Clinical behavior of follicular variant of papillary thyroid carcinoma: presentation and survival

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ABSTRACT

Objective: To determine the prevalence and extent of disease characteristics of the follicular variant of papillary thyroid carcinoma (FV-PTC) and the survival impact of this histopathological diagnosis compared to classical papillary thyroid carcinoma (C-PTC).

Study Design: Cross-sectional population analysis of national cancer database.

Methods: Cases of C-PTC and FV-PTC were extracted from the Surveillance, Epidemiology and End Results database for 1988-2006 and staged. Surgical extent and radioactive iodine (RAI) use were determined. Demographic and staging parameters were statistically compared according to tumor histology. Survival differences according to histology were determined with a Cox proportional hazards model, adjusting for age, sex, T-stage, N-stage, surgical therapy and RAI.

Results: 46,699 patients were identified (68.4% C-PTC and 31.6% FV-PTC). Age at presentation and sex distribution were similar between FV-PTC (47.9 years; 79.3% female) and C-PTC patients (46.2 years; 77.3% female). Although nodal disease prevalence was significantly lower in FV-PTC compared to C-PTC (14.8% versus 27.8%, respectively, p<0.001), T-stage was not significantly different (p=0.450). Mean overall survivals for patients with FV-PTC (204.5 months) and C-PTC (205.3 months) were not significantly different (p=0.373). Cox regression analysis revealed that advanced age (p<0.001), male sex (p<0.001), advanced T-stage (p<0.001), and positive nodal disease (p<0.001) were associated with reduced overall survival, while histopathological subtype was not (p=0.360).

Conclusion: Disease presentation (with exception of nodal metastasis) and survival in patients with FV-PTC are statistically similar to that of C-PTC and accordingly these patients carry very similar prognoses.

INTRODUCTION

- Papillary thyroid carcinoma (PTC) is the most common type of thyroid malignancy, accounting for ~ 80% of thyroid cancers.[1,2]
- Follicular variant of PTC (FV-PTC) comprises as many as 41% of all PTC cases.[3]
- The clinical significance of an FV-PTC diagnosis remains a matter of debate[4] due to the generally favorable prognosis PTC and the limited number of subjects studied in case series.
- The ability of published studies of FV-PTC to draw clinically applicable conclusions was likely limited by small sample sizes and short mean durations of follow-up, which in some cases were confined to just over three years.[4,5]
- We turned to the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database to evaluate the behavior of FV-PTC and its influence on patient prognosis.

METHODS

- Cases of PTC arising in 1988-2006 were extracted from the SEER database. Case data included age at diagnosis, sex, histological type of PTC (FV-PTC versus C-PTC), extent of disease at the primary site and nodal metastasis, extent of thyroidectomy, use of radioactive iodine, vital status, cause of death and duration of follow-up were extracted and exported to SPSS version 17.0.

METHODS (continued)

- Categorizes of surgery included (1) biopsy, (2) thyroid lobectomy, (3) near-total/subtotal thyroidectomy or (4) total thyroidectomy.
- Overall actuarial survival rates at 10 and 15 years were determined for the cohort. Overall survival differences between FV-PTC and C-PTC were determined using the Kaplan-Meier method.
- Cox multivariate regression analysis for overall survival outcomes was conducted with the predictor variables: histopathological type, extent of thyroidectomy, use of RAI therapy, age and sex. Statistical significance was set at p<0.05 for all significance testing.

TABLES & FIGURES

TABLE I.
Distribution of Tumor and Nodal Stages for Follicular Variant and Classical Papillary Thyroid Carcinoma.

	FV-PTC		C-PTC		Total		
	N	%	N	%	N	%	Value
Tumor stage							
T1	8,191	55.5	18,845	59.0	27,036	57.9	
T2	3,419	23.3	5,493	17.2	8,912	19.1	
T3	2,734	18.5	6,175	19.3	8,909	19.1	.450
T4	412	2.8	1,430	4.5	1,842	3.9	
Total	14,756	100.0	31,943	100.0	46,699	100.0	
Nodal status							
N0	12,565	85.2	23,065	72.2	35,630	76.3	
N1	2,191	14.8	8,878	27.8	11,069	23.7	<.001
Total	14,756	100.0	31,943	100.0	46,699	100.0	

FV-PTC = follicular variant papillary thyroid carcinoma; C-PTC = classical papillary thyroid carcinoma.

Table 1. Distribution of tumor and nodal stages for follicular variant and classical papillary thyroid carcinoma.

TABLE II.
Distribution of Patients With Follicular Variant and Classical Papillary Thyroid Carcinoma by Use of RAI Therapy and Extent of Thyroidectomy Surgery.

	FV-PTC		C-PTC		Total	
	N	%	N	%	N	%
RAI therapy						
Yes	6,984	50.0	14,673	48.7	22,461	50.9
No	6,984	50.0	15,477	51.3	21,650	49.1
Surgical extent						
Biopsy only	132	0.9	585	1.9	717	1.6
Lobectomy	2,736	18.7	4,827	15.3	7,563	16.4
Near-total thyroidectomy	3,068	21.0	7,166	22.7	10.234	22.1
Total thyroidectomy	8,682	59.4	19,043	60.2	27,725	60.0

RAI = radioactive iodine; FV-PTC = follicular variant papillary thyroid carcinoma; C-PTC = classical papillary thyroid carcinoma.

Table 2. Distribution of patients with follicular variant and classical papillary thyroid carcinoma by use of RAI therapy and extent of thyroidectomy surgery.

TABLE III.
Mean, 10-Year, and 15-Year Overall Survival for Patients With Follicular Variant and Classical Papillary Thyroid Carcinoma.

	Mean Survival Duration (mo±95% CI)	*P* Value	10-Year Overall Survival %	15-Year Overall Survival %
C-PTC	205.3 ± 1.0	.373	89	81
FV-PTC	204.5 ± 1.8		89	79
Total	205.1 ± 0.9		89	80

CI = confidence interval; C-PTC = classical papillary thyroid carcinoma; FV-PTC = follicular variant papillary thyroid carcinoma.

Table 3. Mean, 10-year, and 15-year overall survival for patients with follicular variant and classical papillary thyroid carcinoma.

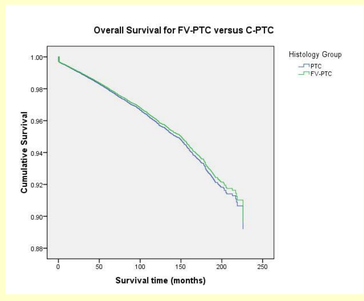

Figure 1. Kaplan-Meier overall survival for papillary thyroid carcinoma based on histopathological subtype, adjusted for age, sex, stage, surgical extent and RAI.

RESULTS

- 31,943 (68.4%) cases of C-PTC and 14,756 (31.6%) cases of FV-PTC were identified, for a combined total of 46,699 patients. The mean age at diagnosis (±SD) for C-PTC and FV-PTC were 46.15 (±15.384) and 47.8 (±15.050) years, respectively.

RESULTS (continued)

- Tumor stage at presentation was not significantly different according to histopathological subtype. The prevalence of nodal disease was significantly higher in C-PTC patients when compared to patients with FV-PTC (p<0.001) (**Table 1**).
- Mean overall survival times (± 95%CI) for all patients with C-PTC (205.3 ± 1.0 months) and FV-PTC (204.5 ± 1.8 months) were not significantly different (p=0.373). Ten-year and 15-year overall actuarial survival for C-PTC were 89% and 81%, respectively, while corresponding survival for FV-PTC were 89% and 79%, respectively (**Table 3**).
- Among patient variables, advanced age (p <0.001), male gender (p<0.001), advanced tumor status (p<0.001) and presence of nodal disease (p<0.001) were associated with reduced survival in Cox multivariate regression. Histopathological subtype (i.e., C-PTC versus FV-PTC) did *not* have a significant impact on survival (p=0.360) (**Figure 1**).

DISCUSSION

- The current literature on FV-PTC only provides a short-term snapshot of the natural course of a long-term disease and is limited to reports on comparisons of its clinicopathologic behavior to C-PTC. Survival data is exceedingly limited. The current analysis sheds some light on the differential disease presentation of FV-PTC relative to C-PTC.
- With respect to staging at presentation, no trend towards earlier or later stage disease for either PTC subtypes was found.
- Twice as many patients with C-PTC presented with nodal disease (27.8%) compared to FV-PTC patients (14.8%) (p<0.001), indicating that FV-PTC has a significantly lower tendency towards nodal disease compared to C-PTC.
- Mean overall survival times were statistically similar, indicating that the prognoses of these patients are similar. Advanced age, tumor stage and male gender were independently associated with reduced overall survival, while tumor histopathological subtype was *not*.
- The diagnosis of FV-PTC has little to no impact on patient survival when compared to patients with C-PTC. Clinicians should be able to definitively provide FV-PTC patients with appropriate counseling on prognosis and to confidently follow C-PTC treatment algorithms for FV-PTC therapy.

CONCLUSIONS

- FV-PTC constitutes a frequently diagnosed subset of PTC, comprising roughly 32% of all PTC cases.
- Although debate has surrounded the differences in the clinical courses and outcomes of patients with FV-PTC, our data suggest that the prognoses of patients with FV-PTC is basically similar to that of C-PTC, and patients should be treated and counseled accordingly.

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