Research Article

What Happens in a 5-Year Follow-Up of Benign Thyroid Nodules

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To determine an optimal time for follow-up of benign thyroid nodules, we retrospectively evaluated 249 euthyroid patients with unimultinodular goiter, who underwent annual visit, and significant events that occurred in 5 years’ time were registered. A significant event (appearance of new nodule, increase of nodule diameter >50%, appearance of compressive symptoms, thyroidectomy, repetition of FNA on the same nodule, and execution of FNA on new nodule) occurred in 26.1% of patients, with more than one event occurring in the same patient in 27.7% of cases. The majority of events (71.9%) were observed at 24- and 36-month follow-up visit. These results suggest that a patient diagnosed with benign nodular goiter may be safely followed-up at a 2-3-year interval time.

1. Introduction

The prevalence of palpable thyroid nodules has been estimated to be around 3–7%, while the prevalence on nonpalpable nodules, detected by thyroid ultrasound or incidentally discovered by MRI or carotid Doppler ultrasound, is much higher (20–76%) [1–3]. Moreover, 20–48% of patients with a palpable nodule have another nodule detected by ultrasound [4, 5]. Once a thyroid nodule has been detected, further investigations are required, like fine-needle aspiration (FNA), thyroid function test, or scintigraphy [6]. Once the diagnosis has been made, the patients may be referred to surgery, radioiodine therapy, laser/radiofrequency ablation, or follow-up. In patients residing in iodine deficient areas, a medical treatment with levothyroxine may be advised. In AACE-AME-ETA guidelines for thyroid nodules, it is indicated that the optimal time interval for patients follow-up is 6–18 months, in lack of specific studies that address this issue [6].

Given the high prevalence of thyroid nodules and the number of patients with cytologically benign nodules with a normal thyroid function that periodically should be checked by ultrasound and thyroid function tests, it is easy to understand the global impact on the health care system deriving from such disease.

The aim of this study is to ascertain an optimal time interval of consultations, in order to guarantee an effective monitoring, but avoid an excessive and useless execution of consultations, function test, and ultrasound, for a benign disease that is also often asymptomatic.

2. Methods

We retrospectively selected patients who in 2007-2008 had their first visit for thyroid disease and had been diagnosed with euthyroid unimultinodular goiter and had cytological benign exam and completed their follow-up for five years (2012-2013), with at least 3 visits during this period (baseline, 60 months, and at least one other visit in between). As per our institutional protocol, patients referred to our clinic for thyroid nodule undergo ultrasound and TSH. Patients are submitted to FNA in case of nodules greater than 10 mm, irrespective to presence or absence of characteristics of malignancy and in case of nodule smaller than 10 mm, just in presence of characteristics of malignancy. Then, from the initial population of thyroid patients we excluded those with hypothyroidism, hyperthyroidism, drugs interfering with thyroid function (as listed in the ATA/AACE guidelines), and positive thyroid antibodies (when available); we also excluded...
those patients who, after their initial workup, underwent thyroid surgery, radioiodine therapy, or ethanol ablation, were lost at follow-up, had nodules smaller than 5 mm, and were submitted to suppressive therapy with levothyroxine.

From such selected population, the following data were recorded: sex, age, TSH, number of nodules, diameter of the nodule in case of uninodeular goiter, and diameter of the major nodule in case of multinodular goiter; for the aim of the study, we considered in five-year follow-up the following events as relevant: appearance of new nodules larger than 10 mm; appearance of new nodules smaller than 10 mm with characteristics of malignancy; increase in nodule diameter greater than 50% from baseline; appearance of dyspnea, dysphonia, dysphagia, and local discomfort; execution of a FNA on the same nodule already examined at baseline or on a new nodule; any other situation that indicates surgery or any other treatment that excluded the patient from follow-up; development of thyroid dysfunction.

Ultrasounds were performed with a 7.5 MHz linear probe (Logiq 7 GE or MyLab25 Gold Esaote) by three endocrinologists with consolidated experience in thyroid ultrasound; the three diameters (anteroposterior, transverse, and longitudinal) of each nodule were usually reported; the major of the three diameters was always reported and used for the present study.

Thyroid cytology categories followed the British Thyroid Association system (THY1–5).

Permission for this review and analysis was granted by the Investigational Review Board at the “V. Fazzi” Hospital. Results are presented according to patient and nodule, respectively, and compared using a t-test or a χ² test, as appropriate. Values of $P < 0.05$ are considered significant.

### 3. Results

In 2007-2008, 1,772 patients had their first visit for thyroid disease. Of these, 555 were hypothyroid, 98 were hyperthyroid and treated with antithyroid drugs, 75 underwent radioiodine treatment for Graves’ disease or Plummer adenoma, 100 underwent thyroid surgery for compressive symptoms or malignancy, 527 had nodules smaller than 5 mm, were lost at follow-up, or had less than 3 visits, 100 had chronic autoimmune thyroiditis in euthyroidism, 23 were treated with ethanol ablation for cystic nodules, and 43 underwent suppressive therapy with levothyroxine for nodular goiter. This latter group of patients spontaneously chose to be treated with levothyroxine, after exhaustive explanation; the treatment was not assigned on medical decision basis; then, the exclusion of this group should not represent a bias in analysis of results. Then, the study population consisted of 249 patients with euthyroid uni-/multinodular goiter, with benign FNA.

Characteristics of study population are described in Table 1.

Almost all patients had 5 consultations (4.98 ± 1.0). A total of 82 events occurred in 65/249 patients (26.1%) in 5-year follow-up period. The events were the following: 38 new nodules, 23 increase of nodule diameter >50% in respect to baseline, 5 increase of nodule diameter <50% but appearance of local discomfort with compressive symptoms, 6 thyroidectomies (with 2 having incidentally discovered micropapillary cancer at histological exam), 5 repetitions of FNA on the same nodule detected at baseline, and 5 FNA on new nodules. The reaspiration of the 5 nodules was done in those who had an increase of diameter >50% in respect to baseline and diameter >20 mm.

In 18/65 patients we recorded more than one event (e.g., increase of nodule diameter >50% and FNA). No patients developed thyroid dysfunction, nor was the appearance of metastatic lymph nodes observed. Of the 5 nodules that were reaspirated, no false-negative FNA was detected. None had a spontaneous reduction of thyroid nodule greater than 50% in respect to baseline.

The 82 events occurred at 36.3 ± 12.8 months from baseline. 71.9% of events (59/82) were detected at 24- and 36-month follow-up visits ($P < 0.01$); appearance of new nodules and increase of nodule >50% represent 50% of all events that occurred in 5-year follow-up ($P < 0.01$) (Figure 1).

### 4. Discussion

Given the high prevalence of benign nodular disease in the general population, an optimal management of such disease would be useful in order to adequately monitor the patients, while minimizing useless consultations, thyroid function test, and ultrasounds. Data of the present study show that, of all the possible events considered, 72% were detected between 2 and 3 years after the initial evaluation and that it is almost unnecessary to reevaluate the patients in 12 months. Indeed,
Conflict of Interests

The author declares that there is no conflict of interests regarding the publication of this paper.
References
