment such as I-131 should be strongly considered. This is because long-term control of

hyperthyroidism with medical management is unlikely to be successful enough to mitigate the detrimental effect of even mild hyperthyroidism on the kidneys.

On the other hand, if renal function declines dramatically after anti-thyroid drug treatment, especially if accompanied by marked clinical deterioration of the cat's renal failure (to mid to late IRIS Stage III or IV) it may be best to maintain the cat on a reversible anti-thyroid therapy. Except in extreme cases, maintaining the cat in a mildly hyperthyroid state is questionable given that uncontrolled hyperthyroidism may be damaging renal function. However, in cats with very late-stage CKD this may be the only palliative option.

The Bottom Line:

1. Cats that are non-azotemic when first diagnosed with hyperthyroidism can have definitive therapy without a methimazole trial. Any underlying CKD is likely to be mild and non-progressive, and survival of cats that do develop azotemia is no shorter than for those whose renal function remained stable.

2. Cats that are azotemic (creatinine >176 umol/L) when first diagnosed with hyperthyroidism should have a methimazole trial.

If renal disease is stable and Stage I or II after a month of being euthyroid, definitive therapy with RAI is recommended.

Final thoughts:

Clients should be aware that a very few cats might not fit neatly into these categories. If they are not comfortable with the odds, then a methimazole trial should be performed.

Conversely, if cats are in Stage III or IV CKD and cannot tolerate methimazole, and the client has realistic expectations for outcomes, duration of survival and support their cat may need, we can consider radioiodine therapy.

Although the median survival is shorter in later stages of CKD (stage 111: 778d, Stage IV: 103 days), the range is extremely wide (Stage III range: 22-2100 days, Stage IV range: 1 – 1920 days) so some late-stage CKD cats may do well with definitive therapy.

For more reading, please visit Dr. Mark Peterson's (from whom we have shamelessly lifted this well-researched information) blog: https://endocrinevet.blogspot.ca/