



Is there a correlation between thyroiditis and thyroid cancer?

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Abstract

Background In the past few decades, the incidence of thyroid cancer has increased significantly all over the world. In the same period, there also seems to have been an increase in the incidence of Hashimoto's Thyroiditis—the most common inflammatory autoimmune thyroid disease. Several studies have linked thyroiditis to thyroid cancer.

Methods In our study, we examined 2304 cases of thyroid surgery collected over a 12-year period starting from 2004. In 2090 cases (90.7%) out of our sample, it has been possible to compare the presence, or lack thereof, of thyroiditis by means of a histological diagnosis post-surgery; 214 (9.3%) cases were excluded from our study due to insufficient data. We then divided the different histological classifications into two groups. Group A included all the benign histological classifications and Group B included all the malignant histological classifications. In each group, we then assessed the presence, or lack thereof, of thyroiditis in order to evaluate if thyroiditis can be linked to a higher incidence of thyroid cancer.

Results Data analysis showed a higher incidence of thyroiditis in Group B, 36.4% (malignant pathology report), than in Group A, 32.4% (benign pathology report), but no statistically significant difference emerged between those two groups ($P > 0.05$).

Conclusions Our conclusion was that a correlation between thyroiditis and a higher incidence of thyroid cancer is still undefined.

Keywords Thyroiditis · Thyroid cancer · Thyroidectomy · Papillary cancer

Abbreviations

HT Hashimoto's thyroiditis
PTC papillary thyroid cancer

Background

In the past few decades, the incidence of thyroid cancer has increased significantly all over the world [1]. This could be related both to an increased rate of detection and to an increased number of cases due to thyroid-specific

carcinogens [2]. In the same period, there also seems to have been an increase in the incidence of Hashimoto's thyroiditis (HT) [3]—the most common inflammatory autoimmune thyroid disease [4]. Several studies have linked thyroiditis to thyroid cancer [5–12], and in particular to papillary thyroid carcinoma (PTC), which is the most common type of thyroid cancer [13]. Dailey et al. were the first to suggest a relationship between PTC and HT [14]. Chronic inflammation was hypothesized as the influencing factor in the correlation between PTC and HT—similar to the development of cancer in other locations [15]—determining an immune response that leads to chronic cell damage, genetic alteration and uncontrolled cell proliferation. It is still not clear whether HT is induced by the tissue response to cancer [16] or if HT induces the development of PTC [17], or if they are just concomitant incidental findings. The clinical importance of this correlation remains unclear. It seems that the concomitant presentation of HT and *well-differentiated thyroid cancer* may correspond to a less aggressive clinical presentation and better prognosis [18].

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The aim of our study was therefore to evaluate if the presence of thyroiditis is related to an increased incidence of thyroid cancer.

Methods

This was a retrospective study involving a series of 2304 total thyroidectomies over a 12-year period between 2004 and June 2016. 214 (9.3%) cases were subsequently excluded from our study due to insufficient data. In 2090 (90.7%) cases out of our sample it has been possible to compare the presence, or lack thereof, of thyroiditis by means of a histological diagnosis post-surgery.

Cases were collected and authorized by an institutional review board database of thyroid surgical operations (thyroidectomy, near total thyroidectomy, hemithyroidectomy), carried out by the General Surgery Unit, Department of Surgery, University Hospital of Parma, Parma, Italy.

The presence of thyroiditis was determined considering histological diagnosis taken post-surgery and we considered all types of thyroiditis, including focal, chronic lymphocytic thyroiditis, etc.

We decided to collect personal data of the patients, authorized by an institutional review board database of thyroid surgical operations, and we considered the correlation between any presence of thyroiditis and all the different final classifications, taken from the histological examination after pathologic analysis.

We then divided the different classifications into two groups: Group A included all the benign histological classifications, and Group B included all the malignant histological classifications. In each group, we then assessed the presence, or lack thereof, of thyroiditis.

This division into two groups was made in order to evaluate the correlation between thyroiditis and thyroid cancer and to assess if the presence of thyroiditis is linked to a higher incidence of thyroid neoplasia.

Data were analyzed using a chi-square test and Fisher's exact test. *P*-values of <0.05 were defined as statistically significant.

Results

A total of 2304 patients were enrolled in our study (1817 female and 487 male; with a mean age of 54.65 ± 13.85).

In 2090 (90.7%) cases out of our sample it has been possible to compare the presence, or lack thereof, of thyroiditis by means of a histological diagnosis post-surgery. 214 (9.3%) cases were excluded from our study due to insufficient data.

After histological examination, Hürthle cell adenoma was found in 75 patients: 27 (36.0%) with thyroiditis and 48 (64.0%) without; follicular adenoma was found in 136 patients, 43 (31.6%) with thyroiditis and 93 (68.4%) without; multinodular goiter was found in 1161 patients, 374 (32.2%) with thyroiditis and 787 (67.8%) without; papillary carcinoma was found in 600 patients, 224 (37.3%) with thyroiditis and 376 (62.7%) without; follicular carcinoma was found in 61 patients, 20 (32.8%) with thyroiditis and 41 (67.2%) without; medullary carcinoma was found in 10 patients, 1 (10%) with thyroiditis and 9 (90%) without; Hürthle carcinoma was found in 46 patients, 16 (34.8%) with thyroiditis and 30 (65.2%) without; anaplastic carcinoma was found in 1 patient, without thyroiditis (Table 1).

In our study, 1372 patients were diagnosed with a benign pathology (Group A) (Hürthle cell adenoma, follicular adenoma, and multinodular goiter), of them 444 (32.4%) had thyroiditis and 928 (67.6%) did not; whereas, 718 were diagnosed with a malignant pathology (Group B) (papillary carcinoma, follicular carcinoma, medullary carcinoma, Hürthle carcinoma, and anaplastic carcinoma), among those 261 (36.4%) had thyroiditis and 457 (63.6%) did not (Table 2).

We therefore found no statistically significant difference between those two groups ($P > 0.05$).

Discussion

In our study, we wanted to evaluate whether there is a correlation between the presence of thyroiditis and an increased risk of developing thyroid neoplasia. This topic has long been debated in scientific literature and over the years some studies have shown that there is a correlation [5–12], while others have supported the opposite hypothesis [17, 19–21]. In 2008, our group was already interested in this subject, and during a study involving 189 patients undergoing thyroid surgery between 2004 and 2007, we

Table 1 Patient's population

Histological classification	No. of patients	No thyroiditis	Thyroiditis
Hurtle adenoma	75	48 (64%)	27 (36%)
Follicular adenoma	136	93 (68.4%)	43 (31.6%)
MNG	1161	787 (67.8%)	374 (32.2%)
Papillary carcinoma	600	376 (62.7%)	224 (37.3%)
Follicular carcinoma	61	41 (67.2%)	20 (32.8%)
Medullary carcinoma	10	9 (90%)	1 (10%)
Hurtle carcinoma	46	30 (65.2%)	16 (34.8%)
Anaplastic carcinoma	1	1 (100%)	0 (0%)
Total	2090	1385 (66.3%)	705 (33.7%)

Table 2 Patients associated to benign pathology and malignant pathology

	Total	Group A (benign pathology)	Group B (malignant pathology)	<i>P</i> -value
No thyroiditis	1385 (66.3%)	928 (67.6%)	457 (63.6%)	> 0.05
Thyroiditis	705 (33.7%)	444 (32.4%)	261 (36.4%)	> 0.05
No. of patients	2090	1372	718	

found that chronic lymphocytic thyroiditis has only minimal impact on the development of thyroid neoplasms [22]. In our current study, involving a sample of 2090 patients, it emerged that Group B—in which we grouped all malignant diseases—is associated with a higher presence of thyroiditis than Group A—which contained all benign pathologies: 36.4% vs. 32.4%. However, this difference was not statistically significant. Even in this study, we did not find a statistically relevant correlation between the presence of thyroiditis and an increased incidence of thyroid neoplasms. Jankovic et al. [23], in a systematic review of studies that have been evaluating the correlation between thyroiditis and thyroid cancer, state that studies suggesting a positive correlation, and in particular those using samples obtained from thyroidectomies, suffer a selection bias. In fact, in most of the studies considered by them, indications for surgical treatment in patients with thyroiditis (HT) were not specified. It is also clear that indications for surgery differ between malignant and benign pathologies. The former are in most cases treated surgically, unlike the latter, and this means that most of the patients with thyroiditis are never candidates for surgery. To minimize this selection bias, Farrel et al. [24] decided to correlate the impact of thyroiditis with the incidence of incidental thyroid neoplasms, i.e. after histological examination, those tumors found outside the nodule that led to the indications for surgical treatment. Their study found that incidental thyroid neoplasms appear to be more common in moderate to severe thyroiditis, whereas mild thyroiditis does not seem to increase the risk of developing such tumors.

Even if, according to some studies, the presence of thyroiditis may promote the development of thyroid neoplasms, it has not yet been possible to find a pathogenic link that could explain this hypothesis [25]. Some authors have hypothesized that Hashimoto's thyroiditis, in the long term, may result in increased TSH serum levels, which seem to stimulate the development of thyroid neoplasms [26, 27]. Others, however, have contradicted to this hypothesis, claiming that Hashimoto's thyroiditis would increase the risk of developing thyroid cancer only in euthyroid patients [24, 28].

Some scientific literature has evaluated the correlation between PTC and HT, not analyzing post-thyroidectomy specimens, but using FNAB. In a study on 10,508 patients, Matesa-Anić et al. [29] failed to show any statistically significant correlation on cytological material. In addition, a Swedish study by Stockholm's Karolinska Hospital showed

no correlation between thyroid cancer, or any other solid neoplasia, and chronic lymphocytic thyroiditis [19].

From our analysis, we found an increased incidence of thyroiditis in malignant diseases compared with benign ones, but no statistically significant correlation between thyroiditis and an increased risk of developing thyroid cancer emerged. However, after postoperative histological examination, we noticed that in the separate analysis of the various classes of pathologies, papillary carcinoma appeared to be more often related to thyroiditis, with a 37.3% incidence in thyroiditis. In the last years also in Italy the number of thyroidectomy related to thyroid cancer is higher than in the past as the number of patients affected by thyroiditis. These two diseases are related to a higher rate of nerve palsy as reported by literature [30]. Especially in these cases the surgeon experience might significantly determine surgical outcome.

Conclusion

Our conclusion was that even if our data evidenced a higher presence of thyroiditis in malignant thyroid pathologies than in the benign ones, this evidence was not strong enough to be statistically significant. We found that papillary carcinoma is more often related to the presence of thyroiditis than all the other groups of thyroid pathologies we analyzed. Our data analysis showed that correlation between thyroiditis and a higher incidence of thyroid cancer remains yet to be defined.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. The datasets used and/or analyzed during the current study are available from the OU of General Surgery of AOU of Parma.

Author contributions All authors contributed significantly to the present research and reviewed the entire manuscript. All the authors have read and approved the final manuscript. P.D.R.: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of the data; also participated substantially in the drafting and editing of the manuscript. C.M.M.: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of the data. FC: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of the data. M.R.: Participated substantially in

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Consent to publish was given by AOU Parma Ethical Committee for Unit of General Surgery, Prot. No. 0047239 of 2017.

Informed consent All patients consented to publish their data.

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