

The Incidence of Carcinoma in Solitary "Cold" Thyroid Nodules

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Two hundred and three patients with single thyroid nodules were referred for radioactive scan of the thyroid. Solitary "cold" nodules were identified in 130 patients and 68 of these patients came to surgery. Of this group, 12 patients were found to have carcinoma. There was no obvious selection process which distinguished the 68 patients who underwent surgery from the 62 who did not. There is a significant risk of thyroid neoplasms occurring in patients with solitary "cold" nodules, and this is particularly true in patients under forty.

Although the proper treatment of nodular goiter continues to be an area of controversy, most physicians are especially concerned about the presence of a single thyroid nodule [1-3]. Despite difficulty in separating solitary thyroid nodules from multi-nodular goiter clinically, thyroid cancer has been found more frequently in single nodules. Since thyroid carcinoma usually does not concentrate radioiodine as well as normal tissue, malignant thyroid nodules commonly appear as hypofunctioning or nonfunctioning areas on the radioactive iodine scan of the thyroid [4]. The reported prevalence of thyroid carcinoma in thyroid nodules has varied widely with the highest prevalence reported in the surgical series. Careful studies have demonstrated an underlying incidence of thyroid carcinoma in as many as 5-6 percent of unselected autopsies [5]. The high incidence of carcinoma found in solitary thyroid nodules has been attributed to a bias of case selection. Since most physicians would refer patients with single thyroid nodules for an isotope scan of the thyroid, examination of this group might avoid the bias of case selection.

MATERIALS AND METHODS

Radioactive Iodine Scans

Examination of the records of the Nuclear Medicine Division at the Yale-New Haven Medical Center indicated that 203 patients with single thyroid nodules were referred for radioactive thyroid scans between July 1970 and June 1973. One hundred and thirty were interpreted as "cold," i.e., hypofunctioning with respect to the rest of the thyroid. Thirty-four thyroid nodules were interpreted as functioning normally, and 39 nodules were interpreted as "hot," i.e., hyperfunctioning with respect to the rest of the thyroid. Seven of these nodules were considered to be autonomous as judged by failure to suppress on thyroid hormone. Sixty-eight patients had surgery following the scan; six patients were lost to follow up.

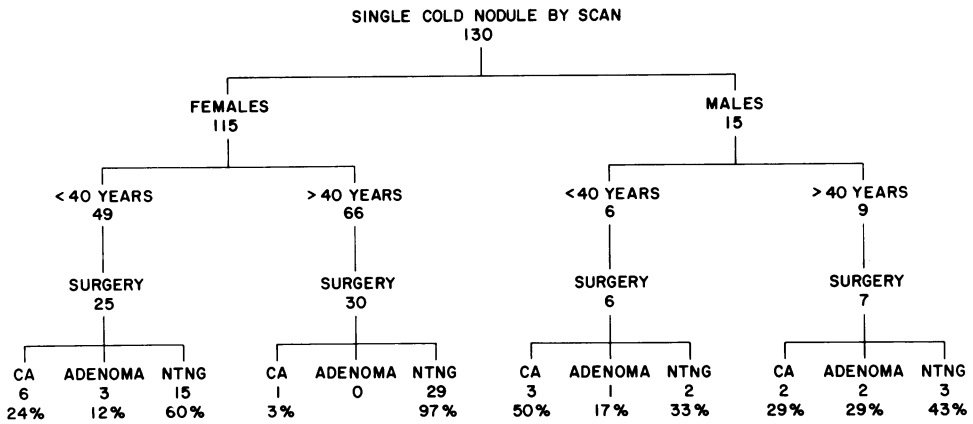


FIG. 1. Distribution of patients with solitary "cold" thyroid nodules on scan by age, sex, and histological diagnosis. One female, less than forty years of age, had Hashimoto's Disease and is not included. (NTNG) Non-toxic Nodular Goiter.

The decision whether or not to operate was made by the individual physician and the active decision process, how individual patients were selected for surgery, is unknown. Only one patient gave a history of previous radiation to the neck. Of the forty-nine females under 40 years, 25 had surgery, 22 did not and 2 patients were lost to follow up. There were 66 females over 40 years and 30 had surgery while 31 were not operated upon and five were lost to follow up. In contrast, of 15 males, 13 came to surgery and one was lost to follow up.

Pathology

All histologic material was reviewed by a single pathologist (V.A.L.).

In nodular goiter, the follicles within the nodules varied greatly in size, many were dilated and filled with colloid. Hemorrhage and scarring were found often. Focally, areas of adenomatous proliferation were noted in some cases. Adenomas considered to be true neoplasms showed a more or less complete capsule, uniformity within the tumor of microfollicular or trabecular zones and the tissue composing the nodule differed from the surrounding normal gland. In this series, the adenomas were follicular in type; no papillary adenomas were identified [6].

Carcinomas were classified into papillary, mixed papillary and follicular, and pure follicular (medullary carcinoma and anaplastic lesions were excluded from this study). Papillary or mixed cancers are considered as one biologic spectrum showing varying degrees of papillary proliferation, calcospherites, large clear nuclei, multifocality and a propensity to lymph node metastases. Pure follicular carcinomas tend to be unifocal, to show capsular and/or angioinvasion and to metastasize via a hematogenous route. No papillary foci or calcospherites are identified and the nuclei demonstrated hyperchromatism and atypia, but not clearing [7].

RESULTS

The patients with solitary "cold" nodules on thyroid scan are distributed by sex, age and histological diagnosis in Fig. 1. There was no obvious selection process which distinguished the 68 patients who were referred for thyroid surgery following a scan from the 62 patients who were not (six of the latter group were lost to follow up).

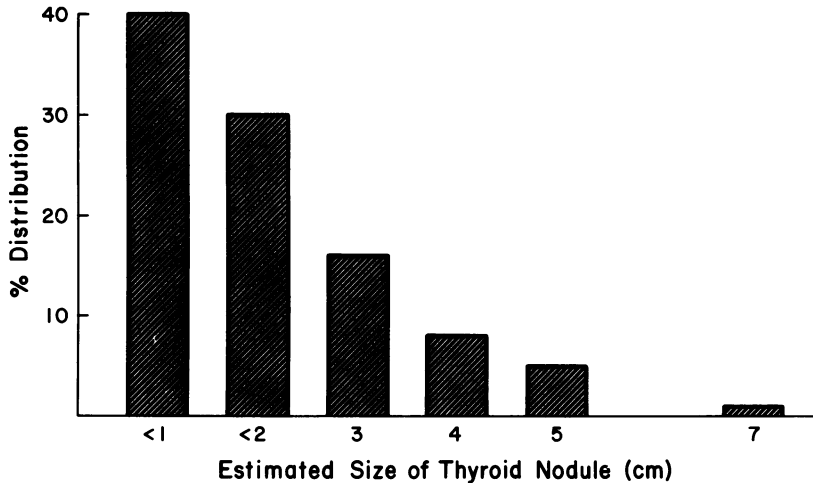


FIG. 2. Percent distribution of solitary "cold" thyroid nodules identified by thyroid scan according to clinically estimated size.

About 70 percent of the thyroid nodules were 2 cm or less in size and were equally distributed between the right and left lobes (Fig. 2). Thirty-seven patients were given thyroid hormone in an attempt to suppress TSH secretion. The majority of patients received 120–180 mg of desiccated thyroid hormone or equivalent for periods ranging from several months to several years. The thyroid nodule decreased or disappeared in 12 patients all of whom were female. In four patients, the thyroid nodule increased in size during thyroid therapy.

Of the 68 patients with single "cold" nodules identified at the time of scan who came to surgery, 49 patients had non-toxic nodular goiters including three cysts; one had Hashimoto's thyroiditis, six had follicular adenoma and 12 had carcinoma. Six of the seven thyroid carcinomas in women occurred in patients under the age of forty while all three follicular adenomas occurred in this age group.

DISCUSSION

To examine the risk of carcinoma in solitary "cold" thyroid nodules, we examined patients who were referred for radioactive scan of the thyroid. Although it is impossible to be certain that some patient selection had not taken place before referral, standard medical practice in the New Haven area is to obtain a thyroid scan on any patient with a thyroid nodule. Approximately half of these patients subsequently underwent thyroidectomy. Again, it is important to know how the decision to operate was made. There was no obvious difference between the operated and non-operated patients in regard to age, sex, nodule size or history of radiation exposure.

The incidence of carcinoma in these patients was 18%. During the period of 1968 to 1973, 93 patients were referred for surgery for a single "cold" nodule and of these 17 or 18% were found to have carcinoma. These figures include most of the group identified by thyroid scan and it is not surprising that the incidence of carcinoma is similar in the two groups. The important question is what is the incidence of carcinoma in the unoperated nodules identified by scan? However, even if all the thyroid nodules in the non-operated group proved to be benign, the incidence of carcinoma in the series would still be 9 percent.

There are certain data available on the prevalence of thyroid neoplasms in the local New Haven population which may be helpful in interpreting the present study. Most patients in our study live in New Haven County which has a population of about 750,000. The Framingham study indicates that about 2.8 percent of individuals between 30 and 59 years have a solitary thyroid nodule on clinical examination [8]. There should be about 21,000 patients with solitary nodules in New Haven County. If the underlying incidence of thyroid carcinoma is 2-3 percent, a similar number of patients with thyroid malignancy should be found. During the five year period of 1968 to 1972, 109 cases of thyroid cancer were diagnosed in New Haven County [9]. Silverberg and Vidone studied the thyroids from 300 autopsies from this institution on patients over twenty years of age [10, 11]. There were eight thyroid carcinomas and nine follicular adenomas in the series for an overall incidence of 6 percent. Seventy-two thyroid glands had one or more nodules which were greater than 1.0 cm. Nineteen thyroids contained gross single nodules with two carcinomas and four follicular adenomas. Thus, in an unselected series from this institution, the chance of a solitary thyroid nodule being a neoplasm was 32 percent, similar to the incidence of thyroid neoplasms of 25 percent in the present study.

Veith and his co-workers reported a series of 299 patients who were found to have single thyroid nodules at the time of surgery [12]. Like the present study, there was a 5:1 female to male ratio and about half the patients were under the age of forty. The overall incidence of thyroid carcinoma in this series was 6.6 percent, the great majority of which were papillary adenocarcinoma. In both studies thyroid carcinoma was more common in women under forty years of age than over forty. The number of males in our study was too small to make meaningful comparisons, but in neither study was there an obvious age difference in the incidence of thyroid carcinoma. Although the numbers were small, males seemed to be at greater risk for thyroid carcinoma.

Whether the higher incidence of thyroid carcinoma in our study can be explained by the fact that the patients had "cold" thyroid nodules on scan is not clear. Kendall and Condon reported a prevalence of malignancy in solitary thyroid nodules of 21 percent [13]. They considered whether the scan was "cold" or not to be of diagnostic value. Shimaoka and Sokal reported a series of 88 patients with areas of hypofunction on radioactive iodine thyroid scan, 38 of which were single thyroid nodules [14]. There were three thyroid carcinomas among these patients. Hoffman reported a series of 202 patients with solitary thyroid nodules with an overall incidence of thyroid carcinoma of 29 percent [1]. He commented that 40 percent of thyroid carcinomas in this series would have been ignored if "cold" thyroid nodules were the sole criterion for operative selection. Messaris studied a group of 416 patients with "cold" nodules by thyroid scan. No mention was made whether the nodules were single or multiple, but there was an overall incidence of thyroid carcinoma of 13 percent.

This present study was designed to answer the question, "What is the risk of carcinoma in a solitary "cold" nodule in the thyroid?" Thyroid carcinoma was found in 18 percent of patients at surgery and another 9 percent had follicular adenomas. Whether case selection occurred to a significant extent in the patients who were referred to surgery is not clear. However, our data indicate that there is a significant risk of thyroid neoplasm in solitary "cold" thyroid nodules, particularly in those patients under the age of forty.

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