Clinical THYROIDOLOGY



A Large Case–Control Study Confirms that Development of Abnormal Thyroid Function Is Associated with Iodinated Contrast Material

Rhee CM, Bhan I, Alexander, EK, Brunelli SM. Association between iodinated contrast media exposure and incident hyperthyroidism and hypothyroidism. Arch Intern Med. 2012;172:153-9.

SUMMARY • • • • • •

Background

From the first days of our endocrine fellowship we are taught about the acute Wolff–Chaikoff effect, escape from it, and its opposite, the Jod–Basedow phenomenon, which can result when the thyroid is exposed to high levels of iodide. Prolonged hyperthyroidism can develop after patients are exposed to iodinated contrast material during computed tomography (CT) scanning or cardiac catheterization (CC), but there have been no large controlled studies examining the incidence of this complication (1-3). This study queried a database of 4.5 million patients in Boston, an iodine-sufficient area, and used a nested case-control study to assess the frequency with which abnormal thyroid function tests were associated with exposure to iodinated contrast materials.

Methods and Results

This carefully constructed retrospective casecontrol study examined the records of adults who had a normal TSH value obtained from January 1, 1990, through June 30, 2010, who had no known history of thyroid dysfunction, thyroid surgery, radioactive iodine thyroid ablation, or use of L-T₄ or antithyroid medication, and who had a second TSH measurement performed 2 weeks to 2 years after the first determination. Patients whose TSH values did not change between the two determinations were used as controls, matched for age sex, race, follow-up TSH interval, and estimated glomerular filtration rate. If the second TSH value was below the lower limit of the reference range, the patient was considered to have hyperthyroidism, whereas if the second TSH value was above the upper limit the patient was considered to have hypothyroidism. During 4096 patient intervals, iodinated contrast material was administered 361 times, leaving 3678 patient intervals that could be used as controls. In the source cohort, 361 subjects (8.8%) received iodinated contrast material in the interval between the two TSH tests (CT alone, 80.9%; CC alone, 13.6%; both CT and CC, 5.5%). A suppressed TSH level occurred in 191 intervals; of those, 178 were matched to 655 controls. Matched analysis revealed a significant association between contrast exposure and incident hyperthyroidism (odds ratio [OR], 1.98; 95% CI, 1.08 to 3.60; P = 0.03). The number needed to harm was 23. In secondary analysis, patients with a TSH of <0.01 mIU/L (considered to have overt hyperthyroidism) were more likely to be female, to have renal dysfunction, and to be of nonwhite race/ ethnicity. An elevated TSH occurred in 227 intervals; of those, 213 were matched to 779 controls. Matched analysis did not reveal a significant association (OR, 1.58; 95% CI, 0.95 to 2.62; P = 0.08). The number needed to harm was 33. However, if the interval for the second TSH determination was less than 180 days, or if the evaluation was limited to severe hypothyroidism (TSH >10), the association with exposure to contrast material did reach significance.

Conclusions

This study demonstrated associations between exposure to iodinated contrast materials from CT scanning and cardiac catheterization and the development of thyroid dysfunction. The strengths of the study include the large number of controls and careful case definitions. The study is limited because of the retrospective nature of the analysis, the variability between the time of exposure to contrast material and the time that follow-up TSH values were obtained, and the lack of a complete set of peripheral hormone levels in most of the patients.

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ANALYSIS AND COMMENTARY • • • • • •

I admit my bias is that the study must be correct, based on the known Wolff–Chaikoff and Jod–Basedow effects and the very high iodine content of contrast media (4). This is a difficult study for a nonstatistician to tease apart, but over 20 years, there were 4096 patient intervals (1 patient can have more than 1 interval that is separated by time) during which the serum TSH was checked twice within 2 years. Only 361 of these intervals were associated with the administration of iodinated contrast material. This means that the study captured only a small percentage of patients who received contrast material. One could ask whether there was a patient bias, since the period of repeating a TSH test (from 2 weeks to 2 years later) is more frequent than the period routinely used to follow patients without thyroid symptoms. This study confirms an association between the development of thyroid dysfunction and the administration of contrast material (1-4), although the design does not allow it to be used to show causality; that would require a prospective study that fully characterizes the patient's thyroid status before and at set times after the administration of contrast material. If the number needed to harm is 1 in 23 for the development of hyperthyroidism, then a prospective study that obtained follow-up samples from at least 2000 patients after they received contrast material would be required in order to obtain a statistically significant difference, a study that would appear to be difficult to perform and fund.

- Stephanie L. Lee, MD, PhD

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