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RESEARCH ARTICLE

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Katanin P60 and P80 in papillary thyroid carcinoma patients: Indicators for exacerbated tumor features and worse disease-free survival

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Abstract

Background: This study aimed to explore the clinical implications of katanin P60 and P80 (katanin P60/P80) regarding their correlations with clinicopathological features and survival profiles in papillary thyroid carcinoma (PTC) patients.

Methods: Tumor tissue and paired adjacent tissue specimens were obtained from 172 PTC patients who underwent lobectomy or thyroidectomy. Besides, immunohistochemistry assay and immunoreactive (IR) score (multiplying staining intensity score by density score) were used to determine katanin P60/P80 expressions. According to IR score (from 0 ~ 12), katanin P60/P80 expressions were classified as low (IR score 0 ~ 3) and high (IR score 4 ~ 12) expressions.

Results: Both katanin P60/P80 expressions were highly expressed in tumor tissue compared with adjacent tissue. Besides, tumor katanin P60 expression positively correlated with tumor katanin P80 expression. Tumor katanin P60 high expression correlated with larger tumor size, extrathyroidal invasion, advanced pT stage, pN stage, and pTNM stage, while no correlation of tumor katanin P60 expression with age or gender was observed; tumor katanin P80 high expression correlated with advanced pN stage and pTNM stage, whereas there was no correlation of tumor katanin P80 expression with age, gender, tumor size, extrathyroidal invasion, or pT stage. Furthermore, both tumor katanin P60/P80 high expressions correlated with shorter accumulating disease-free survival. As for overall survival (OS), neither tumor katanin P60 nor P80 expression correlated with OS.

Conclusion: Katanin P60/P80 measurement might assist with tumor management and prognosis surveillance in PTC patients.

KEYWORDS

katanin P60, katanin P80, papillary thyroid carcinoma, prognosis, tumor stage

1 | INTRODUCTION

Thyroid cancer is one of the most prevalent malignancies in the endocrine system, with an increasing incidence in recent years worldwide.[1] Thyroid cancer is histologically divided into four subtypes: papillary thyroid carcinoma (PTC), follicular thyroid carcinoma, medullary thyroid carcinoma, and anaplastic thyroid carcinoma.[1,2] Among them, PTC, the main histological subtype of

thyroid cancers, is marked by proliferation of follicular cells with distinctive nuclear features such as nuclear grooves and pseudoinclusions, which accounts for approximately 85% of all thyroid cancer cases.[1,3] PTC patients are generally treated by surgical resection, radioactive iodine therapy, and thyroid-stimulating hormone suppression, which achieve with a five-year survival rate of around 97%.[4] Despite the overall good prognosis of PTC, more than 30% of PTC patients suffer from lymph node metastasis, distal metastasis, and recurrence, which is associated with increased mortality.[5,6] Furthermore, no effective biomarker for predicting progression and prognosis of PTC is available to date.[5] Therefore, the discovery of novel biomarkers may offer new prospects for optimizing the tumor management of PTC to reduce the likelihood of recurrence and metastasis.

Katanin, a family of heterodimeric microtubule-severing complex, regulates key cellular activities including cell division, migration, and differentiation through remodeling microtubule-based structures, which consists of P60 subunit and P80 subunit.[7] Previous researches have illustrated that the aberrant expression of katanin P60 or katanin P80 participates in the development and progression of breast cancer, prostate cancer, and non–small-cell lung cancer.[8-13] For instance, katanin P60 represses cell proliferation while enhances cell migration in breast cancer; clinically, katanin P60 is associated with higher N stage, TNM stage and shorter overall survival (OS) in breast cancer patients.[10,11] As for katanin P80, the interaction between katanin P80 and LAPSER1 is involved in cytokinesis, the disruption of which potentially results in genetic instability of prostate cancer; clinically, larger tumor size, lymph node metastasis, and advanced TNM stage were found in non–small-cell lung cancer patients with katanin P80 high expression compared to patients with katanin P80 low expression.[9,13] As for PTC, katanin P60 and P80 (katanin P60/P80) induce mitotic spindle damage, which subsequently trigger chromosomal instability and participate in the tumorigenesis.[8,9,14] However, the clinical relevance of katanin P60/P80 in PTC patients is still unknown. Considering the above data, we hypothesized that katanin P60/P80 might exhibit the potential as biomarkers for progression and prognosis of PTC patients. Therefore, the present study retrospectively assessed katanin P60/P80 expressions in 172 PTC patients and then explored their correlations with clinicopathological features and survival profiles in these patients, aiming to provide new insights for optimizing tumor management and prognostication of PTC in the clinical setting.

2 | METHODS

2.1 | Subjects and specimens

In this retrospective study, a total of 172 PTC tissue and paired adjacent tissue (separate samples of patients' normal tissue) specimens were collected from 172 PTC patients. All specimens were formalin fixed paraffin-embedded (FFPE), and available for immunohistochemical (IHC) assay. As for mRNA derived from FFPE tissues underwent chemical modifications and degradation over time due to the fixation method, katanin P60/P80 mRNA detection by reverse transcription quantitative polymerase chain reaction measurement was not appropriate in this case. All patients had a pathological diagnosis of primary PTC without distant metastases and underwent lobectomy or thyroidectomy in Zhongshan Hospital Affiliated to Xiamen University between January 2015 and December 2019. Besides, all patients met following criteria: age more than 18 years; clinical data and follow-up records were complete; no history of thyroid surgery before thyroidectomy; and no history of other cancers. This study was approved by the Institutional Review Board of Zhongshan Hospital Affiliated to Xiamen University, and written informed consents were obtained from all patients or their family members.

2.2 | Data collection

Clinical data of patients were collected from medical database of Zhongshan Hospital Affiliated to Xiamen University, which comprised of demographics (age and gender), tumor features (tumor size, extrathyroidal invasion status, pathological T stage (pT) stage, pathological (pN) N stage, and pathological TNM (pTNM) stage), and postoperative treatments.

2.3 | IHC assay

Immunohistochemical assay was performed for the assessment of katanin P60/P80 expressions in the tumor tissue and paired adjacent tissues. In brief, the FFPE specimens were sliced as 4 μm sections. The sections were deparaffinized with xylene and rehydrated through graded alcohol washes (100%-70%) followed by antigen retrieval in sodium citrate buffer (10 mmol/L, pH 6.0) with a pressure cooker. After inhibition of endogenous peroxidase activity for 30 minutes with methanol containing 0.3% H_2O_2, the slides were then blocked in normal goat serum. Thereafter, the slides were incubated with primary antibody Rabbit polyclonal to p60 katanin (1:20 dilution, Abcam) or Rabbit polyclonal to KATNB1 (Katanin p80) (1:1000 dilution, Abcam) overnight at 4°C. Next day, the sections were incubated with horseradish peroxidase-conjugated goat-anti-rabbit immunoglobulin G antibody (1:2000 dilution, Abcam). Subsequently, the sections were stained with diaminobenzidine (Dako), counterstained with hematoxylin (Sigma-Aldrich), dehydrated in a graded series of ethanol and xylene, and sealed with neutral resin (Sango Biotech). Finally, the sections were viewed and photographed on a microscope (Nikon Instruments).

2.4 | Katanin P60/P80 expressions evaluation

After IHC staining, katanin P60/P80 expressions in the sections were evaluated using the immunoreactive (IR) score, which was a well-established semi-quantitative scoring system as described in

a previous study.[15] One hundred cells from 5 selected representative high-power fields (HPF, ×200) of each section were counted for the determination of the immunostaining intensity. The staining intensity was interpreted by two experienced pathologists visual scoring as 0 (negative), 1 (weak), 2 (moderate), and 3 (strong), while the staining density was assessed by the percentage of positively stained cells, which was scored from 0 (0%) to 1 (1%-25%), 2 (26%-50%), 3 (51%-75%), and 4 (76%-100%). After multiplying the staining intensity score by the density score, the IR score was obtained, ranging from 0 to 12. A cut-off value of 3 was used to define low and high expression of katanin P60/P80, that is, IR score 0 ~ 3, katanin P60/P80 low expression; IR score 4 ~ 12, katanin P60/P80 high expression.

2.5 | Treatment and follow-up

All patients were treated by lobectomy or thyroidectomy with or without radioactive iodine therapy, followed by thyroid-stimulating hormone (TSH) suppression therapy according to the American Thyroid Association Risk Stratification System.[16] Follow-up schedule for patient was based on the risk stratification for recurrence, and the follow-up tools varied according to the tumor histotype, initial treatment, initial risk of persistent/recurrent disease, and responses to treatment. Serum thyroglobulin (Tg) test and neck ultrasound were the mainstays of PTC follow-up. Based on the follow-up records, disease-free survival (DFS) and OS were evaluated. The DFS was defined as the duration from lobectomy or thyroidectomy to disease recurrence or death; for patients without known disease recurrence or death were censored at the last date of their examination. The OS was defined as the duration from lobectomy or thyroidectomy to death; for patients not known to have died at last follow-up, they were censored on the date they were last known to be alive.

2.6 | Statistical analysis

Categorical data were presented as described as number (percentage), and continuous data were presented as mean and standard deviation (SD). Comparison of katanin P60/P80 expression between tumor and adjacent tissue was determined by McNemar's test. Correlation between tumor katanin P60/P80 was analyzed by chi-square test, while correlation of tumor katanin P60/P80 with clinical features of patients was determined by Spearman's rank correlation test or chi-square test. Kaplan-Meier curves were plotted to displayed DFS and OS, and the comparison for curve was determined by log-rank test. Factors predicting DFS or OS were analyzed by univariable and forward stepwise multivariable Cox's proportional hazard regression. All statistical analyses were performed by SPSS 22.0 statistical software (IBM, USA), and all figures were made by GraphPad Prism 7.01 (GraphPad Software Inc, USA). P value <.05 was considered as statistically significant.

TABLE 1 Characteristics of PTC patients

Items	PTC patients (N = 172)
Demographics	
Age (years), mean ± SD	43.6 ± 11.8
Gender, No. (%)	
Female	128 (74.4)
Male	44 (25.6)
Tumor features	
Tumor size (cm), mean ± SD	3.0 ± 1.5
Extrathyroidal invasion, No. (%)	
No	102 (59.3)
Yes	70 (40.7)
pT stage, No. (%)	
T1	49 (28.4)
T2	34 (19.8)
T3	34 (19.8)
T4	55 (32.0)
pN stage, No. (%)	
N0	72 (41.9)
N1	100 (58.1)
pTNM stage, No. (%)	
I	120 (69.8)
II	25 (14.5)
III	17 (9.9)
IV	10 (5.8)
Postoperative treatment	
Radioiodine, No. (%)	
No	124 (72.1)
Yes	48 (27.9)
TSH-suppression therapy, No. (%)	
No	0 (0.0)
Yes	100 (100.0)

Abbreviations: PTC, papillary thyroid carcinoma; SD, standard deviation; TSH, thyroid-stimulating hormone.

3 | RESULTS

3.1 | Characteristics

The mean age of PTC patients was 43.6 ± 11.8 years, and there were 128 (74.4%) females/44 (25.6%) males (Table 1). Regarding tumor features, the mean tumor size was 3.0 ± 1.5 cm; 70 (40.7%) patients had extrathyroidal invasion; 49 (28.4%), 34 (19.8%), 34 (19.8%), and 55 (32.0%) patients presented with pT stage T1, T2, T3, and T4, respectively; 72 (41.9%) and 100 (58.1%) patients exhibited pN stage N0 and N1, respectively; 120 (69.8%), 25 (14.5%), 17 (9.9%), and 10 (5.8%) patients displayed pTNM stage I, II, III, and IV, respectively. In terms of postoperative treatment, 48 (27.9%) and 100 (100.0%) patients received radioiodine and TSH-suppression therapy, respectively.

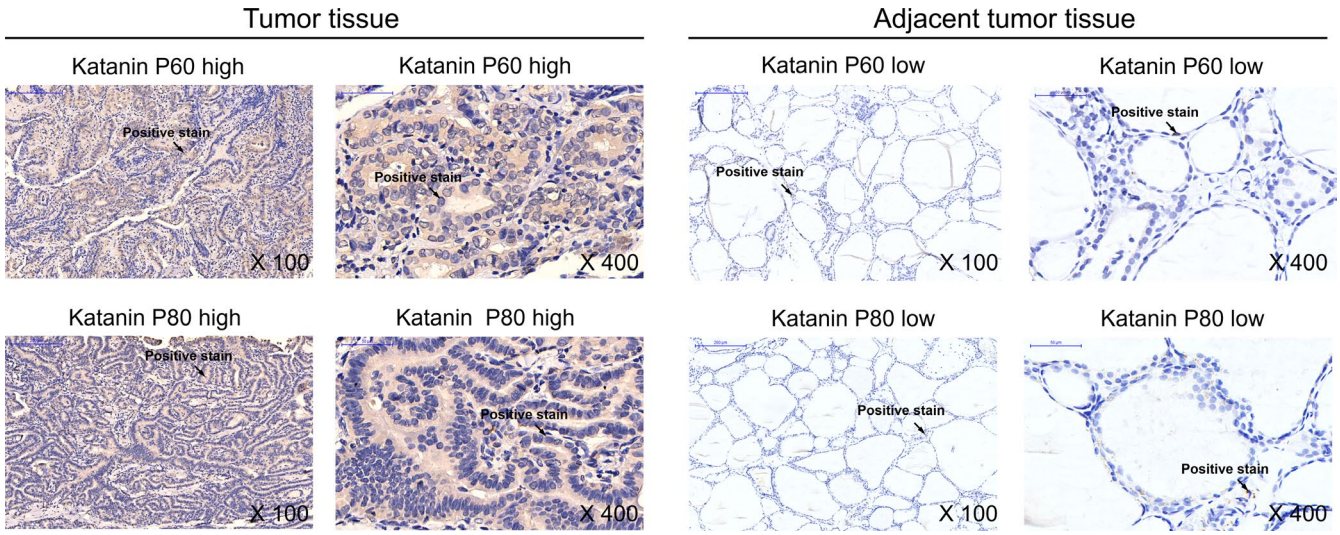

FIGURE 1 Representative IHC staining images of tumor tissue with katanin P60/P80 high expression and adjacent tumor tissue with katanin P60/P80 low expression. IHC, immunohistochemistry; katanin P60/80, katanin P60, and P80

TABLE 2 Comparison of katanin P60/P80 expressions between tumor tissue and adjacent tissue

	Katanin P60		Katanin P80	
Items	**Low**	**High**	**Low**	**High**
Tumor tissue, No. (%)	80 (46.5)	92 (53.5)	70 (40.7)	102 (59.3)
Adjacent tissue, No. (%)	124 (72.1)	48 (27.9)	120 (69.8)	52 (30.2)
P value	<.001		<.001	

Note: Comparison was determined by McNemar's test.

TABLE 3 Correlation between katanin P60 and katanin P80 in tumor tissue

		Katanin P80		
Items		**Low (n = 70)**	**High (n = 102)**	***P* value**
Katanin P60	Low (n = 80)	54 (31.4)	26 (15.1)	<.001
	High (n = 92)	16 (9.3)	76 (44.2)	

Note: Correlation was determined by chi-square test.

3.2 | Katanin P60/P80 expressions in tumor tissue and adjacent tissue

IHC assay was performed to assess katanin P60/P80 expressions in the tumor tissue and adjacent tissue. Then, katanin P60/P80 expressions were classified as low expression (IR score 0 ~ 3) and high expression (IR score 4 ~ 12) based on IR score (from 0-12). IHC staining image samples of tumor katanin P60 high expression, tumor katanin P80 high expression, adjacent katanin P60 low expression, and adjacent katanin P80 low expression were shown in Figure 1. As for katanin P60, 80 (46.5%) and 92 (53.5%) tumor tissue were of katanin P60 low expression and P60 high expression, respectively; 124 (72.1%) and 48 (27.9%) adjacent tissue were with katanin P60 low expression and P60 high expression, respectively; these revealed that katanin P60 was highly expressed in tumor tissue ($P < .001$) (Table 2). Regarding katanin P80, 70 (40.7%) and 102 (59.3%) tumor tissue exhibited katanin P80 low expression and P80 high expression, respectively; 120 (69.8%) and 52 (30.2%) adjacent tissue displayed katanin P80 low expression and P80 high expression, respectively; these disclosed that katanin P80 was highly expressed in tumor tissue ($P < .001$). Besides, katanin P60 was positively associated with katanin P80 in tumor tissue ($P < .001$) (Table 3).

3.3 | Correlation of tumor katanin P60/P80 expressions with patients' characteristics

Tumor katanin P60 high expression correlated with larger tumor size ($P = .031$), extrathyroidal invasion ($P = .008$), advanced pT stage ($P = .002$), pN stage ($P = .020$), and pTNM stage ($P = .026$), while no correlation of tumor katanin P60 expression with age ($P = .387$) or gender ($P = .851$) was observed (Table 4). Tumor katanin P80 high expression correlated with advanced pN stage ($P = .001$) and pTNM stage ($P = .001$), while it did not correlate with age ($P = .466$), gender ($P = .498$), tumor size ($P = .380$), extrathyroidal invasion ($P = .156$), or pT stage ($P = .101$) (Table 4).

3.4 | Correlation of katanin P60/P80 expressions with accumulating DFS

Accumulating DFS was decreased in PTC patients with tumor katanin P60 high expression compared to PTC patients with tumor katanin P60 low expression ($P = .009$) (Figure 2A). Meanwhile, accumulating

TABLE 4 Correlation of katanin P60/P80 with demographics and tumor features

	Katanin P60			Katanin P80		
Items	**Low (n = 80)**	**High (n = 92)**	***P* value**	**Low (n = 70)**	**High (n = 102)**	***P* value**
Age, No. (%)						
<45 y	47 (58.8)	48 (52.2)	.387	41 (58.6)	54 (52.9)	.466
≥45 y	33 (41.2)	44 (47.8)		29 (41.4)	48 (47.1)	
Gender, No. (%)						
Female	59 (73.8)	69 (75.0)	.851	54 (77.1)	74 (72.5)	.498
Male	21 (26.2)	23 (25.0)		16 (22.9)	28 (27.5)	
Tumor size, No. (%)						
<4 cm	64 (80.0)	60 (65.2)	.031	53 (75.7)	71 (69.6)	.380
≥4 cm	16 (20.0)	32 (34.8)		17 (24.3)	31 (30.4)	
Extrathyroidal invasion, No. (%)						
No	56 (70.0)	46 (50.0)	.008	46 (65.7)	56 (54.9)	.156
Yes	24 (30.0)	46 (50.0)		24 (34.3)	46 (45.1)	
pT stage, No. (%)						
T1	30 (37.4)	19 (20.7)	.002	24 (34.3)	25 (24.5)	.101
T2	19 (23.8)	15 (16.3)		14 (20.0)	20 (19.6)	
T3	12 (15.0)	22 (23.9)		14 (20.0)	20 (19.6)	
T4	19 (23.8)	36 (39.1)		18 (25.7)	37 (36.3)	
pN stage, No. (%)						
N0	41 (51.2)	31 (33.7)	.020	40 (57.1)	32 (31.4)	.001
N1	39 (48.8)	61 (66.3)		30 (42.9)	70 (68.6)	
pTNM stage, No. (%)						
I	62 (77.4)	58 (63.1)	.026	58 (82.9)	62 (60.8)	.001
II	11 (13.8)	14 (15.2)		8 (11.4)	17 (16.7)	
III	4 (5.0)	13 (14.1)		3 (4.3)	14 (13.7)	
IV	3 (3.8)	7 (7.6)		1 (1.4)	9 (8.8)	

Note: Correlation was determined by chi-square test or Spearman's rank correlation test.

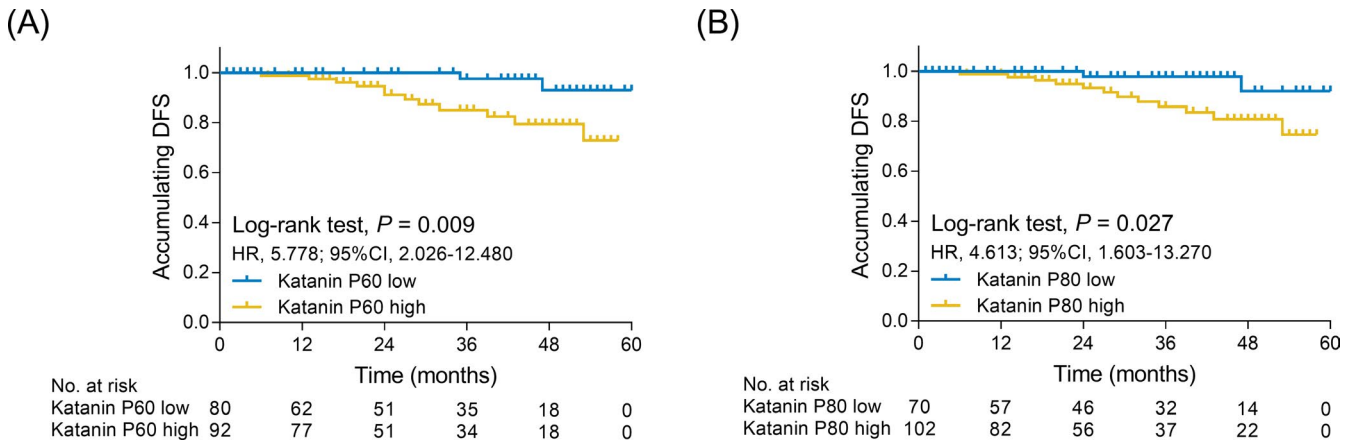

FIGURE 2 Katanin P60/P80 correlated with accumulating DFS in PTC patients. Accumulating DFS between PTC patients with tumor katanin P60 low expression and PTC patients with tumor katanin P60 high expression (A). Accumulating DFS between PTC patients with tumor katanin P80 low expression and PTC patients with tumor katanin P80 high expression (B). Katanin P60/80, katanin P60 and P80; DFS, disease-free survival; PTC, papillary thyroid carcinoma

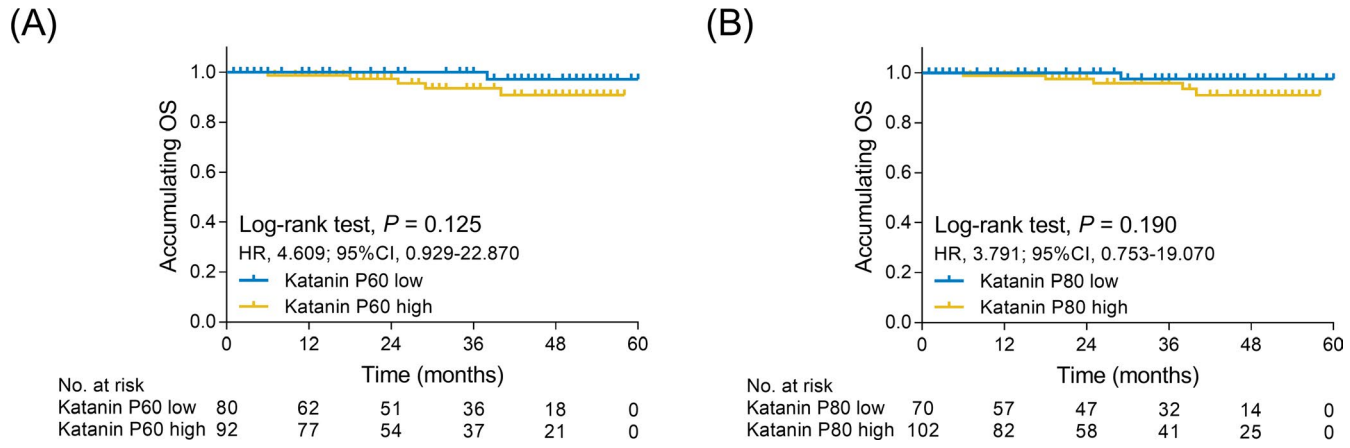

FIGURE 3 Katanin P60/P80 did not correlate with accumulating OS in PTC patients. Accumulating OS between PTC patients with tumor katanin P60 low expression and PTC patients with tumor katanin P60 high expression (A). Accumulating OS between PTC patients with tumor katanin P80 low expression and PTC patients with tumor katanin P80 high expression (B). Katanin P60/80, katanin P60 and P80; OS, overall survival; PTC, papillary thyroid carcinoma

TABLE 5 Univariate and multivariate Cox's proportional hazard regression model analyses of factors predicting DFS

	Cox's proportional hazard regression model			
			95% CI	
Items	*P* value	HR	Lower	Higher
Univariate Cox's regression				
Katanin P60 high	.021	5.808	1.298	25.988
Katanin P80 high	.045	4.619	1.033	20.646
Age ≥45 y	.026	5.497	1.228	24.616
Male	.553	1.395	0.465	4.189
Tumor size >4 cm	.078	2.568	0.900	7.332
Extrathyroidal invasion	.127	2.294	0.789	6.666
pT stage	.034	1.731	1.043	2.873
pN stage	.029	5.303	1.185	23.727
pTNM stage	<.001	2.316	1.456	3.685
Radioiodine	.392	1.589	0.551	4.587
Forward stepwise multivariate Cox's regression				
Katanin P60 high	.056	4.362	0.962	19.781
pTNM stage	.002	2.142	1.314	3.491

Note: Factors predicting DFS were analyzed by univariate Cox's regression and forward stepwise multivariate Cox's regression.
Abbreviations: CI, confidence interval; DFS, disease-free survival; HR, hazard ratio.

DFS was also attenuated in PTC patients with tumor katanin P80 high expression compared to PTC patients with tumor katanin P80 low expression ($P = .027$) (Figure 2B).

3.5 | Correlation of katanin P60/P80 expressions with accumulating OS

Accumulating OS was not differed between PTC patients with tumor katanin P60 low expression and PTC patients with tumor katanin P60 high expression ($P = .125$) (Figure 3A). Besides, no difference of accumulating OS was observed between PTC patients with tumor katanin P80 low expression and PTC patients with tumor katanin P80 high expression ($P = .190$) (Figure 3B).

3.6 | Factors predicting DFS

Univariate Cox's regression analysis found that katanin P60 high expression ($P = .021$, HR = 5.808), katanin P80 high expression ($P = .045$, HR = 4.619), age ≥ 45 years ($P = .026$, HR = 5.497), pT stage ($P = .034$, HR = 1.731), pN stage ($P = .029$, HR = 5.303), and pTNM

TABLE 6 Univariate and multivariate Cox's proportional hazard regression model analyses of factors predicting OS

	Cox's proportional hazard regression model			
			95% CI	
Items	*P* value	HR	Lower	Higher
Univariate Cox's regression				
Katanin P60 high	.163	4.618	0.539	39.562
Katanin P80 high	.224	3.795	0.443	32.504
Age ≥ 45 y	.224	59.390	0.082	42 985.255
Male	.214	2.760	0.557	13.682
Tumor size >4 cm	.019	12.979	1.515	111.218
Extrathyroidal invasion	.603	1.529	0.308	7.584
pT stage	.086	2.310	0.888	6.013
pN stage	.232	55.969	0.076	41 405.470
pTNM stage	.003	2.873	1.420	5.813
Radioiodine	.357	2.122	0.427	10.538
Forward stepwise multivariate Cox's regression				
Tumor size >4 cm	.027	11.868	1.324	106.399
pTNM stage	.019	13.454	1.545	117.158

Note: Factors predicting OS were analyzed by univariate Cox's regression and forward stepwise multivariate Cox's regression.

Abbreviations: CI, confidence interval; HR, hazard ratio; OS, overall survival.

stage ($P < .001$, HR = 2.316) could predict shorter DFS, while male ($P = .553$, HR = 1.395), tumor size > 4 cm ($P = .078$, HR = 2.568), extrathyroidal invasion ($P = .127$, HR = 2.294), or radioiodine ($P = .392$, HR = 1.589) could not predict DFS in PTC patients (Table 5). Further forward stepwise multivariate Cox's regression analysis reported that only pTNM stage ($P = .002$, HR = 2.142) independently predicted decreased DFS in PTC patients.

3.7 | Factors predicting OS

Univariate Cox's regression analysis displayed that tumor size >4 cm ($P = .019$, HR = 12.979) and pTNM stage ($P = .003$, HR = 2.873) could predict reduced OS, while katanin P60 high expression ($P = .163$, HR = 4.618), katanin P80 high expression ($P = .224$, HR = 3.795), age ≥45 years ($P = .224$, HR = 59.390), male ($P = .214$, HR = 2.760), extrathyroidal invasion ($P = .603$, HR = 1.529), pT stage ($P = .086$, HR = 2.310), pN stage ($P = .232$, HR = 55.969), or radioiodine ($P = .357$, HR = 2.122) could not predict OS in PTC patients (Table 6). Further forward stepwise multivariate Cox's regression analysis showed that tumor size >4 cm ($P = .027$, HR = 11.868) and pTNM stage ($P = .019$, HR = 13.454) independently predicted attenuated OS in PTC patients.

4 | DISCUSSION

Several studies have highlighted the implication of both katanin P60/P80 in the oncogenesis and progression of cancers.[8-13] For instance, overexpression of katanin P60 suppresses cancer cell proliferation but promotes cancer cell migration in prostate cancer; and a clinical study reveals that breast cancer patients with katanin P60-positive expression were of more advanced N stage and TNM stage compared to patients with katanin P60-negative expression.[8,11] As for katanin P80, it is illustrated that breast cancer patients with katanin P80-positive expression exhibit more advanced N stage, TNM stage, and reduced OS compared to patients with katanin P80-negative expression.[12] In addition, katanin P60/P80 mediate dysfunction of the mitotic spindle checkpoint and chromosomal instability that participate in the pathogenesis of PTC.[14] Therefore, it was speculated that katanin P60/P80 might have clinical implication in the tumor development and progression of PTC. The present study detected katanin P60/P80 expressions in PTC patients and unrevealed that both katanin P60/P80 expressions were highly expressed in tumor tissue compared with adjacent tissue, and katanin P60 expression was positively associated with katanin P80 expression in PTC patients. These findings could be explained by that (a) katanin P60/P80 might cause mitotic spindle damage and chromosome instability, which subsequently enhanced the neoplastic transformation of cells.[9,17] Thus, katanin P60/P80 were highly expressed in tumor tissue; and (b) katanin P80, the regulatory subunit of katanin P60, might form a complex with katanin P60 to markedly promote the microtubule-binding and microtubule-severing activities of katanin P60.[18] Thereby, katanin P60 expression positively correlated with katanin P80 expression.

Additionally, the present study investigated the correlation of tumor katanin P60/P80 expressions with clinicopathological features and found that tumor katanin P60 high expression correlated with larger tumor size, extrathyroidal invasion, more advanced pT

stage, pN stage, and pTNM stage; tumor katanin P80 high expression correlated with more advanced pN stage and pTNM stage. The possible explanations might involve that (a) katanin P60 might facilitate cancer cell proliferation, migration, and metastasis via dysregulating mitotic cellular events (such as G2/M arrest and formation of cellular pseudopodia).[10,17] Thereby, tumor katanin P60 high expression was associated with advanced tumor features in PTC patients; and (b) katanin P80 might induce the malformation of the central spindle and genetic instability through disrupting the interaction with LASER1, which promoted cancer cell mitosis, migration, and metastasis.[9] Thereby, tumor katanin P80 high expression was associated with more advanced tumor stage in PTC patients.

Data from prior studies illustrate the prognostic value of tumor katanin P60 or P80 in breast cancer and non–small-cell lung cancer.[11-13] In breast cancer, tumor katanin P60 positive expression is associated with worse OS in patients with $HER2^{+}HR^{+}$, $HER2^{+}HR^{-}$ and $HER2^{-}HR^{-}$.[11] In non–small-cell lung cancer, DFS and OS are both attenuated in patients with tumor katanin P80 high expression compared with tumor katanin P80 low expression.[13] However, data regarding the correlation of tumor katanin P60/P80 expressions with prognosis in PTC patients are still unclear. In the present study, Kaplan-Meier analyses disclosed that tumor katanin P60/P80 high expressions were associated with shorter DFS but not OS in PTC patients. Interestedly, subsequent multivariate Cox's regression analyses observed that katanin P60/P80 high expressions could not interpedently predict DFS in PTC patients. To explain these results, the following reasons have been suggested: (a) According our findings, tumor katanin P60 high expression correlated with larger tumor size, extrathyroidal invasion, and more advanced tumor stage, and tumor katanin P80 high expression correlated with more advanced tumor stage; thereby, both tumor katanin P60/P80 high expressions correlated with worse DFS in PTC patients. (b) Tumor katanin P60/P80 might stimulate the microtubule-severing activities and enhance microtubule instability, which promoted cancer cell migration to other sites of body, leading to tumor metastasis.[9,10] Thereby, tumor katanin P60/P80 high expressions were associated with reduced DFS in PTC patients. (c) Katanin P60/P80 might interact with pN stage to indirectly result in worse DFS; thus, they could not independently predict DFS in PTC patients. (d) Tumor katanin P60/P80 expressions did not correlate with OS in PTC patients, which might be explained by that few PTC patients died during the follow-up that markedly reduced the statistic power.

The present study was the first to explore the clinical value of katanin P60/P80 for the progression and prognosis of PTC, while several limitations should be noticed. First, the experiments regarding the mechanism of katanin P60/P80 in the pathogenesis of PTC were not conducted in the present study; thus, further experiments would be desirable. Second, PTC patients with distant metastasis were not included; thus, the clinical significance of katanin P60/P80 in these patients were not analyzed. Third, we found that tumor katanin P60/P80 did not correlate with OS, which was likely explained by that few PTC patients died during the follow-up period that greatly reduced the statistic power; thereby, further studies with extended follow-up duration were needed for evaluating the impact of katanin P60/P80 on OS more objectively. Lastly, all PTC patients were recruited from one hospital, which might result in selection bias.

In conclusion, katanin P60/P80 are both highly expressed in PTC tumor tissues, which correlate with exacerbated tumor features and worse DFS in PTC patients. These findings might aid in tailoring tumor management and predicting prognosis of PTC.

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