TURNITIN_Hormone_and_Macroscopic_Profile

by Edmond Rukmana Wikanta

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Original Article

Hormone and Macroscopic Profile of Classical and Follicular Variant Papillary Thyroid Carcinoma

Alin Nabila[1], Hermawan Istiadi[2], Edmond Rukmana Wikanta[3], Ika Pawitra Miranti[2], Dik Puspasari[2]

[1]Faculty of Medicine, Diponegoro University
[2]Department of Anatomy Pathology, Faculty of Medicine, Diponegoro University
[3]Department of Surgery, Sub-Division of Oncology Surgery, Faculty of Medicine, Diponegoro University

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Author Affiliation:
Faculty of Medicine,
Diponegoro University

Author Correspondence:
Alin Nabila
Jl. Prof. H. Soedarto, SH., Tembalang,
Semarang, Central Java 50275,
Indonesia

Email Address:
alinnabilala@gmail.com

Abstract

Background : New cases of Papillary Thyroid Carcinoma (PTC) patients at Dr. Kariadi Hospital, Semarang is quite high, where the most types are Classical Papillary Thyroid Carcinoma and Follicular Variant Papillary Thyroid Carcinoma. On the other hand, in diagnosing PTC, histopathological examination which is a gold standard sometimes has a subjective value. Therefore, it is necessary to have a correlation with the clinical characteristics of the patient in order to get a correct diagnosis. The aims of this study was to understanding the differences in age category, tumor macroscopic size and hormone profile between patients at Dr. Kariadi Hospital, Semarang.
Methods : Analytic observational research with cross sectional design. Obtained a total sample of 38 patients who were recorded in CM in which 18 cases of Classic Papillary Thyroid Carcinoma and 20 cases of Follicular Variant Papillary Thyroid Carcinoma. Data with anominal scale, namely age category were analyzed using the Fisher exact test to test the significance of the comparative hypothesis, while the data with a numerical scale, namely the macroscopic size of the tumor and the hormone profile, were tested for normality of Saphiro Wilk then continued with the Mann-Whitney test.
Results : Based on the Fisher exact test, there wassignificant difference (p=0.009) between age category and Classical Papillary Thyroid Carcinoma and Follicular Variant. In the Mann–Whitney test there was no significant difference (p=0.3) between the macroscopic size of the classical papillary carcinoma and follicular variant and there was no significant difference TSHs (p = 0.501) and fT4 (p = 0.953) hormone profiles between Classic Papillary Thyroid Carcinoma and Follicular Variant.
Conclusion : There wassignificant difference between the category of age at diagnosis, and there was no significant difference between the macroscopic size of the tumor and the hormonal profile of Classical Papillary Carcinoma and Follicular Variant in Dr. Kariadi Hospital, Semarang.

Keywords : Age category; Classical Papillary Thyroid Carcinoma; Follicular Variant Papillary Thyroid Carcinoma;Hormone profile; Tumor macroscopic size.

INTRODUCTION

Thyroid carcinoma is a malignancy that occurs in the endocrine gland, which is most often found, which is about 95% of all endocrine malignancies in Asia.Thyroid malignancy with the highest incidence is PTC.[1,2] A new case of a patient with a PTC at Dr. Kariadi Hospital, Semarang is quite high, where the most types are classic PTC and PTCVF with an incidence of 90%. However, the high incidence of PTC is not comparable with publications regarding clinical comparisons of the two types of PTC. On the other hand, in diagnosing PTC, histopathological examination which is the gold standard sometimes has a subjective value, where the criteria for benign or malignant are only based on papillary nuclear features and microscopic architecture. Therefore, it is necessary to correlate with the clinical characteristics of the patient in order to obtain a correct diagnosis.

The hypothesis of this study is that there are differences in the age category, tumor macroscopic size and hormone profile between Classical Papillary Thyroid Carcinoma and Follicular Variant Papillary Thyroid Carcinoma patients in Dr. Kariadi Hospital, Semarang. The purpose of this study was to determine the differences in age characteristics, tumor macroscopic size, and hormone profile between classical papillary thyroid carcinoma and follicular variant papillary thyroid carcinoma in Dr. Kariadi Hospital, Semarang

METHODS

This research has received permission from the Ethics Commission for Health Research, Faculty of Medicine, Diponegoro University. Permit was granted on April 14, 2020 with number No. 37 / EC / KEPK / FK-UNDIP / IV / 2020. This research is an observational-analytic study with a cross sectional design usingsecondary data from medical records inpatients. This research was carried out in the medical record section of Dr. Kariadi Hospital, Semarang. The time of the data to be examined is from January to June 2019.

In this study, a consecutive sampling technique was used where medical record data that met the inclusion criteria were used as the study sample. The sample in this study were patients who had been diagnosed with classical papillary carcinoma and follicular variant in Dr. Kariadi Hospital, Semarang who met the inclusion criteria to prevent bias. The inclusion criteria in this study were all medical records of patients diagnosed with Classical Papillary Thyroid Carcinoma and Follicular Variants which included age category (≤55years or > 55 years)[3], macroscopic size of the tumor that measured in dimensions length x width x high and hormone profile (TSHs and fT4). Based on the cross sectional formula, the minimum required sample size is 30 samples.

The medical record data that had been collected were analyzed using the Statistical Product and Service Solutions (SPSS) 25 program, where the nominal scale data, namely age category were analyzed by fisher exact test, while the numerical scale data were the macroscopic tumor size and hormone profile by Saphiro Wilk normality test is then continued with the Mann–Whitney test. Then it is presented in descriptive form in the form of tables and narration.

RESULTS

This study was conducted for approximately 3 weeks between June – July 2020. From the samples obtained, the number of patients diagnosed with Classic Papillary Thyroid Carcinoma was 33 and the number of patients diagnosed with Follicular Variant Papillary Thyroid Carcinoma was 51 but only 18 cases of Classical Papillary Thyroid Carcinoma and 20 cases of Follicular Variant Papillary Thyroid Carcinoma that matched the inclusion criteria. Variables observed included age category at diagnosis, macroscopic size of the tumor and hormone profile (TSHs and fT4). Patient clinicopathological data can be seen in table 1.

This study shows that most of the Classical PTC patients at Dr. Kariadi Hospital, Semarangwas diagnosed at the age category of less than 55 years as many as 17 patients while 1 patient were diagnosed at the age category of more than 55 years. Likewise, with PTCVF patients at Dr. Kariadi Hospital, Semarang where most of the patients were diagnosed at the age of less than 55 years, 11 patients and 9 patients were diagnosed at the age of more than 55 years with the number of Classical

TABLE 1
Clinicopathological Data for Patients with Classical PTC and PTCVF

	Classical PTC (n= 18)	PTCVF (n= 20)
Age Category		
≤55 years	17	11
>55 years	1	9
Macroscopic Size Tumor	2.5 ± 4.4*	7.4 ± 15.6*
	0.014 – 14.095^	0.004 – 65.253^
Hormone Profile		
TSHs	7.9 ± 14.1*	8.3 ± 26.9*
	0.04 – 47.04^	0.02 – 122.43^
fT4	13.8 ± 3.5*	13.9 ± 3.6*
	3.59 – 18.06^	2.43 – 19.65^

Description: * Mean ± standard deviation, ^ Minimum – maximum

TABLE 2
Saphiro Wilk Normality test Result

		p (Classical PTC)	*p* (PTCVF)
Macroscopic size tumor		0.000	0.000
Hormone profile	TSHs	0.000	0.000
	fT4	0.044	0.022

Description: * Mean ± standard deviation, ^ Minimum – maximum

TABLE 3
Mann-Whitney Test result

		p
Macroscopic size tumor		0.300
Hormone profile	TSHs	0.501
	fT4	0.953

Description: * Mean ± standard deviation, ^ Minimum – maximum

TABLE 4
Fisher's Exact test results

	p
Age Category	0.009
≤55 years	
>55 years	

PTC patients as many as 18 people and PTCVF as many as 20 people. The overall mean macroscopic tumor size of Classical PTC patients was 2.5 ± 4.4 cm3. Whereas in PTCVF patients it was 7.4 ± 15.6 cm3. Furthermore, the average profile of the TSHs hormone in Classical PTC patients was 7.9 ±14.1 µIU / mL and in PTCVF it was 8.3 ± 26.9 µIU / mL. For the mean fT4 hormone profile in Classical PTC patients was 13.8 ± 3.5 pmol / L. Whereas in PTCVF patients is 13.9 ± 3.6 pmol / L.

Data Normality Test

Numerical scale data such as tumor microscopic size and hormone profile were tested for normality using the Saphiro Wilk test.

From the normality test of Saphiro Wilk, it was found that the p value was <0.05. So, it can be concluded that the distribution of data is not normal, so it continues with the Mann Whitney test.

Test Analytics Statistics

After the Mann Whitney test, it was found that the Classical PTC patients have a mean macroscopic tumor size smaller than in PTCVF patients. Classical PTC patients also had lower mean TSHs and fT4 hormone levels than PTCVF patients. However, there were no significant differences in tumor macroscopic size, TSHs and fT4 hormone levels statistically between Classical PTC and PTCVF patients.

Furthermore, for variables on annominal scale, namely the age category at diagnosis, a non-parametric Fisher's Exact test was performed with a significance of $p < 0.05$.

Based on the results of the Fisher's Exact test, it was found that classic PTC and PTCVF patients had statistically significant differences at the age category of diagnosis with a *p value* <0.05 (0.009).

DISCUSSION

Differences in age category between Classical Papillary Thyroid Carcinoma and Follicular Variant

Based on this study, both Classical PTC and PTCVF patients at Dr. Kariadi Hospital, Semarang is mostly diagnosed at the age category of less than 55 years. This is in accordance with the literature which states that the average patient is diagnosed with PTC at the age of 30–50 years.[4] Because in this age range the proliferation and activity of thyroid cells is faster and increases.[5] From epidemiological studies also obtained results where the average The average age of patients diagnosed with Classical PTC and PTCVF is >45 years. This is because the proportion of positive BRAFV600E gene mutation expression is higher in the age category > 45 years.[6,7] This statement is in line with studies conducted in the USA where the average age of patients when diagnosed with a Classical PTC is 43 years and the average age of patients when diagnosed with PTCVF was 44 years with a *p–value* of 0.435 ($p>0.05$).[8] Research conducted in Korea also stated that the average age of patients when diagnosed with Classical PTC and PTCVF was 46 years with a *p–value* of 0.861 ($p>0.05$).[9] The results of this study and previous studies both state that the average age of patients diagnosed with Classical PTC and PTCVF was more at the age of less than 55 years.[8,9]

Based on statistical tests, the statistics in this study obtained a *p–value* of 0.009 ($p<0.05$), which means that there was significant difference between the age category when diagnosed with Classical PTC and PTCVF at Dr. Kariadi Hospital, Semarang. This is difference with previous studies which state that there is no significant difference between age category when diagnosed with Classical PTC and PTCVF.[8,9]

Difference in tumor macroscopic size between classical papillary thyroid carcinoma and follicular variant

Based on this study, the mean macroscopic tumor size in Classical PTC patients after total thyroidectomy at Dr. Kariadi Hospital, Semarang is 2.5 cm and in PTCVF patients is 7.4 cm. The results of this study are in accordance with the literature which states that usually the tumor mass in Classical PTC patients is 2–3 cm in size, while the tumor mass in PTCVF patients is 5–10 cm in size and even bigger. This is because PTCVF involves the RAS gene which consists of guanine nucleotide proteins that play a role in controlling cell growth and differentiation and if malignancy occurs there is a RAS gene mutation that allows the protein to be active and results in abnormal cell growth.[4] China where the tumor mass in Classical PTC patients was between 0.9 – 3.5 cm while the tumor mass in PTCVF patients was between 3–10 cm with a *p-value* of 0.03 ($p<0.05$).[10] This is also consistent with with a study conducted in the USA where the results showed that the tumor mass in PTCVF patients was greater than the tumor mass in Classical PTC patients with a *p value* of <0.001.[8]

Based on the statistical test in this study, the *p-value* was 0.3 ($p> 0.05$), which means that there was no significant difference between the macroscopic size of the Classical PTC tumor and PTCVF tumor in Dr. Kariadi Hospital, Semarang. This is different from previous studies conducted in China ($p<0.05$) and in the USA ($p<0.001$), which means that there is a significant difference between the macroscopic size of the Classical PTC tumor and PTCVF.[8,10] This is probably due to the lack of variation in data when compared to previous studies where in the previous study there were 542 samples.[8]

Difference in hormone profile (TSHs and fT4) between classical papillary thyroid carcinoma and follicular variant

Based on this study, the mean levels of TSHs and fT4 hormones in Classical PTC patients at Dr. Kariadi Hospital, Semarang was 7.9 µIU / mL and 13.8 pmol / L, while the mean levels of TSHs in PTCVF patients were 8.3 µIU / mL and 13.9 pmol / L. From these results it can be interpreted that the average level of TSHs in both Classical PTC and PTCVF patients increases where the normal level of TSHs is 0.51 – 4.94 µIU / mL. Meanwhile, the mean levels of the fT4 hormone in the classic PTC and PTCVF patients in this study were classified as normal, where the normal levels of the fT4 hormone were 10.6 - 19.4 pmol / L. Increased levels of TSHs in patients with a diagnosis of Classic PTC can be related to mutations in the BRAFV600E gene which result in overactivation of RAF Kinase which interferes with the proliferation and differentiation processes and results in uncontrolled cell division and hormonal imbalance.[11,12] This is in accordance with the literature which states that in PTC patients, both classic and PTCVF TSHs levels tended to be higher / within normal limits while fT4 levels tended to be lower / within normal limits.[13] Higher TSHs levels were associated with a higher incidence and advanced stage of malignancy.[14] The results of this study are consistent with research conducted in Hawaii which states that an increase in TSHs hormone levels in all variants of PTC and an increase in TSHs hormone levels is associated with a poor prognosis. Meanwhile, the results of this study indicate that fT4 is lower / within normal limits and is not significantly related to the incidence of PTC.[15] The results of previous studies conducted in Departement of Anatomy Pathology, Faculty of Medicine USU/ Haji Adam Malik Hospital Medan, Indonesia also stated that both Classical PTC and PTCVF levels of TSHs increased while fT4 was within normal limits / tended to be lower.[13]

Based on the statistical test in this study, the *p-value* was 0.501 ($p>0.05$) for the difference in TSHs levels between Classical PTC and PTCVF patients. Whereas for the difference in fT4 levels between Classical PTC and PTCVF patients, the *p-value* was 0.953 ($p> 0.05$), which means that there was no significant difference between thehormonal profiles of both TSHs and fT4 in patients with Classical PTC and PTCVF. This is in line with previous research conducted in Hawaii with a *p-value* >0.05 and previous studies in Indonesia with a *p-value* of 0.328 ($p>0.05$), which means that there is no significant difference between the hormonal profiles of both TSHs and fT4 in Classical PTC patients and PTCVF.[13,15]

Suggestions for further research are the need for further research on other clinical aspects that can distinguish classical papillary carcinoma from follicular variants, and direct intervention is needed in patients with classical papillary carcinoma and follicular variants to find environmental factors.

CONCLUSION

The conclusion of this study is that there was significant difference between the category of age at diagnosis, and there was no significant difference between the macroscopic size of the tumor and the hormonal profile of Classical Papillary Carcinoma and Follicular Variants in Dr. Kariadi Hospital, Semarang.

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