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## Multifocality of thyroid carcinomas: a “privilege” of papillary tumors or not?

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**SUMMARY: Multifocality of thyroid carcinomas: a “privilege” of papillary tumors or not?**

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*Aim. To study the frequency of multifocality in well-differentiated non-medullary thyroid carcinomas and correlate it with various epidemiological factors, as well as with patients' survival.*

*Patients and methods. A retrospective study was conducted on 80 patients who underwent total thyroidectomy from January 1985 to December 2004 in the First Department of Surgery of University General Hospital of Alexandroupolis, Democritus University of Thrace, Greece, for well-differentiated non-medullary thyroid cancer (papillary and follicular). Patients' medical records and demographics, including age, gender, histological type (papillary, follicular), multiple foci of tumors, overall and specific survival were analyzed.*

*Results. Multifocality was established in 17/80 patients (21,25%). Multifocal tumors were found in 4/20 male patients (20%) and 13/60 female ones (21,67%), percentages which are almost identical. Increased rates of multifocal tumors were found in the age groups of 20-29, 30-39 and 70-79 years old, while low rates were documented in the age groups of 0-9, 10-19 and 60-69 years old. Follicular tumors had a 20% rate, similar to papillary tumors (22,2%), and an impressive multifocal rate of mixed papillary-follicular neoplasms (75%) was found. Finally, survival was not found to be influenced by the multifocality of the tumor, under the prerequisite that total thyroidectomy is applied.*

*Conclusions. Multifocality should not be considered as a “privilege” of papillary thyroid tumors, but as a privilege of thyroid carcinomas in general. If total thyroidectomy is applied in all benign and malignant thyroid diseases, the presence of multiple foci does not affect the prognosis and the survival of the patients.*

**RIASSUNTO: Multifocalità dei carcinomi tiroidei: un “privilegio” dei tumori papillari o no?**

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*Obiettivo. Studio della frequenza della multifocalità nei carcinomi tiroidei ben differenziati non midollari e della sua correlazione con diversi fattori epidemiologici, oltre che con la sopravvivenza dei pazienti.*

*Pazienti e metodi. Lo studio è stato condotto in 80 pazienti sottoposti a tiroidectomia totale dal gennaio 1985 al dicembre 2004 nel Primo Dipartimento di Chirurgia della Università della Tracia Democritus, Grecia, per carcinoma ben differenziato (papillare e follicolare). Sono stati analizzati età, sesso, tipo istologico, multifocalità dei tumori, sopravvivenza.*

*Risultati. La multifocalità è stata identificata in 17/80 pazienti (21,25%). Tumore multifocalizzato è stato trovato in 4/20 (20%) e in 13/60 donne (21,67%), in percentuali quindi sovrapponibili. Alta frequenza di multifocalità si è trovata nei seguenti gruppi di età 20-29, 30-39 e 70-79, bassa frequenza è stata trovata nei gruppi 0-9, 10-19 e 60-69 anni. La frequenza nei follicolari è stata del 20%, analoga a quella dei papillari (22,2%). Invece, frequenza molto alta è stata trovata nei tumori misti papillari-follicolari (75%). La sopravvivenza non è influenzata dalla multifocalità del tumore.*

*Conclusioni. La multifocalità non deve essere considerata un “privilegio” dei tumori tiroidei papillari, ma caratteristica comune dei carcinomi tiroidei. In caso di tiroidectomia totale la presenza di multifocalità non influenza ovviamente la prognosi e la sopravvivenza del paziente.*

KEY WORDS: Thyroid cancers - Multifocality.  
Carcinomi tiroidei - Multifocalità.

## Introduction

Thyroid carcinomas are usually papillary or follicular tumors, arising from the thyroid follicles. Until now, it is believed that multifocal tumors are, in majority, variants of papillary carcinomas. Estimates of the frequen-

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cy of multifocal papillary tumors vary in literature, ranging from 18%, up to 87% (1-5). On the contrary, various studies report a multifocal trend of appearance in follicular carcinomas as well (6-8), a form of presentation that in at least one study (9) affects the prognosis.

We report a series of thyroid tumors with multifocal origin, in which follicular tumors are found to be multifocal in at least the same frequency as the papillary tumors.

## Patients and methods

A retrospective study was conducted on 992 patients who underwent total thyroidectomy from January 1985 to December 2004 in the First Department of Surgery of an academic tertiary referral medical center (University General Hospital of Alexandroupolis, Democritus University of Thrace, Greece) for several thyroid diseases. Well-differentiated non-medullary thyroid cancer (papillary and follicular) was documented by histologic examination in 80 patients (8,1%).

Patients' medical records and demographics, including age, gender, histological type (papillary, follicular), multiple foci of tumors, overall and specific survival were analyzed using Statistical Package for the Social Sciences (SPSS), version 11.0 (SPSS, Inc., Chicago, IL, USA). Multifocality was defined as the presence of two or more loci, at distinctive positions of the thyroid gland, at the final pathology report.

## Results

Multifocality was documented in 17/80 patients (21,25%). Multifocal tumors in the same thyroid lobe as the primary site were found in 10/17 patients (58,8%), while malignant foci in the contralateral lobe were found in 7/17 patients (41,2%). The rate of patients with disease influencing both thyroid lobes was 7/80 patients (8,8%).

Regarding gender, male patients were 20/80 (25%) and female patients 60/80 (75%). Multifocal tumors were found in 4/20 male patients (20%), while the female group was presented with 13/60 ones with multiple loci (21,67%), percentages which are almost identical, without any statistical difference.

Age was another factor studied regarding the multifocality of thyroid cancer. The mean age of the study was  $45,55 \pm 15,05$  years. Increased rates of multifocal tumors were found in the age groups of 20-29, 30-39 and 70-79 years old, with 36,4%, 30,8% and 33,3% respectively, while low rates were documented in the age groups of 0-9, 10-19 and 60-69 years old (0%, 0% and 8,3%) (Fig. 1). Overall, a trend is observed, with multifocality appearing mainly in patients in the third and fourth decade of their life, while the increased rate in group 70-79 was insignificant, due to the small number of patients (1/3).

Histology was studied as another factor influencing

multifocality. Papillary tumors (papillary and mixed papillary-follicular neoplasms, 45/80 patients) had a multifocality rate of 22,2% (10/45 patients), while follicular tumors (including Hürthle carcinomas, 35/80 patients) had a 20% rate (7/35 patients), a rate similar to papillary tumors. More thorough analysis showed impressive multifocal rate of mixed papillary-follicular neoplasms (75%), low frequency of papillary carcinomas (10,8%) and multifocality rate of Hürthle carcinomas to be 0%, while the rate of follicular carcinomas was found statistically similar with that of the general population (24,1%) (Fig. 2).

Overall survival in the study was 93,8% (75/80 patients), with a mean follow-up time of  $95,25 \pm 74,42$  months. In the multifocality patients' group, the survival was found to be 94,1%, while in the patients with solitary tumors' group the survival was 93,7%, results that are statistically identical, thus documenting that survival is not influenced by the multifocality of the tumor, under the prequisition that total thyroidectomy is applied.

## Discussion

Multifocality of thyroid carcinomas is a characteristic documented in many patients undergoing surgery for various benign and malignant thyroid diseases. This characteristic is mainly identified in patients with papillary thyroid cancer, a histologic type that mostly gives metastases through the lymphatic system, which inside the gland forms a network of intralobular lymphatic vessels that connect the two lobes. In papillary carcinomas, the rate of multiple foci varies in the literature, ranging from 18% up to 87% (1-5). In our study, the rate of papillary multifocal tumors was found to be 22,2%, a value similar to the lower rates reported in the literature and similar to the overall rate of multifocality in our study (21,25%). This low rate is probably due to the application of total thyroidectomy for all benign diseases in our Department, a surgical practice which diagnoses papillary microcarcinomas in an early stage, before producing intrathyroidal metastases.

An extremely high rate of multifocality was found in patients with follicular variant of papillary carcinomas (75%). This is, to our knowledge, a result that is first documented in the literature, although the rate of multiple foci in these patients is reported high in some studies (8). The authors believe that more studies should be designed in this direction to verify this result or not, in order to examine the possibility of a second look in the treatment of patients with small incidental thyroid mixed-type tumors. Authors believe that all thyroid malignancies, even <1 cm, should be treated as potentially lethal, and total thyroidectomy should be applied all cases.

Follicular tumors were found to have almost similar

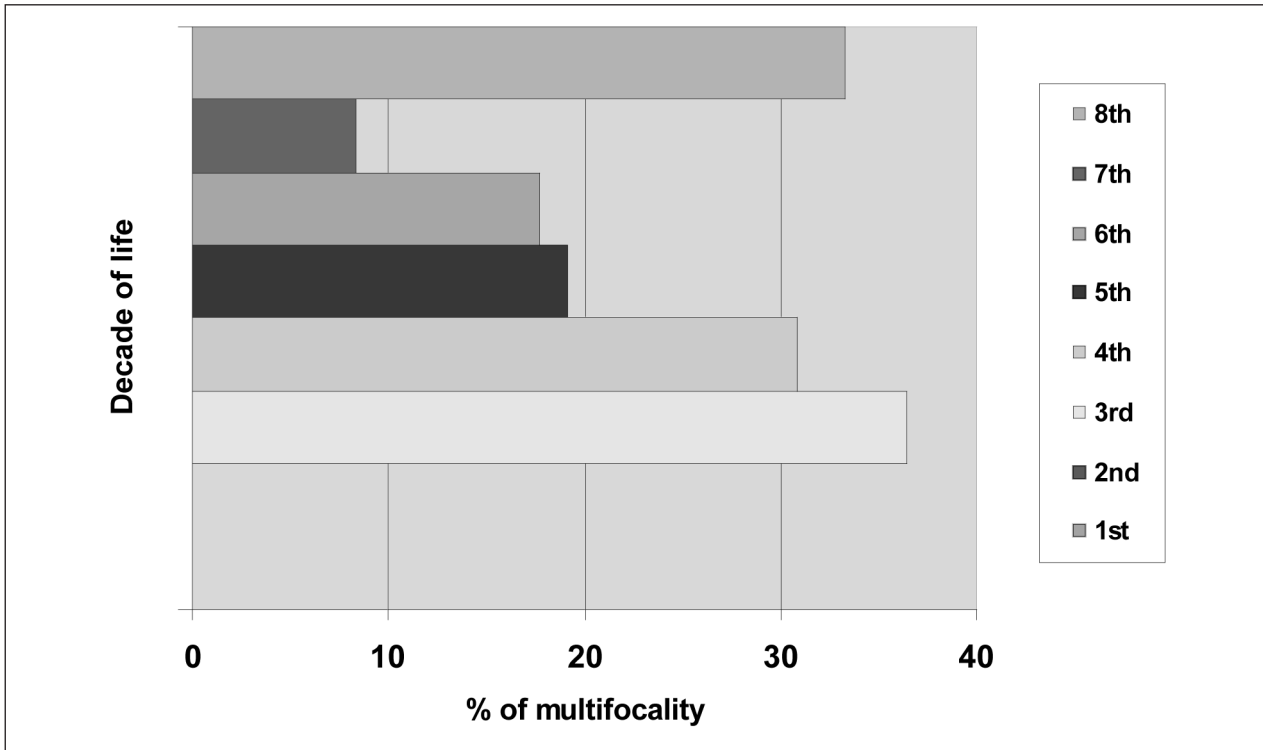


Fig. 1 - Age and multifocality.

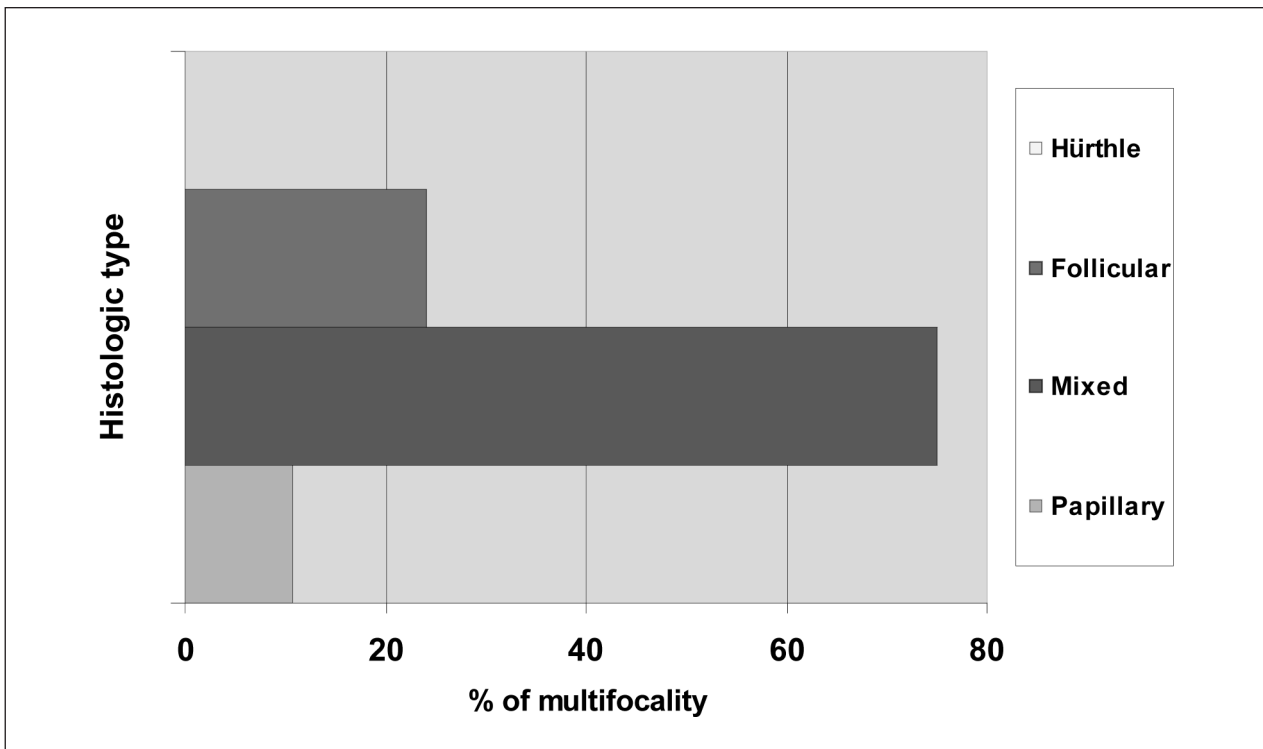


Fig. 2 - Histologic type and multifocality.

frequency of multifocality with papillary tumors (20% *vs* 22,2%). This is another result of our study that is extremely interesting, since until nowadays, it is believed that multifocality is a characteristic found in papillary tumors. Some authors report high rate of multiple loci in follicular neoplasms (6-8), but the rate of multifocality in follicular cancer is not yet clarified.

Hürthle-cell carcinomas were found to have a very low (0%) rate of multifocality. This is a finding that, although is recorder in a small population (6 patients), comes in consent with previous studies (7, 8) which documented the very low frequency of multiple foci in this type of cancer.

Gender was not found to be a significant factor for the presence of multifocal tumors. On the contrary, age was found to play a significant role in the appearance of multifocality. From the results of our study, patients between 20-39 years old seem to have an increased risk for developing multiple thyroid tumors. This result is very important and should be put under further investigation, in order to confirm it or not and to possibly re-examine the surgical treatment applied on these patients for various benign and malignant diseases, and especially multinodular goitre.

Finally, survival does not seem to be influenced by

the presence of multifocality in thyroid tumors. The survival rates in patients with or without multiple loci were found to be identical, in contrast with previous studies that report multifocality as a factor that worsens prognosis (9). This is a finding that, although important, should not misguide the surgeon in performing operations other than total thyroidectomy, because these results come from a Department that performs total thyroidectomy in all cases, thus eliminating the possibility of presence of thyroid carcinomas in the contralateral lobe, carcinomas that are misdiagnosed when performing less-extensive procedures.

## Conclusions

Multifocality should not be considered as a “privilege” of papillary thyroid tumors, but as a privilege of thyroid carcinomas in general. It could be present in all histologic types of non-medullary thyroid cancers, with a very high frequency in follicular variants of papillary carcinomas, especially in younger patients (20-39 years old). If total thyroidectomy is applied in all benign and malignant thyroid diseases, the presence of multiple foci does not affect the prognosis and the survival of the patients.

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