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Original article

## Thyroid surgical practices shaping thyroid cancer incidence in North-Eastern Italy



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### ABSTRACT

**Aim:** To investigate the effects of changing surgical practices on thyroid cancer incidence in the Veneto Region (North-Eastern Italy).

**Methods:** Hospital discharge records of the period 2000–2010 were analyzed to detect trends in thyroid surgery rates by type of surgery and diagnosis. The association between surgery rates for benign and malignant diseases across the 21 Local Health Units (LHUs) was assessed by Poisson regression. In a second step, clinical and pathological charts of the year 2010 were retrieved from the larger regional surgical center. The proportions of total and incidental papillary thyroid micro carcinoma (PTMC) were compared with historical data. Factors influencing an incidental diagnosis of PTMC were analyzed by logistic regression.

**Results:** Among 26,000 procedures performed in the Region, there was an increase with time in the proportion of total thyroidectomies (from 67% to 78%) and surgeries with a diagnosis of thyroid cancer (from 17% to 28%). Cancer surgery rates across LHUs resulted associated to surgery rates for benign diseases ( $P < 0.001$ ). In the largest regional center, the proportion of PTMC increased from 35% to 56%, of whom almost 60% were incidental cases. The probability of finding an incidental PTMC was higher in total thyroidectomies than in other procedures (odds ratio = 1.84, 95% confidence interval 1.08–3.14).

**Conclusion:** Data from the Veneto Region suggest that the increase in PTMC is due to several factors: increased preoperative diagnosis, total gland removal, extensive histological examination. Moreover, geographical variations in cancer incidence were associated to surgery rates for benign diseases.

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## 1. Introduction

Thyroid cancer incidence is steadily increasing both in the US and Europe [1,2], with the largest increase observed for tumors  $\leq 10$  mm in diameter [1]. Thyroid cancer  $\leq 10$  mm has been defined as thyroid microcarcinoma, usually papillary (papillary thyroid microcarcinoma, PTMC); in a review of the literature published in 1966–2008, PTMC represented 28.8% of papillary thyroid cancer, 22.9% of all thyroid cancer, and 3.8% of all thyroidectomies [3].

However, these figures are raising over time: in France, the proportion of microcarcinomas among operated cancer increased from 18.4% in 1983–1987 to 43.1% in 1998–2001 [4]. In a study

from Italy, the prevalence of PTMC increased from 7.3% of all thyroid cancer in 1985–1994 to 36.4% in 1995–2005 [5]; another series from Central Italy showed a raise of microcarcinomas among differentiated thyroid cancer from 7.9% in 1969–1989 to 28.7% in 1990–2004 [6].

The increase of PTMC is therefore a main determinant of the raise in overall thyroid cancer incidence and can be explained by two main trends: first, an expansion in the rate of preoperative diagnosis of small lesions due to the widespread use of high resolution cervical ultrasound and fine needle aspiration biopsy (FNAB) [7]; second, an increase in the proportion of incidental thyroid cancer in patients undergoing surgery for preoperatively benign diseases. The latter proportion varies greatly between published reports, for example 5.0% in subtotal or total thyroidectomies performed in 1999–2004 in Poland [8]; 10.4% in patients operated in 2003–2005 in Central Italy [9]; 12.0% in patients operated from 2000 to 2008 in the US [10].

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The rate of incidental thyroid cancer at a population level can be heavily influenced by different surgical and pathological practices, which can be summarized in the following issues:

- overall surgical rates for benign thyroid disease: in France among women, the incidence of microcancers (but not that of all thyroid cancers) was correlated to the intervention rate for benign thyroid pathologies [11];
- extension of thyroid surgery: the prevalence of incidental thyroid carcinoma in patients operated for multinodular goiter was 10.7% in total thyroidectomies and 4.7% in subtotal resections [12];
- changing pathology workout, namely an increase in the number of slides derived from each surgical specimen. In patients undergoing surgery for retrosternal goiter in Australia (with no role for enhanced surveillance by ultrasonography), incidental thyroid cancer increased from 3.6% in 1966–1975 to 7.5% in 1996–2006; this rise was entirely due to PTMC and paralleled the increasing number of blocks sampled [13]. Furthermore, the prevalence of PTMC in thyroid surgery increased in Austria from 0.3% in 1975–1984 to 5.4% in 1995–2005, while the number of paraffin blocks per resected thyroid raised from 2.2 to 7.5 [14].

Aim of the paper is to investigate the effects of the above dynamics in the Veneto Region (North-Eastern Italy) in a two-step study. The first step was to analyze discharge records in the period 2000–2010 to assess trends for: overall thyroid surgery rates, type of surgery, and proportion of malignancies among operated subjects. The second step was to retrieve clinical and pathological data from the larger surgical center in the Region for the year 2010 to assess: the proportion of incidental PTMCs in surgeries for benign thyroid disease, the proportion of PTMCs among all thyroid cancers, and differences with historical data from a previous study carried out in the same institution [15].

## 2. Methods

### 2.1. Analysis of discharge records

On January 1, 2010, the total population of the Veneto Region was about 4,900,000 inhabitants; the Region is subdivided in 21 Local Health Units (LHUs), and there were about 900,000 discharges from regional hospitals each year. Discharge diagnoses and procedures are recorded according to the International Classification of Diseases, 9th Revision-Clinical Modification (ICD9-CM); the regional archive of hospital discharge records includes all hospitalizations in regional hospitals, as well as discharges of residents hospitalized outside the region, assuring a complete coverage of all major surgical procedures performed in the population.

All discharges of Veneto residents from January 1, 2000, to December 31, 2010 were selected if thyroid surgery was performed, classified in total thyroidectomy (ICD9-CM procedural codes 06.4, 06.50, 06.52) and other procedures, including lobectomy or other partial thyroidectomy (codes 06.2, 06.3, 06.51). Underlying pathologies were grouped in thyroid cancer (ICD9-CM diagnostic code 193), thyroid adenoma and few cases of thyroid/endocrine neoplasms of uncertain behavior (codes 226, 237.4, 239.7), and non-neoplastic thyroid diseases (codes 240–246); a limited proportion of discharges (about 1.5%) with other or inconsistent diagnoses were excluded from analyses. In case of subjects submitted to repeated surgical procedures, only the first hospitalization was considered.

Population surgery rates (overall thyroid surgery, and surgery for benign thyroid diseases and for thyroid cancer) were computed using denominator data from the National Institute for Statistics

[<http://demo.istat.it/>]; associations between procedural rates were tested by means of Poisson regression analysis.

### 2.2. Analysis of clinical charts at a tertiary institution

According to the regional discharge archive, about one-third of all thyroid procedures and above 40% of those with a diagnosis of cancer are performed in the Department of Special Surgery at the University of Padova. Clinical and pathological charts were therefore retrospectively reviewed for all thyroid surgeries performed in the Department during the year 2010.

Information was abstracted on: age and gender of patients; preoperative thyroid cytology and clinical indication for surgery; type of surgery (lobectomy, near-total thyroidectomy, total thyroidectomy); final histology of the removed gland; in case of malignancy, cancer histotype (medullary, anaplastic, follicular, papillary), cancer diameter, presence of multifocality, presence of lymph node metastases, and TNM staging. A PTMC was defined incidental when discovered at histologic analysis of the removed gland, in the absence of a malignant or suspect cytology, and in any other case (e.g. follicular cytology, or cytology not retrievable/inadequate) of a preoperative diagnosed benign disease. The local ethics board waived the requirement for informed consent for this retrospective study.

Bivariate associations between categorical variables were evaluated by the Chi-square test and between interval variables by the Wilcoxon rank-sum test. Factors influencing an incidental diagnosis of PTMC were assessed by means of logistic regression analysis. Analyses were repeated including or excluding subjects living outside the Veneto Region. All analyses were carried out by means of the statistical package Stata 11.

## 3. Results

### 3.1. Discharges for thyroid surgery

Overall from 2000 to 2010, about 26,000 thyroid surgeries were performed among residents in the Veneto Region. Through the study period, there was a limited increase in the yearly number of procedures, in the mean age of patients, and in the proportion of male subjects (Table 1). Crude intervention rates increased slightly, especially among the regional male population. There was a clear shift in the surgical approach, with a 10% rise in the proportion of total thyroidectomies among all thyroid

**Table 1**

Rates of thyroid surgery, type of procedure, reported diagnosis, and demographics of operated patients according to discharge records: residents in the Veneto Region, 2000–2010.

	2000–2003	2004–2007	2008–2010
<i>Surgeries, n/year</i>	2233	2344	2548
<i>Mean age, years</i>	51.9	52.7	53.3
<i>% males</i>	20.6%	21.1%	23.2%
<i>% total thyroidectomies</i>	67.0%	73.4%	77.6%
<i>Diagnosis</i>			
% thyroid cancer	17.8%	23.6%	28.0%
% adenoma	18.2%	17.2%	16.9%
% other thyroid diseases	64.0%	59.2%	55.1%
<i>Overall thyroid surgery rate (<math>\times 10^5</math>)</i>			
Males	20.8	21.5	24.8
Females	76.4	76.8	78.6
<i>Thyroid cancer surgery rate (<math>\times 10^5</math>)</i>			
Males	4.2	5.5	8.1
Females	13.2	17.8	20.9

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