Association between Different Variants of Papillary Thyroid Carcinoma and Risk-Group According to AMES (Age, Metastasis, Extent and Size) Classification System

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Objective: *To study the association between cell variants of papillary carcinoma and AMES (Age, Metastasis, Extent and Size) risk classification.*
Material and Method: *One hundred and twenty-one cases of papillary thyroid carcinomas were subclassified for cell type and risk-groups according to AMES classification system. Correlations between both variables are evaluated.*
Results: *Among different cell variants of papillary carcinoma, solid cell pattern has the highest proportion of high-risk tumor classified by the AMES criteria, comprising 75% followed by tall cell subtype with 33.3% of high risk patients. Conventional papillary carcinoma has only 8.3% of high-risk group. Follicular and encapsulated variants as well as microcarcinoma (< 1 cm) are all categorized as low-risk neoplasms.*
Conclusion: *The present study indicates that there is association between cell variants and AMES prognostic index. The authors, therefore, emphasize the importance of cell variants in predicting the prognosis of papillary carcinoma.*

Keywords: *Papillary thyroid carcinoma, Cell variants, AMES*

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Many studies have demonstrated a number of factors which are of prognostic importance in papillary thyroid carcinoma. These factors include age and gender of the patients, size of the tumor, multiplicity, extrathyroid invasion and metastasis of the diseases[1-6].

Apart from these features, cell variant is believed to be another factor to affect patients' outcome[6-12]. For example, tall and columnar cell variants of papillary carcinoma tend to behave more aggressively than the conventional type of neoplasms[9-11].

The aim of this work was to find the association between different cell variants of papillary thyroid carcinoma and risk group classification according to AMES (Age, Metastasis, Extrathyroid invasion and Size) scoring system[13].

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Material and Method

A retrospective study included all medical records with papillary thyroid carcinoma, totaling 121 cases, recorded in the files at the Department of Pathology, Faculty of Medicine, Chulalongkorn University from January 2001 to June 2004.

The data on age, sex, size, extrathyroid invasion and morphologic variants of the tumor were collected. The cases were divided into two risk groups using criteria proposed by Cady et al[13] which is known as AMES (Age, Metastasis, Extrathyroid invasion and Size). Classification of the details is demonstrated in Table 1.

Statistical analysis of the clinical and pathologic data was performed using descriptive statistics and Student's *t* test and chi-square analysis. A p-value of less than 0.05 was considered statistical significance.

Results

Of the 121 cases, 106 patients (87.6%) were

Table 1. Risk group definitions according to AMES classification[13]

Low-risk group
- A. All younger patients without distant metastases (men < 41 years; women<51 years)
- B. All older patients with:
  1. Intrathyroidal papillary involvement follicular carcinoma and
  2. Primary cancers < 5 cm in diameter and
  3. No distant metastases

High-risk group
- A. All patients with distant metastases
- B. All older patients with:
  1. Extrathyroidal papillary cancer or major tumor capsular involvement follicular carcinoma and
  2. Primary cancers 5 cm in diameter or larger regardless of extent of disease

females and 15 of them (12.4%) were males. The age ranged from 9 to 77 years with the mean of 41.4 years (SD = 14.4). There were 61 cases (50.4%) of classical papillary carcinomas, 21 cases (17.4%) of tall cell type, 15 cases (12.4%) of follicular cell variant, 11 cases (9.1%) of encapsulated tumor,8 cases (6.6%) of microcarcinoma, 4 cases (3.3%) of solid cell pattern and 1 case (0.8%) of columnar cell type. Using AMES classification system, 105 patients (86.8%) were categorized as the low-risk group and 16 cases (13.2%) were subclassified as high-risk patients.

The associations of different prognostic features and cell variants are summarized and shown in Table 2. When compared to the risk groups according to AMES classification (Table 2 and Fig. 1), solid cell variant (Fig. 2C) had the highest proportion of high-risk tumors, comprising 75% of all cases followed by tall cell subtype (Fig. 2B) with the percentage of the high-risk group of about 33.3%. For the usual type of papillary carcinoma (Fig. 2A), high-risk patients comprised only 8.3%. All cases of microcarcinoma, follicular (Fig. 2D) and encapsulated variants were categorized as low risk neoplasms.

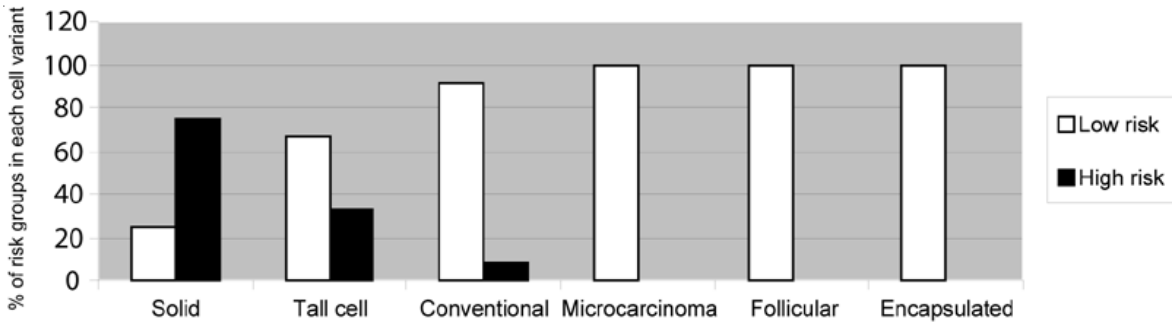
Discussion

It has been recognized that, for many cancers, one factor that may influence the diseases' outcome is cell variant[6-12,14-16]. For example, different subtypes of squamous cell carcinoma (eg. verrucous carcinoma,

Table 2. Association between different prognostic features and cell variants of papillary carcinoma

	Variants					
	Conventional	Follicular	Encapsulated	Solid	Tall cell	Microcarcinoma
Mean Age (years)	40.6	37.2	36.5	61.2*	44.9	45
Sex (F/M)	9.3:1	13:1	5:1	4:0	7:1	7:1
Tumor size (mean)(cm)	2.4	2.3	1.9	N/A	2.8	0.6*
Extrathyroid Invasion (%)	28.1	40.0	0.0*	75.0*	57.9*	0.0
Multifocal Involvement (%)	60.7	100.0*	18.2*	N/A	52.6	0.0*
Distant Metastasis (%)	1.7	0.0	0.0	25.0*	4.8	0.0
AMES (% high-risk)	8.3	0.0	0.0	75.0*	33.3*	0.0

* $p < 0.05$ (compared with conventional carcinoma)
Abbreviations: N/A, not available



	Solid	Tall cell	Conventional	Micro	Follicula	Encapsulated
Low risk	25	66.7	91.7	100	100	100
High risk	75	33.3	8.3	0	0	0

Fig. 1 Proportion of risk groups in different types of papillary carcinoma according to AMES classification

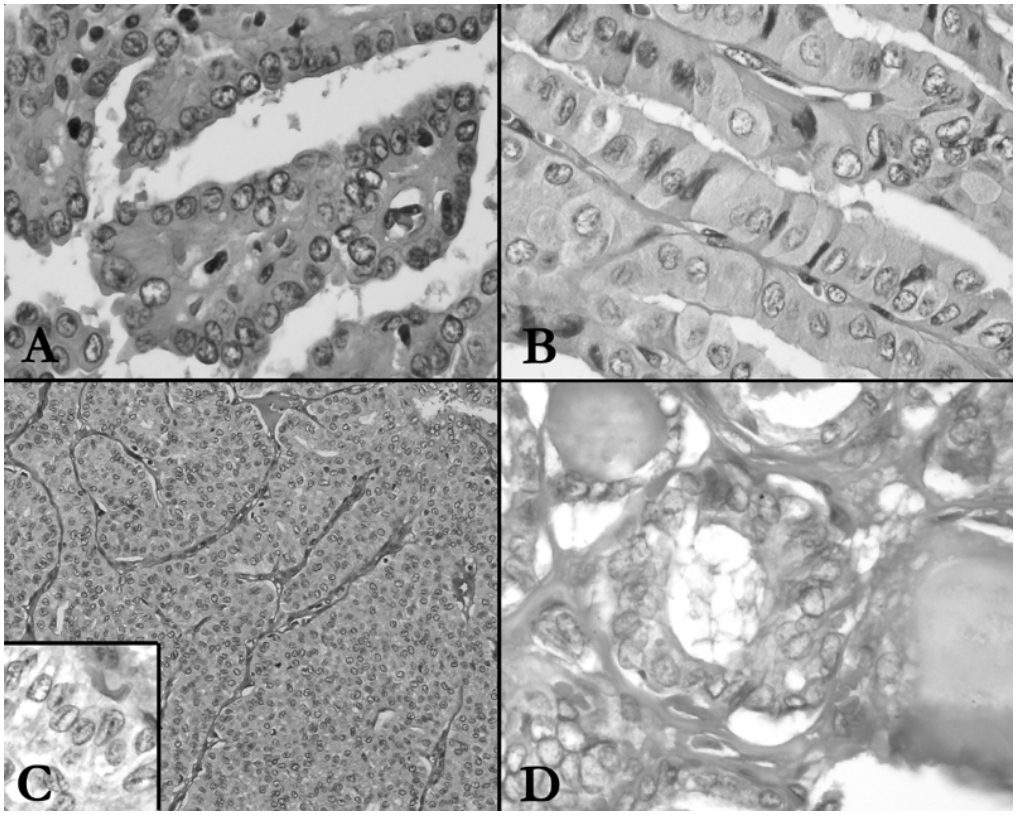


Fig. 2 Morphologic appearances of different variants of papillary carcinoma
(A) Usual type of papillary carcinoma(H&E x 400)
(B) Tall cell variant. The tumor cells have a height that is at least twice the width. These type of cells comprise at least 30% of the neoplasm (10) (H&E x 400)
(C) Solid variant. The tumor cells grow in solid and trabecular pattern by at least 70% of the primary tumor nodule (12) (H&E x 100). Cytologic features of papillary carcinoma such as nuclear grooves (inset) are preserved
(D) Follicular variant. Most of the tumor cells (at least 80%) show follicular architecture (28) (H&E x 400)

basaloid squamous cell carcinoma) and certain kinds of soft tissue tumors (malignant fibrous histiocytoma for instance) carry different prognosis[14-16]. Papillary thyroid carcinoma is also one malignancy which has been documented that morphologic variant has an impact on the tumors behavior [6-12].

There are several prognostic scoring systems developed to predict the outcomes of the thyroid cancers[5,13,17-25]. Various prognostic variables such as age, gender, tumor size, histologic grades, local (extrathyroidal) invasion, completeness of primary tumor resection and distant metastasis are used in combination to categorize patients into different risk groups[5,13,17-25]. None of these systems, however, incorporates tumor cell variants into the classification as a prognostic parameter.

The aim of the present study was to find relationship between cell variants and prognostic groupings using criteria described in AMES classification system. The findings indicate that there is association between different cell variants and risk groups. The tumors which are known in the literature to be more aggressive like tall cell and solid cell types[10,12] are more frequently classified in the high-risk group while follicular, encapsulated variants and papillary microcarcinoma tend to be associated with better prognosis since all of them are in the low-risk category (Table 2 and Fig. 1). This emphasizes the impact of cell variants on the prognosis of the tumors. In addition, the data from the present study, like other series, show that most papillary carcinomas are not aggressive neoplasms for 86.8 percent of the patients who have low-risk tumors.

The solid variant in the present series was more common in older patients (mean age 61.2 years) compared with other cell subtypes (Table 2). The findings are contrary to other reports which showed a higher trend of solid cell type of papillary carcinoma to occur in younger individuals[12,26-27], particularly in the children exposed to radiation after the Chernobyl nuclear accident, in which up to 34% of all tumors had a predominantly or exclusively solid growth pattern[26,27].

The authors also found that follicular variant has more multicentric lesions (100% in the present series) when compared with other cell types (Table 2). The findings are different from the series reported by Tielens et al. in which multicentricity was present with similar frequencies in the follicular variant and conventional papillary carcinoma[28].

In summary, the present study supports the studies in the literature that cell variants are important for the prognosis of the papillary thyroid carcinoma. Therefore, they should be emphasized in the pathological reporting. Also, the importance of cell variants of the malignancy should be recognized by the clinicians as one prognostic parameter in order to make a proper management plan.

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ความสัมพันธ์ระหว่างมะเร็งต่อมธัยรอยด์ แพพพิลารี่ คาร์ซิโนมา ชนิดต่าง ๆ และการแบ่งกลุ่มเสี่ยงตามการพยากรณ์โรคด้วยระบบ AMES (Age, Metastasis, Extent and Size)

สมบูรณ์ คีลาวัฒน์, อุบล พุ่มสุข

วัตถุประสงค์: *เพื่อศึกษาความสัมพันธ์ระหว่าง แพพพิลารี่ คาร์ซิโนมาที่มีลักษณะและรูปร่างพิเศษชนิดต่าง ๆ และการแบ่งกลุ่มตามการพยากรณ์โรคด้วยระบบ AMES*

วัสดุและวิธีการ: *ตัวอย่างที่ศึกษาได้จากผู้ป่วยด้วยมะเร็งต่อมธัยรอยด์ชนิด แพพพิลารี่ คาร์ซิโนมาจำนวน 121 ราย โดยได้รวบรวมข้อมูลต่าง ๆ จากผู้ป่วยเหล่านี้เพื่อนำมาจัดกลุ่มคนไข้ตามการพยากรณ์โรคด้วยระบบ AMES และนำข้อมูลที่ได้มาหาความสัมพันธ์กับแพพพิลารี่ คาร์ซิโนมาที่มีลักษณะและรูปร่างพิเศษชนิดต่าง ๆ*

ผลการศึกษา: *ในระหว่างแพพพิลารี่ คาร์ซิโนมาที่มีรูปร่างต่าง ๆ มะเร็งที่มีรูปแบบการเรียงตัวเป็นแบบ solid มีสัดส่วนของผู้ป่วยที่จัดอยู่ในกลุ่มเสี่ยงสูง มากที่สุดโดยมีสัดส่วนสูงถึงร้อยละ 75 รองลงมาได้แก่แพพพิลารี่ คาร์ซิโนมาที่มีลักษณะแบบเซลล์ทรงสูง ซึ่งพบมีคนไข้กลุ่มเสี่ยงสูง ร้อยละ 33.3 ในส่วนของแพพพิลารี่ คาร์ซิโนมาที่มีรูปร่างแบบปรกติธรรมดานั้น พบคนไข้กลุ่มเสี่ยงสูง เพียงร้อยละ 8.3 เท่านั้น ส่วนเนื้อร้ายในกลุ่มที่เหลือ ซึ่งได้แก่ กลุ่มที่มีการเรียงตัวเป็น follicles และชนิดที่มีแคปซูลหุ้ม (capsular variant) รวมทั้งมะเร็งที่มีขนาดเล็กกว่า 1 เซนติเมตร นั้น คนไข้ทุกรายถูกจัดอยู่ในกลุ่มเสี่ยงต่ำ*

สรุป: *ผลการศึกษานี้ได้แสดงให้เห็นถึงความสัมพันธ์ระหว่างรูปร่างและลักษณะแบบพิเศษชนิดต่าง ๆ ของมะเร็งแพพพิลารี่ คาร์ซิโนมา และการแบ่งกลุ่มคนไข้ตามการพยากรณ์โรคด้วยระบบ AMES ซึ่งบ่งชี้ว่าแพพพิลารี่ คาร์ซิโนมาที่มีลักษณะหรือรูปร่างพิเศษต่าง ๆ มีการพยากรณ์โรคที่แตกต่างกัน ดังนั้นแพทย์ผู้รักษาและพยาธิแพทย์จึงควรให้ความสำคัญกับลักษณะและรูปร่าง ของแพพพิลารี่ คาร์ซิโนมา เพื่อเป็นส่วนช่วยในการพยากรณ์โรคของคนไข้*