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Radioactive iodine scanning is not beneficial but its use persists for euthyroid patients

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Abstract

Background—Radioactive iodine (RAI) scanning is a method of determining the functional status of thyroid nodules. Historically, practitioners thought “cold,” or inactive nodules were more likely malignant. However, surgeons now do not find these scans helpful for preoperative management of euthyroid patients. The purpose of this study was to evaluate the utility of RAI scans.

Methods—We retrospectively reviewed cases of euthyroid patients (TSH > 1.0 mIU/L) who underwent RAI scans prior to thyroid surgery at our institution between 1994 and 2011. We correlated the RAI scan results with final pathology. We considered RAI scans concordant with pathology when a malignancy was found on the same lobe as a cold nodule. We also tabulated the specialty and affiliation of the ordering physicians.

Results—109 euthyroid patients underwent RAI scanning as part of their preoperative workup. 88 patients (81%) had a cold nodule. A malignancy concordant with the RAI scan findings occurred in only 15 (17%) of these patients. Non-surgical specialties ordered 90 scans (95%). Only 11 of these scans (10%) were performed in the last 5 years, and physicians outside of the academic institution ordered all 11 (100%) of these. A linear regression of RAI scanning per year yielded a slightly negative slope ($m = -0.32$).

Conclusions—RAI scanning is not useful for the surgical management of thyroid disease in euthyroid patients since it poorly predicts malignancy. The overall use of RAI scans is trending downward, but they are still ordered by non-surgical referring physicians.

Keywords

Radioactive iodine scan; euthyroid; thyroid nodules

Introduction

Higher quality computer tomography (CT) and ultrasonography (U/S) detect thyroid nodules more frequently in the clinical setting. One U/S study revealed thyroid nodules in 67% of the population [1]. An estimated 4-7% of the U.S. population has a palpable nodule [2]. Despite this prevalence, only 5% of clinically discovered nodules are malignant [3]. Surgical

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excision is performed when the nodule is large, symptomatic, malignant, or when cytology results cannot rule out malignancy.

Physicians use radioactive iodine (RAI) scanning to determine the functional status of thyroid nodules. Commonly used radioactive substances include, I-131, technetium-99m pertechnetate, or iodine-123. The degree of RAI absorption differentiates a hyperactive, or “hot” nodule, from a hypoactive, or “cold” nodule. In the 1940’s physicians learned that malignant nodules exhibited poor uptake of RAI. Thus, RAI scans became a fixture in the evaluation of thyroid nodules [4]. Studies estimate that 85% of nodules are cold nodules. Historically, cold nodules had a 15% risk for malignancy [5].

Today, RAI scans provide diagnostic benefits in select situations. Most notably, RAI scans support the diagnosis of a patient with clinical symptoms of hyperthyroidism and/or suppressed TSH levels. The first recommendation in the guidelines for thyroid nodules, published by the American Thyroid Association (ATA), is to measure serum TSH initially and perform radionuclide testing if a subnormal TSH value is reported [6]. With such guidelines for limited use, RAI scans would not be expected to be helpful for euthyroid patients preoperatively. Rather, treatment guidelines deemed fine-needle aspiration (FNA) as the gold standard for determining malignancy because it has more impact on surgical management [6, 7]. From the surgeon’s perspective, euthyroid patients do not always need RAI scans. This paper aims to evaluate the prevalence and utility of RAI scans for euthyroid patients in a modern university setting.

Method

We performed an IRB approved retrospective review of a prospectively collected Endocrine Surgery Database of patients that underwent thyroid surgery between 1994 and 2011 at the University of Wisconsin. The inclusion criteria for this study were (1) a TSH value of greater than 1.0 mIU/L (2) a RAI scan prior to surgery. For analysis, we collected patient characteristics, FNA results, final pathology results, RAI scan findings, the specialty and the institution of the ordering physicians. Linear regression was performed to fit a trend line for the volume of RAI scan orders per year.

Our method for correlating the RAI scan results with final pathology was as follows. We labeled the findings from the RAI scan according to the side (left versus right) involved. We also categorized the final pathology report by the side involved. We considered RAI scans concordant with pathology when a malignancy was found on the same lobe as a cold nodule.

Results

Patient characteristics

Of the 2,154 patients available in the database, 255 patients (12%) had RAI scans and 109 of these were euthyroid. Of the 109 patients that met our inclusion criteria, 28 were male and 81 were female (Table 1). The mean age of the study group was 48 ± 2 years of age at the time of their thyroid surgery (Table 1). The average TSH level at the time of surgery was 2.57 ± 0.2 mIU/L (Table 1). We categorized cases into one of five reasons for surgery: 28 patients (26%) for enlargement, another 28 patients (26%) had a cancer diagnosis (PTC, MTC, follicular carcinoma), 20 patients (18%) had indeterminate cytology (follicular cell neoplasm, Hurthle cell neoplasm, FLUS), 18 patients (16%) had surgery due to compressive symptoms (dysphagia, stridor, pressure), and lastly, 15 patients (14%) to rule out malignancy because of inadequate FNA evaluation or other clinical suspicions (Table 1).

Lobectomies were performed on 72 patients (66%), total thyroidectomy on 35 patients (32%), and subtotal thyroidectomy on 2 patients (2%). Malignant pathology was discovered in 25 patients (23%). Of these 25 patients, 21 of them (19%) had PTC and 2 had MTC (1.8%) and 2 had follicular carcinoma (1.8%).

RAI scan correlation with cytology and histology

The RAI scans for the 109 patients indicated that 88 patients (81%) had a cold nodule (Table 2). 61 patients with a cold nodule (69%) underwent FNA (Table 3). The FNA results revealed 22 patients (36%) with neoplasm, 17 patients (28%) with benign results, 10 patients (16%) with malignant cytology, 7 other patients (12%) had cytology that was suspicious for malignancy, and lastly, 5 patients (8%) had non-diagnostic FNAs (Table 4).

Of the 88 patients with a cold nodule, 15 (17%) had malignant pathology results. 9 patients with a cold nodule (10%) had both a malignant pathology result and a malignant FNA result (Table 4). 6 patients (7%) had a malignant pathology result and a non-malignant FNA result. 4 patients (5%) had a malignant FNA result and a non-malignant pathology result. Specifically, in three of these cases, the FNA location did not correlate with the cold nodule location. Lastly, in 69 patients (78%), both FNA and pathology results were not malignant. The sensitivity and specificity of RAI scans in identifying malignancy, was 0.60 and 0.13, respectively. The positive predictive value and negative predictive values were 0.17 and 0.52, respectively. The sensitivity and specificity for hyperthyroid patients were not included because this study is focused on the euthyroid patient population specifically.

Ordering provider

We obtained information about the physicians that ordered RAI scans for 95 cases. Non-surgical specialty physicians ordered 90 of the 95 scans (95%) (Table 5). The most represented physician specialties were family medicine, internal medicine and endocrinology with 31 (33%), 29 (31%), and 28 (30%) scans ordered, respectively. Physicians ordered 14 scans in 1996, the most in any single year (13%) (Figure 1). Physicians ordered 53 scans (49%) during the five-year period from 2000 to 2004. Starting in 2004, the number of scans dropped sharply. In the past five years, physicians ordered only 11 scans (10%). Outside providers ordered all 11 of these scans (100%). A linear regression of the volume of RAI scans per year resulted in a slightly negative slope ($m = -0.32$), indicating a progressive decline in RAI scan use.

Discussion

RAI scanning predicts only a low percentage of malignancy among cold nodules seen in a euthyroid patient group. In our study, RAI scanning showed 88 cold nodules in 109 cases (81%), but only 15 (17%) of those cold nodules were malignant. FNA accurately predicted malignancy in 9 cases (60%). Though, reports described 4 of the 6 malignancies without a malignant FNA as “suspicious for malignancy.” FNA gave an indication of malignancy in 13 out of 15 cases (87%), from which our surgeons could more confidently perform the appropriate surgical procedure. Therefore, FNA, more so than RAI scanning, solidifies surgical decision-making. The study done by Greenblatt and colleagues showed a sensitivity and specificity of FNA for thyroid cancer of 89% and 92%, respectively. They also compared the percentage of patients that received optimal surgical treatment (defined as no need for completion thyroidectomy for PTC and MTC and as no unnecessary surgery for lymphoma) in a FNA group and a no-FNA group, which was statistically in favor of the FNA group [7].

In some instances, guidelines recommend RAI scanning in conjunction with FNA. These situations occur after the initial diagnosis and involve a FNA result of follicular neoplasm, which has a 20-30% risk of malignancy. The ATA recommends that a RAI scan may be considered, especially if the TSH is in the low-normal range. This recommendation is given a C rating on an A-I rating scale [6]. If the nodule is hot, observation is sufficient in euthyroid patients. If the nodule is cold, surgery is warranted [8]. Since most nodules are cold on a scan and only a small minority is malignant, this adds to the inefficiency surrounding RAI scanning [9]. In most institutions, a follicular neoplasm is managed with a lobectomy regardless of the nodule's functional status because clinicians are uncomfortable with a 20-30% cancer risk. In our study, follicular neoplasm was the leading result for cold nodules with a FNA. This situation may have contributed to the larger volume of RAI scans in the early years of this study.

RAI scans are important in the diagnosis of patients that demonstrate thyrotoxicosis. In these cases, RAI scans help pinpoint the etiology of the thyrotoxicosis. Hyperthyroidism, one type of thyrotoxicosis, results in increased uptake. Specifically, Graves' disease has a homogenous uptake pattern, toxic thyroid adenoma has one hyperactive nodule, while a toxic multinodular goiter has multiple hyperactive and hypoactive nodules.

Thyroiditis, a second cause of thyrotoxicosis, on the other hand, shows low uptake [10]. Hashimoto's thyroiditis is the most common acquired form of hypothyroidism. Though, the disease can demonstrate biochemical hyperthyroidism, which is called Hashitoxicosis, due to inappropriate release of remaining thyroid hormone. RAI scans can differentiate between the transient hyperthyroidism of Hashitoxicosis and Graves' disease [11]. With scanning, Hashitoxicosis exhibits low uptake, while Graves' disease exhibits higher uptake. Physicians may have ordered 11 of the 109 (10%) RAI scans for this reason. In these cases, the final pathology indicated Hashimoto's thyroiditis. Hashimoto's thyroiditis pathology applied to only 2 of the 11 RAI scans (18%) ordered in the last 5 years.

The downward trend of RAI scan use is ongoing as some physicians still utilize them on euthyroid patients. At our institution, these physicians were mostly non-surgeons, specifically internal medicine, family practice, and endocrinology physicians (Table 5). Most recently, they have been referring physicians from outside our institution. In 2010, there was a sharp increase in the volume of RAI scans. Of the 7 scans in 2010, 5 were done for patients referred from out of state.

These two traits suggest a few reasons for continued use of RAI scans. One reason may be physicians' use of RAI scans as part of their workup for thyroid nodules is out of habit. But, in the last five years, endocrinologists ordered only 2 of the 11 scans (18%). This suggests that this specialty group, in particular, recently changed their practice to match published guidelines, which emphasize FNA to diagnose thyroid nodules in euthyroid patients.

The 1996 ATA guidelines on thyroid nodule management, similar to the 2009 version, suggested that RAI scanning be confined to hyperthyroid patients and recommended FNA as an alternative [13]. The adoption of this stance likely led to the decreased RAI scanning in the initial workup of thyroid nodules, when it was previously a staple. A survey of North American members of the ATA in 1998 revealed that only 23% of physicians would order a RAI scan in a euthyroid patient scenario [12]. Our data depicted this evolution between 1994 and 2011 as fewer euthyroid patients received RAI scans. Though, we did not see significant change until 2006 in our study.

It is difficult to judge how rooted the method of practice was prior to these recommendations. Thus, we suspect a period of time was necessary for this knowledge to predominate. Physician attitudes towards clinical practice guidelines can affect the length of

the lag time. Surveys of physicians showed that they generally view guidelines as beneficial, but there are disputes about putting them into practice [14]. Such views would cause improvements in care to be less than expected or postponed. Nevertheless, our data shows an overall negative trend in the use of RAI scans for euthyroid patients, indicating that the guidelines are slowly taking effect.

The retrospective nature of this study made it problematic to discern physicians' motivations to order a RAI scan. Since we selected patients based on TSH values, the study may include cases where the patient had a history of hyperthyroidism but that history may have not been distinguishable in our database. Another limitation of this study was that not all patients had FNA evaluations because other compressive symptoms or suspicious imaging studies negated the need for FNA.

In conclusion, this paper was intended to review the use of radioactive iodine scanning utility in the modern setting. We found that the use of RAI scans is decreasing, but continues to persist at low levels. Going forward, RAI scans should be reserved for nodules in patients with clinical or biochemical indications of hyperthyroidism because they do not efficiently diagnose malignant nodules in euthyroid patients. Further, physicians should use FNA as the main diagnostic method for hypoactive nodules found via palpation or other imaging. Better communication of protocols could facilitate additional decreases in RAI scanning.

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Figure 1. Linear regression of RAI scans ordered per year

Figure 2. Algorithm for assessing thyroid nodules

Table 1**Patient characteristics**

Age (yrs)	48 ± 1.5
Female (%)	74
TSH (mIU/L)	2.57 ± 0.2
Reason for Surgery	
Enlargement	28 (25.7%)
Cancer	28 (25.7%)
Neoplasm	20 (18.3%)
Compressive symptoms	18 (16.5%)
Rule out malignancy	15 (13.8%)

N = 109; Data shown as mean ± SEM; TSH = Thyroid stimulating hormone

Table 2
Results of RAI scans performed on the study group patients

Scan result	#	%
Cold nodule	88	80.7%
Heterogeneous	11	10.1%
Normal	9	8.3%
Diffuse cold	1	0.9%

N = 109

Table 3**Cold nodule FNA results**

Follicular neoplasm or Hurthle cell	22	36.1%
Benign	17	27.9%
Malignant	10	16.4%
Suspicious for malignancy	7	11.5%
Non-diagnostic	5	8.2%

N = 61

Table 4
Cold nodule correlation with cytology and histology

FNA	Pathology	# (%)
+	+	9 (10.2%)
-	+	6 (6.8%)
+	-	4 (4.6%)
-	-	69 (78.4%)

N = 88; (+) = malignant; (-) = non-malignant

Table 5**Ordering Physician Specialty**

Non-surgical specialty	90	94.7%
Family Medicine	31	32.6%
Internal Medicine	29	30.5%
Endocrinology	28	29.5%
Pediatrics	2	2.1%
Surgical specialty	5	5.3%
Otolaryngology	3	3.2%
General surgery	2	2.1%

N = 95