

# The Assessment of Prognostic Histopathological Parameters Depending on Histological Patterns of Papillary Thyroid Carcinoma

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**ABSTRACT:** Papillary thyroid carcinoma represents common injuries that can have different histological variants that may influence the patient's prognosis. The study included a total of 44 papillary thyroid carcinomas, for which were followed a series of histological factors of aggressiveness for grading tumors. Most studied papillary carcinomas corresponded to the conventional type, followed by the follicular, micropapillary and tall cell variants. Depending on the presence of nuclear atypia, tumor necrosis, the frequency of mitosis, also the vascular invasion and the extrathyroidian extension there were distributions differences of the cases according to the tumor type, most of the cases belonged to the conventional and tall cell types. The assessment of histopathological parameters of aggressiveness with certain types known to have an unfavorable behavior, justify the use of the histological grading of papillary thyroid carcinomas.

**KEY WORDS:** papillary thyroid carcinoma, histological grade, tumor type

## Introduction

Papillary carcinoma is a well-differentiated malignant tumor developed from the thyroid follicular cells, which shows a series of characteristic nuclear changes and in even with the growth pattern is frequently papillary, it is not required for the diagnosis [1].

Papillary thyroid carcinoma (PTC) represents 1% of all malignances [2] and about 70-80% of all thyroid cancer [3]. The incidence of thyroid carcinoma types is quite different in various studies [4-7]. In a study, conventional papillary carcinoma was 46% of the carcinomas, followed by the micropapillary carcinoma with 27,8%, by follicular variant (17,6%), tall cell variant (4%) and the diffuse sclerosing variant (1,8%), rarely been noticed the variants: solid, diffuse follicular, papillary carcinoma with focal insular component, columnar cells, necrotising-like stroma and oncocytic one.

Differentiated tumors, papillary and follicular, are mostly treatable and curable. Most of the patients with PTC have good prognosis and long-term survival in cases without distant metastases. Though, have been reported different histological patterns that may influence these patients prognostic.

In this study we followed some histological factors of aggressiveness for grading tumors and the association with the different variants of papillary carcinomas.

## Material and Methods

The current study included a total of 44 papillary thyroid carcinomas from patients hospitalized and operated in Surgery Clinics of Emergency County Hospital of Craiova, in the period 2008-2012. The surgical pieces were fixed in 10% buffered formalin, processed by the usual technique with paraffin embedding and Hematoxylin-Eosin stain. Classification of the tumors was made in accordance with literature data. Tumors subclassification has been made considering that must contain at least 75% (arbitrary cutoff value) of the tumor composition of a given tumor type before being detected as specific sub-type and the variant follicular it must be 100% [8, 9].

For all investigated cases we were interested in a series of histological features as: presence/absence of nuclear atypia, presence/absence tumor necrosis, mitotic frequency on 10 areas with 40x microscopic field (MF), presence/absence of vascular invasion, presence/absence of capsular invasion and the presence/absence of extrathyroidian extension.

The histological grade of the examined tumors was defined as a summary of this histological features, grade 1(G1) was recorded when none of the histological features were

present and grade 2 (G2) was recorded when one or more of these features were present.

Parameters recorded were stored in an electronic database and statistically analyzed using SPSS 10 automatic software by using chi-square test, which analyzed the dependence between the classification factors, values below 0.05 being considered significant.

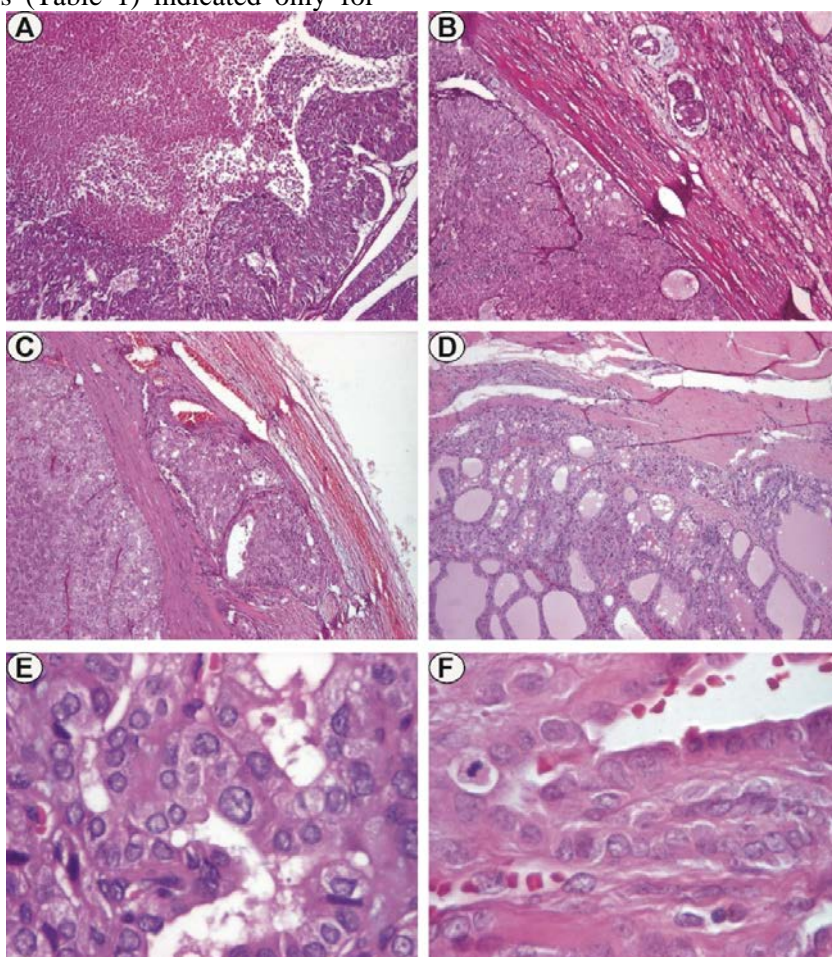
## Results

The analysis of the 44 studied papillary thyroid carcinomas noticed that most of investigated papillary carcinomas corresponded to the papillary conventional type with 25 cases (56,8%), followed by the follicular variant in 11 cases (25%), micro papillary carcinomas in 5 cases (11,4%) and the tall cell variant in 3 cases (6,8%).

The analysis of histopathological parameters of aggressiveness (Table 1) indicated only for

the tall cell variant of papillary carcinomas the association in all cases with the presence of aggressiveness markers. The three papillary carcinomas, tall cell variant presented in all cases necrosis (Fig.1A), nuclear atypia and mitosis, more frequently than the rest of the tumors (3-4 mitosis on 10 areas/ 40x MF), and also vascular invasion (Fig.1B), capsular invasion (Fig.1C) and extrathyroidian in the tracheal muscle.

In contrast, papillary microcarcinomas and most of the follicular variant of papillary carcinomas didn't associated these features. For the follicular variant of papillary carcinomas we observed the absence of nuclear atypia, of tumor necrosis and the vascular invasion. However we found for 5 cases the capsular invasion and in one case even the extrathyroidian one (Fig.1D) but the mitosis were 1-2 on 10 areas/40x MF.



**Fig.1. A. Extensive necrosis, tall cell variant of papillary carcinoma, HE stain, x 40; B. Tumor capsular vessels invasion, tall cell variant of papillary carcinoma, HE stain, x 40; C. Tumor capsular invasion, tall cell variant of papillary carcinoma, HE stain, x 40; D. Tracheal muscular tunic invasion, follicular variant of papillary carcinoma, HE stain, x 40; E. Low atypia, conventional variant of papillary carcinoma, HE stain, x 400; F. Atypical mitosis, conventional variant of papillary carcinoma, HE stain, x 400**

In case of conventional papillary carcinomas we noticed the nuclear atypia (Fig.1E) in 5

cases, focal necrosis in 2 cases and in 3 cases 3-4 mitosis on 10 areas/40x MF (Fig.1F). Vascular

invasion was noticed in 4 cases, capsular invasion in 6 cases and extrathyroidian extension in 4 cases.

In relation with the differentiation degree, papillary micro carcinomas, conventional papillary carcinomas and the follicular variant

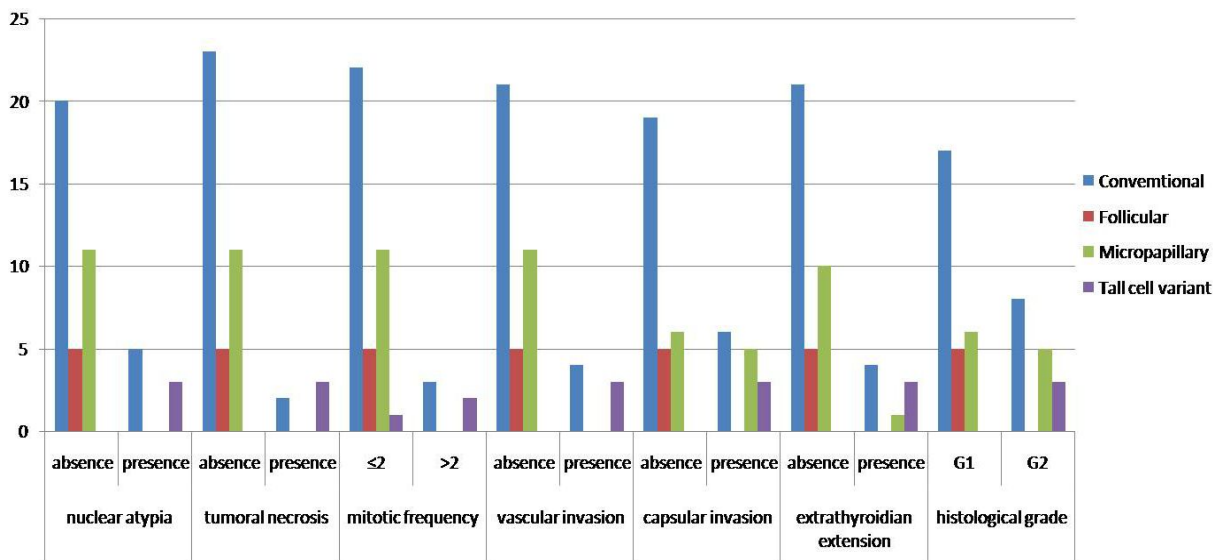
present tumoral degree 1 in most of the cases (100%, 68% respective 54,5%), while all the tall cell carcinomas have degree 2, aspects which were statistical significant ( $p < 0,05$ , chi square test) (Table 1).

**Table 1. Cases distribution in relation to the analyzed histopathological parameters and tumor type**

Parameters/ Tumoral type		Conventional	Micro papillary	Follicular	Tall cell variant	P value
nuclear atypia	absence	20	5	11	0	0,001
	presence	5	0	0	3	
tumoral necrosis	absence	23	5	11	0	0,000
	presence	2	0	0	3	
mitotic frequency	≤2	22	5	11	1	0,011
	>2	3	0	0	2	
vascular invasion	absence	21	5	11	0	0,000
	presence	4	0	0	3	
capsular invasion	absence	19	5	6	0	0,000
	presence	6	0	5	3	
extrathyroidian extension	absence	21	5	10	0	0,000
	presence	4	0	1	3	
histological degree	G1	17	5	6	0	0,003
	G2	8	0	5	3	

The statistical analysis of the cases distribution regarding the tumor type and the histopathological parametres of interest, indicated significant differences (table 1). Thus, in relation with the presence of nuclear atypia, tumor necrosis, mitosis frequency, and also the

vascular invasion and the extrathyroidian extension there were differences of distribution according to the tumor type, most of the cases being the conventional papillary type and the tall cell variant ( $p < 0,05$ , chi square test) (Fig.2).



**Fig.2. Graphic distribution of the cases in relation with the classification factors**

Regarding the follicular variant of papillary carcinomas a small number of cases associated the extrathyroidian extension, capsular invasion being more frequent ( $p < 0,05$ , chi square test).

### Discussions

In the current study involving 44 papillary thyroid carcinomas more than half were

conventional type (56,8%), followed in order of frequency by the follicular variant in quarter of cases (25%), more rare being the papillary micro carcinomas (11,4%) and the tall cell carcinomas (6,8%). The papillary carcinomas subclassification may be difficult in most of cases with more than one architectural type or cellular patterns, tumors shoulding have at least 75% of tumor component of a certain type before they were classified as a specific subtype and for the follicular variant is practically 100%. [8, 9] The patients with papillary carcinomas have the best surviving rate from all types of thyroid cancers, with a 10 year rate up to 95% [10] or by other studies the survival at 5 years is 96% and at 10 years of 93% [11]. Though, these values can be modified depending on other prognostic factors. Pathological variables associated with poor prognostic include the presence of less differentiated or solid areas, vascular invasion and aneuploid cell population [8, 12-15]. These features are well known as aggressiveness factors in most of the malignant tumors and can be evaluated independent of growth pattern and the tumor cells type [8], which may be an advantage in the cases in which the subclassification is difficult because of the complex and heterogeneous tumors structure. Some authors recommend that for all papillary carcinomas to be given a histological grade based on the combined examination of nuclear atypia, tumor necrosis and vascular invasion [8]. It is believed that at least four subtypes of papillary carcinomas should be considered with unfavorable prognosis: tall cell variant, diffuse sclerosing variant, solid variant and follicular variant [16].

All tall cell papillary carcinomas were associated with the aggressiveness factors, the 3 cases corresponding to grade 2. The local recurrences and the tracheal invasion are not rare, the last one complication being fatal sometimes [16]. In a recent study, 278 patients with tall cell variant of papillary carcinoma had a higher rate of extrathyroidian extension (53,6% vs 30,2%,  $p < 0,0001$ ) and lower specific survival with no disease at 5 years (81,9% vs. 97,8%,  $p < 0,0001$ ) compared to 2522 patients with conventional papillary carcinoma [17].

Conventional carcinomas corresponded in 8 cases to grade 2 (32%), being associated with nuclear atypia (5 cases), tumor necrosis (2 cases), and presence of 3 mitosis on 10 ares/40x MF (3 cases), vascular invasion (4 cases), capsular invasion (6 cases) and extrathyroidian extension (4 cases). Even if the papillary thyroid

carcinomas prognostic is in generally good, some tumors are more aggressive, their evolution being related with some histopathological features.

The classification of these features in 2 risk groups indicated in some studies that patients with high-grade tumors present 50% death risk trough thyroid cancer after 15 years, compared to only 5% for patients with low-grade tumors.

We identified nuclear atypia in 8 cases (18,1%) of investigated papillary carcinomas, of which 5 cases were the conventional type and 3 cases tall cell variant, aspects that were statistically significant ( $p < 0,05$ , chi square test). The nuclear atypia was recognized as an important prognostic factor for papillary carcinomas [18], and the marked nuclear atypia can be associated with DNA aneuploidy.

In our study, vascular invasion was noticed in all tall cell variant of papillary carcinomas, in 6 cases of follicular variant (54,5%) and in 5 cases of conventional variant (20%) ( $p < 0.05$ ). Identification of the tumor vascular invasion it is an aggressiveness sign, because it leads to hematogenous invasion, distant metastasis, and therefore unfavorable prognosis [19]. For the differentiated thyroid carcinomas it was found that intra or extrathyroidian vascular extension goes to local recidives and distant metastasis, more frequent in papillary carcinomas [20].

Extrathyroidian extension of tumors was identified behind tracheal wall, at the muscular tunic, in all tall cell papillary carcinomas, in 4 cases of conventional carcinomas (16%) and in one case of follicular variant of papillary carcinomas (9,1%), which was statistically significant ( $p < 0,05$ , chi square test). Tumor extension beyond the thyroid capsular is in generally associated with unfavorable prognosis and some studies, by multivariate analysis, indicated that as a negative prognostic factor [21].

## Conclusions

The association of histopathological parameters of aggressiveness with certain variants known to have an unfavorable behavior, justifies the useful of the histological grading of papillary thyroid carcinomas.

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