

**UNIVERSITY OF MEDICINE AND PHARMACY
CRAIOVA**

SUMMARY

DOCTOR'S DEGREE THESIS

**THE ROLE OF EPITHELIOMESENCHYMAL TRANSITION IN
THYROID CARCINOGENESIS**

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INTRODUCTION

The Thyroid Carcinoma represents 1% of all malignant diseases, with a continuous growth of its incidence in the last 30 years.

The Thyroid Nodules are a very frequent pathology, almost 5% of their total being malignant. The importance of the pre-surgical diagnosis is significant in order to avoid a large number of useless surgical interventions. The history of the clinical exam, lab analysis and imagistic methods (especially the ecography) can only bring partial information. High hopes relies now on immunohistochemical methods of analysing harvested tissue by aspiration biopsy puncture with thin needle in order to obtain a pre-surgical diagnosis.

This study aims to emphasize the role of the epitheliomesenchymal transition in Thyroid Carcinogenesis and the role of some specific markers in identifying carcinomas with progression risk and metastasis.

Actual Data Regarding Carcinogenesis

During the last few years, a challenging progress was recorded in understanding the molecular pathogen process of Thyroid Cancer and in solving the role of many major signalling ways and of molecular damages implied, which lead to identifying new molecular markers useful in the diagnosis and prognosis of Thyroid Cancer. §

The most important signalling ways in Thyroid Cancer are:

- The way RAS/ RAF/ MEK/ ERK= the way MAPK (mitogen protein kinase activated)
- The way RI 3K/ AKT/ mTOR – the way lipid kinase- phosphoinositide 3- kinase

Cellular signals which influence the genes expression, which manage the cellular process.

Encoding protein genes from the signalling process (RET,RAS, BRAF, PI3K, PTEN, AKT) are mutant or abnormal expressed in Thyroid Cancer derived from follicular thyroid cells.

- Another important mechanism in Thyroid Tumour's genesis is the activation of suppressor tumour genes suppressed epigenetically by hypermethylation (Rap 1 GAP, RAS, p16).
- The prognosis factors used in most of the prognosis (AGES, MACIS, AMES, EORTC, GAMES, IGR, SAG, MTCTCS, UAB and MDA, pTNM) are: age, sex, family history, tumours' dimensions, localizing and infiltrating beyond the tumour capsule, tumour subtype , vascular invasion and ganglion metastasis. The most used assessment system is TNM.

Molecular factors involved in Thyroid Tumour Genesis

- The study of oncogene changes as possible mechanism of Thyroid tumour genesis lead to uncertain results yet regarding the possibility of using those as markers.
- The RAS oncogene activation as early event in Thyroid carcinogenesis, the BRAF mutations as marker of aggressive subtypes of Papillary Thyroid Cancer, the mutations of P53 gene as late events related to unfavourable prognosis, the assessment of genes NM 23, CD 44V6, EGFR as markers of metastasis are just few of the mechanisms which actual studies rely on as regarding the possibility of their use as markers in the evolution of carcinogenesis.

To be also mentioned galectin 3, oncogene c-Met, the protein family MMP, thelomerasis, the expression hTERT, which make the object of many recent studies.

The Purpose and Motivation of the Study

This study has as goal the expansion of knowledge on Thyroid Carcinogenesis with a particular focus on the study of action mechanisms of different factors involved in epitheliomesenchymal transition, its role in tumour progression with the purpose of identifying the most specific markers of invasive differentiated and metastatic Thyroid Tumours prognosis.

To reach out this goal, I focused on:

- Identifying and defining the parameters clinical-epidemiological and ecographic specific to differentiated Thyroid Cancers.
- Identifying and defining the parameters histopathological and immunohistopathological specific to differentiated Thyroid Carcinoma.

Methods used:

- Analysis of parameters clinical-epidemiological
- Histopathological Analysis – the assessment of tumour type and subtype
- Immunohistochemical Analysis- markers' analysis in order to establish significant bridges to the early diagnosis, the progression and prognosis of Thyroid Cancer.

Study Material and Methods

- Researched material – 49 differentiated Thyroid Carcinoma were studied, selected on a 8 years interval (2007-2014) from the patients hospitalized and operated in Surgery Clinics of Emergency County Hospital of Craiova, and histologically diagnosed in the Anatomical-Pathology Lab of the above mentioned hospital (SCJU- Craiova).
- For the clinical-epidemiological study we investigated the patients' past and present observation charts.
For the imaging study, we made ecographic investigations 2B, Doppler. The morphology study aimed to identify the macro and microscopic parameters of tumours.
- For the immunohistochemical analysis, 43 cases were selected. The antibodies used in this study aimed to identify: CK 19, Vimentin, E-cadherin, N-cadherin, Twist.

Results

The study included 49 differentiated Thyroid Carcinoma, 44 cases of Papillary Carcinoma and 5 cases of Follicular Carcinoma.

The clinic-epidemiological study showed an incidence growth of Thyroid Carcinoma in the last 4 years of the study. The patients' age varied between 22 and 83 years with a maximum incidence around the age of 60. The undeniable dominance of female sex in patients with Thyroid Carcinoma was F/M of 8, 8/1

The risk factors analyzed were:

- Radiation exposure – the irradiation for diagnosis purposes was identified in all patients compared to the irradiation for therapy purpose only found in 7 patients. The period of time between the irradiation and tumour identifying varied between 11-15 years.

- Personal or heredo-collateral past history of Thyroid disease indicated its presence in 30,6% of cases (15).

TABLE1. CLINICO-EPIDEMIOLOGICAL PARAMETERS ACCORDING TO CARCINOMA TYPES

PARAMETERS		PAPILLARY CARCINOMA		FOLICULARRY CARCINOMA	
		No.cases	Percentages%	No.cases	Percentages%
Age	< 45	16	32,7	1	2
	≥ 45	28	57,1	4	8,2
Sex	female	39	79,6	5	10,2
	male	5	10,2	0	0
Therapy irradiation		7	14,3	0	0
Thyroid Adenoma	personal	3	6,2	0	0
	Family	1	2	0	0
Family Thyroid Cancer		1	2	0	0
Endemic goiter		3	6,2	0	0

The imagistic study of differentiate Thyroid Carcinoma. Thyroid Tumours were hypoecogenous 89,8% , solid in 71,5% of cases, 2% cysts, 26,5% with mixed structure. Smooth calcified shapes were present in 65,3% of u. Mixed vascular activity was present in 31 cases, central in 10 and only peripheral in 8 cases. 59,2% had 2,1-4 cm maximum diameter when found Metastatic adenopathy was present in 20,4% of cases (10). Morphology study- the macroscopic study confirmed the results of the ecography. The study of histological patterns on differentiate Thyroid Carcinomas had as result the discovery of 44 papillary carcinomas and only 5 follicular carcinomas (89,8%).

TABLE 2. THE DISTRIBUTION OF PAPILLARY CARCINOMAS ACCORDING TO THE TUMORAL SUBTYPE

HISTOPATHOLOGICAL TYPE	NO.CASES	PERCENTS%
Conventional	23	52,3
Follicular	13	29,5
Papillary microcarcinoma	4	9,1
With high cells	3	6,8
Oxyphilic	1	2,3

TABLE 3. HISTOLOGICAL VARIANTS OF FOLLICULAR CARCINOMAS

VARIANT	CONVENTIONAL	ONCOCYTIC	WITH CLEAR CELLS
No. Cases	3	1	1
percents%	60	20	20

Study of Aggressive Histopathological Parameters in Follicular Carcinomas

TABLE 4. VARIOUS FOLLICULAR CARCINOMAS ACCORDING TO THE PARTICULARITIES OF THE CAPSULAR INVASION

TUMOR SUBTYPE	FC WITH MICROSCOPIC CAPSULAR INVASION	FC WITH MACROSCOPIC CAPSULAR INVASION	FC WITH ANGIO INVASION
No. Cases	2	1	4
percents%	50	25	80

Risk and TNM Stadialization of Thyroid Carcinomas

TABLE 5. TNM STADIALIZATION OF DIFFERENTIATE THYROID CARCINOMAS

STAGE	TNM	NO.CASES	PERCENTS%
Under 45 years old			
I	any T any N M0	16	32,6
Over 45 years old			
I	T1 N0 M0	4	8,2
II	T2 N0 M0	18	36,7
III	T3 N0 M0	2	4,1
	T1 N1a M0	2	4,1
	T2 N1a M0	2	4,1
	T3 N1a M0	2	4,1
IVA	T4a N1 M0	3	6,1

Immunohistochemical Study of Differentiate Thyroid Carcinomas

We analyzed a number of 43 Thyroid Carcinoma. For all cases studied, we compared progressively some of the markers::CK 19, Vimentin, E- cadherin, N-cadherin and Twist, as well as correlations with clinical-pathological studied factors. For CK19, in Papillary Carcinomas the reaction was intense, with a marked percentage of 79,8% compared to the Follicular Carcinomas with moderate intensity reaction and a marked cells number of 10%, these differences being significant- statistically speaking.

For Vimentin, its analysis regarding the percentage and intensity of the marking for the two types, the results were significant different for the two large classes of Thyroid Carcinomas: in primitive and metastatic Papillary Carcinomas, it was identified in 48,8% base subnuclear, in the Follicular ones, it was identified diffuse cytoplasmatic in 75% of the cases. Significant variations of the Vimentin positivity were also recorded in the subgroups from the two large patterns of the Thyroid Carcinoma.

The immune-expression of E-cadherin was identified at membrane and cytoplasmatic level in 84,6% of Papillary Carcinomas and only with membrane localizing in all Follicular Carcinomas analyzed.

Also, the values of E-cadherin immune expression varied significantly according to the tumour' s degree, being undeniably larger in stages T1-T2 compared to T3-T4.

The N-cadherin immune expression was identified both at membrane and cytoplasmic level in 76,9% of Papillary Carcinomas and only with membrane localizing in all cases of Follicular Carcinomas analyzed.

The metastasis had the same reaction as the primitive tumour. We identified significant differences of N-cadherin immune colouring according to the dimension and extension of the tumour (T category), as we recorded increased values in advanced stages and with ganglion metastasis.

TWIST immune expression (factor of nuclear transcription) was found in 79,5% of Papillary Carcinomas and in all cases of Follicular Carcinomas analyzed, without significant marking differences. The metastasis corresponding to the investigated tumours were positive to this marker. We noticed significantly statistic differences of the Twist marking according to the dimension and extension of the tumour.

Discussions

The increase of the Thyroid Cancer's incidence is usually seen as a real increase of the disease but also it can reflect the change of histopathological diagnosis criteria or as being the result of the increase of diagnosis investigations. (60;61). As the diagnosis techniques for the Thyroid Carcinoma became more and more sensitive, as such the ecography and aspiration puncture with thin needle, it made possible to detect subclinical lesions.

In our study, differentiate Thyroid Carcinomas were diagnosed in 49 cases, meaning 92,4% from the total of malign Thyroid tumours in an interval of 8 years. The number increased from 4-5 per year in the first 4 years to 8-9 new cases/year in the last 4 years. The tumours' incidence was 89,8% in female cases, this ratio of 8/1 being higher than in studies done in America and Europe but lower compared to the figures from the studies published in Japan, 13:1 (147).

The analysis of age groups distribution of the 49 cases studied showed an increasing trend from the third decade of life with a maximum at 60 years old; data similar to the ones in the literature.

The past history of irradiation for diagnosis purposes, studied as risk factor, was present in all the cases of our study, confirming the data from the literature according to whom (324,291,315) the external irradiation of the throat during childhood increases the risk of Papillary Thyroid Carcinoma.

The most frequent first sign of Thyroid Cancer is the nodule (139). In our study, the majority of patients were asymptomatic, the reason for coming to the doctor being a Thyroid mass or a palpable / felt lump in the throat's area.

The ecography represents the ideal imagistic method in order to detect and assess a Thyroid nodule, allowing: detection, nodule or metastasis specification and follow up after a surgical treatment. It is used as guiding system for the biopsy with thin needle puncture. The malignity criteria are: hypoechogenic, the report high/large >1, nonhomogenous structure, the presence of calcifications, uncertain/irregular shape. In Doppler mode, mixed hypervascularity (central and peripheral) is a criteria of malignity.

In our study, 89,8% of Thyroid Carcinoma were hyperechogenic, 59,18% had diameter between 2,1-4cm and 18% had maximum diameter > 4cm, 94,75% were solid, 26,5% had mixed structure, 34 cases (69,4%) had calcifications, from which 32 were punctiform (65,3%) – the data confirms the literature statistics (383).

In our study, all tumours had imprecise shapes.

As for the vascularisation, 63,2% (31 cases) was mixed (central and peripheral). The majority of studies concluded that the presence of central vascularisation supports the malignity diagnosis (11;39) Bakhshae and co. (14) find that 90% of the nodules with mixed vascularisation are malign.

The current study reveals metastatic adenopathies present in 10 cases (20,4%), with calcifications in 8 cases and cyst aspects-associated or not to micro calcifications- in 3 cases. There are authors (192) who consider that all adenopathies with microcalcifications or cyst aspect should be regarded as malign. The peripheral vascularisation of these lumps – associated or not with hilar vascularisation- is also a malignity criteria. In the histopathological study were analyzed 49 Thyroid Carcinoma, from which 44(89,8%) were Papillary Carcinoma and only 5 (10,2%) Follicular Carcinoma. In the specific literature, Papillary Thyroid Carcinoma represents the most common type of Thyroid Cancer (70-80% of all cases of Thyroid Cancer) (184). Similar studies reported 88% Papillary Cancer, 9% Follicular Cancer and 3% low differentiate Carcinoma.

Papillary Thyroid Carcinoma represents 1% from the total of malign diseases (178). The subtype of Papillary Carcinoma-conventional variant- represented 56,8% of all Papillary Cancers analyzed, in the specific literature being reported in almost 46% from Papillary Thyroid Cancers.

The microscopic characteristics of Papillary Carcinomas are: larger nucleus than the one of neoplastic cells (30-40 μm^2 la 97-110 μm^2)(173), irregularities of nuclear shapes, the presence of nuclear incisions and in 50% of the cases (2) the presence of nuclear inclusions. The psammatosae bodies are distinctive calcifications found in 40-50% of Papillary Carcinomas (109,40). They can be isolated. In our study, they were present in 14 of the conventional Papillary Carcinoma analyzed. They can be also found in benign cases (83). Other changes as: cellular necrosis on top of papillae, sclerotic type fibrosis or rarely desmoplastic, scumous metaplasia, a certain degree of cystic transformation are to be found with a variable frequency in the Papillary Cancer.

Beside the conventional shapes, the Papillary Carcinomas can represent a great variety of histological patterns. During our study, we found the Follicular variant in 13 cases (29,5%), Papillary Micro carcinomas in 3 cases (6,8%) and the oxyphilic in just one case (2,3%).

The microscopic characteristics of the Follicular variant are the nuclear particularities specific and present on the entire tumour and/or if there is a capsular invasion and/or capsular vessels. (203).

The variant with high cells is characterized by high cells, disposed „standing” (H/ L >2) with intense eozinofilic cytoplasm and pattern with well developed papillae, elongated (389, 64, 92).

Follicular Carcinoma represents 10-17% from Thyroid malign tumours (329; 94). During our study, we identified 5 cases (10,2%). The growth pattern varies from small or medium folliculae which contain colloid to the ones trabecular or solid. The diagnosis of Follicular Cancer is conditioned by the identifying of the capsule and /or vascular invasion. (329). Some authors consider that capsular invasion without vascular invasion does not justify the diagnosis of Follicular Carcinoma (144).

The most popular standard system of Thyroid Carcinoma is UICC/TNM, based mainly on the tumour's degree and the patients' age.

During the current study of the 49 carcinoma analyzed, 20 cases (40,8%) corresponded to stage I , 18 cases (36,7%) to stage II, 8 cases (16,4%) to stage III and 3 cases (6,1%) to stage IV.

Recently, according to this system, it was defined an European agreement which establishes three risk categories (262):

- Low risk: T1, one-focal (<1cm),N0 M0 without extension beyond the Thyroid capsule and with favourable histology (classical variant of Papillary Carcinoma or Follicular Carcinoma)
- Moderate Risk: T1 (>1cm) or T2N0M0 – or multifocal T1N0M0
- High Risk: any T3 and T4 or any T with N1 or M1.

In patients with differentiated Thyroid Carcinoma, the prognosis is clearly related to the stage of the disease. In patients with stage I Carcinoma, the specific cause mortality is of almost 1% at 20 years, but it rises to 25-45% at 10 years for patients on stages III-IV.

Immunohistological Study of Differentiated Thyroid Carcinoma

The epithelial-mesenchymal transition (EMT) is a differentiation process transforming epithelial cells into a mesenchymal phenotype and it is part of the cancer's progression (343). It is a mechanism that endows the epithelial cells with significant migratory mesenchymal properties, playing an important role in metastasis and tumour recurrences (158, 380). EMT also acts by introducing a high resistance to apoptotic factors (212, 357).

Being regarded as a fundamental process for tumour dissemination, we researched the exploitation of this mechanism with the purpose of finding ways to inhibit or even reverse this process and, by consequence, to inhibit the tumour metastasis (343).

For this purpose also, we searched to assess the expression of a panel of markers containing: cytokeratin 19, Vimentin, E- and N- cadherin and TWIST.

Cytokeratin 19 (CK 19) – cytokeratin with large molecule, the synthesis of its expression being encoded by other genes than the ones encoding the rest of cytokeratins (336). It is a sensitive marker but nonspecific of the Papillary Thyroid Carcinoma (318).

In our study, CK19 indicated positivity in 79% of differentiated Thyroid Carcinomas, 84,6% for Papillary Carcinomas and only 25% for Follicular Carcinomas – data very close to those published in similar studies (318, 186, 48).

Vimentin – we observed its positivity in 48,8% of Papillary Carcinomas and in 75% of Follicular Carcinomas. Some studies report the constant expression of Vimentin in Thyroid Carcinomas (231). Buley ID and co. confirm the data of other studies regarding the co-expression of cytokeratins and Vimentin in Thyroid Cancers (37), but this behaviour is also present in normal structures. Other studies noticed that the distribution of CK19 and vimentin in neoplastic cells seems to be in inverse ratio with the degree of differentiation of neoplastic Thyroid cells (122).

In the current study, the association of some superior scores of Vimentin for Carcinoma in primary stages, without Thyroid extension and without metastasis, places it as a protection factor from the point of view of TEM presence.

The Cadherins are cellular adhesion molecules depending on Ca (171). It was established that the E-cadherin plays an important role in the tumour progression and metastasis because we observed that the loss of E-cadherin expression is correlated with the invasive and non-differentiated phenotype (371). It seems to have a protective role in Cancer (26). In this study, the positivity to E-cadherin was present in 86% of analyzed cases, in 84% of Papillary Carcinomas and in all Follicular Carcinomas. Similar studies report similar figures (294, 326, 240, 28, 159).

To be also mentioned in the current study the complete loss of E-cadherin expression that was correlated to the presence of metastatic tumour, as Brabant also notices (28).

In our study it was a positive linear relation between the expressions of Vimentin, E-cadherin and CK-19, which indicates the fact that the increased expression of these 3 markers is associated to Carcinomas with favourable prognosis, in early stages, without extra Thyroid extension and metastasis.

N-cadherin is another member of cadherin family, molecules of cellular adhesion, Calcium dependent, associated with TEM, crucial in cancer progression regarding both the metastasis and the resistance to chemotherapy (375). In our study, N-cadherin was identified in 76,9% of Papillary Carcinomas and in all cases of Follicular Carcinomas. Also, the scores of N-Cadherin were undeniably superior in cases of Carcinomas with high cells, fact signifying lesions with risk for TEM.

The process of E-cadherin loss expression and increase of the N-cadherin expression is named „the switch of cadherins”, specific and important sign of TEM (347; 160; 246).

In the study, the high expression of N-cadherin was associated to invasive Carcinomas of large dimensions or with extra Thyroid extension and ganglion metastasis.

TWIST –is a member of the transcription factors’ class, one of the molecules involved in adjusting TEM by the adjustment of key proteins which keep the epithelial characteristics of cells that represent the mesenchymal phenotype (361).

It is considered to have oncogene potential by the promoting of proliferation and inhibiting apoptosis (361).

The current study analyzed the Twist expression in 35 Thyroid Carcinoma. For both Papillary and Follicular Thyroid Carcinomas, we noticed variable immune- reactions, having cases with low or high Twist expression, without significant statistic differences compared to the tumour subtype. The scores for the variant with high Papillary Carcinoma cells were superior to the Papillary or conventional variant and Papillary Follicular. The low expression of TWIST was present in 33,3% on Papillary Carcinomas, moderate in 30,8%, and high in 8% of these lesions. In Follicular Carcinoma, 50% of the cases had low expression and in 50% the expression was moderate.

We also noticed in our study the differences of TWIST marks compared to the tumour stage (stage I/ II versus III/ IV) and the presence if metastasis, immune expression of the protein being significantly superior in the case of invasive tumours in adjoining structures and in case of u with metastasis.

The tandem TWIST/ N-cadherin represented a straight positive relationship in this study being specific to invasive and metastatic Carcinomas

In this current study, the data from literature indicates TWIST as tumour aggressive marker, being associated to invasive and metastatic forms of Carcinoma, including the Thyroid level (279, 214, 364, 36, 117).

Conclusions

The study made on 49 differentiate Thyroid Carcinomas during the period 2007-2014 allowed us to make the following observations:

- Differentiate Thyroid Carcinomas represented 92,4% of malign tumours with this particular location.
- The most common imagistic aspects in patients with differentiate Thyroid Carcinoma were represented by dimensions between 2,1-4 cm (59,2%), hypoeogenous (89,8%), with solid structure (71,5%), with calcifications (63,3%), the absence of halo and irregular margins in all cases , mixed vascular activity (63,3%) and metastatic adenopathy (20,4%).
- The macroscopic exam of tumours confirmed the imagistic aspects, the lesions being unique in almost all cases (96%).
- The histopathological analysis identified Papillary Carcinoma in 89,8% of cases and Follicular Carcinoma in 10,2% of the cases studied.
- The analysis of histopathological aggressive parameters, meaning necrosis, the nuclear atypical behaviour and mitosis were present in all cases of Papillary Carcinoma with high cells and also in 21,7% , respectively 8,7% and 13% of conventional Papillary Carcinoma.
- The vascular invasion was observed in 17,4% of conventional Papillary Carcinoma, as well as in oxifilous and high cells variants.
- Capsular invasion was present in 26,1% of conventional Papillary Carcinoma, 38,4% of Papillary Follicular Carcinoma, as well as in oxifilous and high cells variants.

- The extra Thyroid extension was observed in 13% of conventional Papillary Carcinoma, 23,1% of the Papillary Follicular ones, as well as in oxifilous and high cells variants.
- Ganglion metastasis were present in 20,4% of Papillary Carcinoma analyzed, the cases belonging to conventional, Follicular and high cells variants.
- Follicular Carcinomas were capsulated, with microscopic capsular invasion in 40% of cases, macroscopic capsular invasion in 20% of cases, angio-invasion being identified in 80% of cases.
- Stadiation pTNM indicated the predominance of Carcinomas in stages I and II, respectively 40,8% and 36,7% of cases, compared to the lesions in stages III and IV, respectively 16,4% and 6,1% of cases.
- Immunohistochemical analysis indicated the positivity of CK19 in 79% of the analyzed cases, high scores being statistically associated to Papillary Carcinomas, respectively with their conventional and Follicular variants.
- The immune reaction of Vimentin was observed in 55,8% of the investigated cases, the medium scores of markings being significantly superior in Follicular Carcinomas compared to Papillary Carcinomas, as well as in conventional and Follicular variants of Papillary Carcinoma compared to the high cells variant.
- The Vimentin markings were superior in tumours of small dimensions or the ones with Thyroid location (T1/T2). Although the reaction was superior in the specific case of early stage and free of ganglion metastasis Carcinomas, the aspect was statistically insignificant.
- E-cadherin was identified in 86% of cases, without significant differences in medium scores for the Papillary and Follicular Carcinomas.
- The E-cadherin markings were superior in cases of tumours of small dimensions or Thyroid located (T1/T2) compared to the large and with extra Thyroid extension ones (T3/T4), and at the level of ganglion metastasis analyzed, the reaction was negative.
- This study showed a linear positive reaction between the expression of Vimentin and E-cadherin, as well as between E-cadherin and CK19, fact that indicates the marking decreasing of the three proteins associated to Carcinomas in advanced stages and with extra Thyroid extension (T3/T4) and ganglion metastasis, specific aspects for the phenomenon of epitheliomesenchymal transition.
- N-cadherin immunohistochemical markings were identified in 79% of cases and were significantly superior in Follicular Carcinomas, in high cells variants of Papillary Carcinomas, in lesions with increased dimensions or advanced extension, respectively in advanced stages and ganglion metastasis Carcinomas.
- The „switch” of cadherins specific to epitheliomesenchymal transition was recorded by the linear negative correlation existing between E-cadherin and N-cadherin.
- The immune expression of TWIST was observed in 81,4% of Carcinomas, the markings being significantly superior in increased and advanced extension tumours, respectively in advanced stages and with ganglion metastasis Carcinomas. The values of TWIST represented a linear relation compared to the ones of N-cadherin, fact that lets us plead for the use of these markers in order to identify the Thyroid Carcinomas well differentiated and with progression potential.
- In the current study, the investigation of epitheliomesenchymal transition in differentiated Thyroid Carcinomas supports the use of protective markers (CK19, Vimentin, E-cadherin) and the aggressive ones (N-cadherin and TWIST) for the layering of risk patients and it can provide therapy targets for future researches in this field.