Clinical values of preoperative red blood cell distribution width and platelet parameters in patients with papillary thyroid carcinoma

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Abstract. The prevalence of thyroid carcinoma is increasing, and papillary thyroid carcinoma (PTC) is the most frequent subtype. More and more attention is being concentrated on the association between inflammation indicators and malignant tumors. The aim of the present study was to analyze whether the preoperative red blood cell distribution width (RDW) and platelet parameters, including mean platelet volume (MPV) and platelet distribution width (PDW), can be applied to distinguish between patients with PTC or papillary thyroid microcarcinoma (PTMC) and healthy controls, and to explore the associations with clinicopathological characteristics. The study retrospectively compared the RDW, MPV and PDW values of 780 patients with PTC or PTMC against a healthy control group. Receiver operating characteristic (ROC) curves were conducted to determine diagnostic accuracy. Furthermore, the clinicopathological features of the patients with PTC or PTMC were compared between higher and lower platelet parameter groups based on the RDW, MPV and PDW values. Significantly higher preoperative RDW, MPV and PDW values were found in patients with PTC or PTMC compared with those of the healthy group. ROC curve analysis showed that the area under the curve (AUC) plus 95% confidence interval (95% CI) values of RDW, MPV and PDW were 0.808 (0.780-0.835), 0.771 (0.743-0.799) and 0.711 (0.681-0.742), respectively. When RDW and MPV were combined together, the AUC (95% CI) value was enhanced to 0.858 (0.835-0.881) for the patients with PTC. For the patients with PTMC, RDW, MPV and PDW had AUC (95% CI) values of 0.812 (0.783-0.840), 0.779 (0.749-0.808) and 0.718 (0.685-0.751), respectively. When RDW and MPV were combined together, the AUC (95% CI) value was enhanced to 0.858 (0.835-0.881). A higher RDW was significantly associated with being female, deeper tumor infiltration, and normal FT3 and FT4 levels. A higher PDW was significantly associated with elevated thyrotropin receptor antibody levels. In conclusion, as convenient and available inflammation indicators, RDW, PDW and MPV have diagnostic ability and can distinguish between patients with PTC or PTMC and healthy controls. In addition, the combined application of RDW and MPV can improve the diagnostic power. The values of RDW and MPV were associated with clinicopathological characteristics. To the best of our knowledge, this is the first study to prove the usefulness of preoperative RDW combined with MPV in diagnosing patients with PTC or PTMC.

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Introduction

Carcinoma of the thyroid gland, which is the most common endocrine malignant tumor (1), has experienced an increasing incidence globally in the past decades. In 2011, the incidence of thyroid carcinoma has accounted for 1 to 2% of all emerging tumors in the world (2). Papillary thyroid carcinoma (PTC) is the major subtype, which accounts for 80% of all malignant thyroid tumors (3). Inflammation is an important component of the tumor microenvironment that contributes to cancer development and progression. Selected chronic inflammatory conditions enhance the risk of developing cancer (4). These inflammation-driven markers significantly contribute to tumor occurrence, growth and progression (5). The focus on establishing novel non-invasive and sensitive predictive indicators from hematological parameters for inflammatory diseases and tumors has been continuously increasing in recent years.

Although a complete blood count can be routinely obtained from patients for clinicians, the roles of some parameters in the diagnosis and treatment of malignancy, such as red blood cell distribution width (RDW) and platelet parameters, including mean platelet volume (MPV) and platelet distribution width (PDW), remain obscure. RDW is a laboratory parameter widely used for diagnosing anemia (6). However, recent studies have indicated that RDW can be applied as a

laboratory diagnostic parameter for inflammatory diseases and tumors, such as atherosclerosis, inflammatory bowel diseases, lung cancer and breast cancer (7-10). PDW is a measurement of change in platelet size and is a direct platelet volume flow cytometric measurement. PDW has been assessed as a biomarker for determining platelet morphology and activation (11,12). A previous study has also shown the association of PDW with complete blood count and C-reactive protein, and indicated the broad association between platelets and inflammation (13). MPV, another hematological parameter that serves as a marker of platelet size and activity, has been considered as a potential biomarker of platelet function and activation (14). MPV is associated with inflammation-induced arterial and venous thrombosis (15), and large platelets are considered to be more reactive than small platelets, as they are more easily stimulated to release chemical mediators (16). Therefore, the present study aimed to assess whether the three laboratory parameters could be biomarkers used to evaluate disease diagnosis through retrospective analysis of the association between the values of RDW, MPV and PDW, and the clinical data of patients with PTC.

Materials and methods

Study population. The clinicopathological data of 780 patients with PTC, including 542 patients with PTMC (defined as a PTC ≤10 mm in maximal diameter), with a mean age of 46 years and a male:female ratio of 1:3, who had undergone clinical thyroid examination and fine-needle aspiration biopsy (FNAB) for diagnosis were retrospectively analyzed. The data of 400 healthy subjects, with a mean age of 43 years and a male:female ratio of 1:3, were included as the control. All individuals were assessed at Shandong Provincial Hospital Affiliated to Shandong First Medical University (Jinan, China) between January 2017 and December 2018. The diagnosis of papillary thyroid carcinoma/microcarcinoma in all patients was histopathologically reconfirmed by reassessment of biospsy slides by two pathologists. Patients were included in this study based on the following inclusion criteria: A confirmed histopathological diagnosis of PTC/PTMC; a complete whole blood count assessment prior to FNAB; and available clinicopathological data. Patients with clinical signs of acute infection, anemia, hematological disease, diabetes mellitus, cirrhosis, kidney disease, autoimmune disease, severe coronary heart and artery disease, and other malignant tumors were excluded. All clinicopathological data were obtained from medical records. All patients were staged based on the American Joint Committee on Cancer (AJCC) Staging Guidelines (8th edition) (17). Considering the potential for certain patients with PTMC to be overlooked, caution was taken when choosing the healthy controls. The 400 healthy controls were selected from the Medical Examination Center of Shandong Provincial Hospital Affiliated to Shandong First Medical University, and were subjects whose examination results were normal, including blood test, B-ultrasound and computed tomography examination results. This study was approved by the Ethics Committee of Shandong Provincial Hospital Affiliated to Shandong First Medical University (approval no. 2018-456) and written informed consent was obtained from all participants.

Blood sampling and laboratory assays. The RDW, MPV and PDW laboratory parameter values of the patients were assessed 1 week before FNAB with the fully automated hematological analyzer XE-2100 (Sysmex Corporation). Thyroid functional biomarkers, such as free triiodothyronine (FT3), free thyroxine (FT4), anti-thyroglobulin antibodies, anti-thyroperoxidase antibody (anti-TPO) and anti-thyrotropin receptor antibody (TRAB) were also detected within 1 month of FNAB using a Cobas e601 analyzer (Roche Diagnostics). The median values of RDW, MPV and PDW were calculated in all 780 patients with PTC and in the 542 patients with PTMC, respectively. The median values were applied as cut-off values to divide patients into higher and lower RDW, MPV and PDW groups.

Statistical analysis. All statistical analyses were performed using SPSS software version 20.0 (IBM Corp.). The normal distributions of continuous data are displayed as the mean ± standard deviation, and the non-normal distributions of continuous data are expressed as the median. Categorical variables are presented as percentages. Unpaired Student's t-test was performed for comparisons of the mean differences in RDW, MPV and PDW between groups. The χ^2 test was performed to assess the differences between categories of each clinicopathological feature. Receiver operating characteristic (ROC) curves were applied to evaluate the diagnostic accuracy. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Differences between patients with PTC or PTMC and the healthy controls. The preoperative RDW values in the 780 patients with PTC and the 400 healthy controls were 13.13±0.8550 and 12.40±0.5820%, respectively. The RDW value in the PTC group was significant higher than that in the control group ($P<0.001$; Fig. 1A). The preoperative PDW value in the PTC group was 13.05±1.963%, which was significantly higher than the 11.65±1.591% in the control group ($P<0.001$; Fig. 1B). The preoperative MPV values in the PTC and control groups were 10.96±0.8945 and 10.08±0.7724%, respectively. Similar to the other laboratory parameters, there was a significant difference in the MPV values between the two groups ($P<0.001$; Fig. 1C).

The values of RDW, PDW and MPV were also analyzed in the 542 patients with PTMC, which were recorded as 13.16±0.8845, 13.08±1.938 and 10.99±0.8887%, respectively. Significant differences were noted when the values of each group were compared with those of the control group (all $P<0.001$; Fig. 1D-F).

Diagnostic accuracy of RDW, MPV and PDW. ROC curves were used to verify the ability of RDW, PDW and MPV in predicting the presence of PTC and PTMC. For PTC, the diagnostic values of RDW, MPV and PDW for differentiating patients with PTC or PTMC from healthy controls are shown in Table I and Fig. 2A. When the optimal cut-off point was 12.65, RDW had sensitivity (SEN) and specificity (SPE) values of 0.772 and 0.722, respectively. When the optimal cut-off point was 10.45, MPV had SEN and SPE values of 0.694 and

Table I. Evaluation of diagnostic values (normal and papillary thyroid carcinoma or papillary thyroid microcarcinoma).

Variables	Cut-off point	Sensitivity	Specificity	AUC (95% CI)
RDW	12.65	0.772	0.722	0.808 (0.780-0.835)
MPV	10.45	0.694	0.702	0.771 (0.743-0.799)
PDW	12.15	0.652	0.662	0.711 (0.681-0.742)
RDW + MPV		0.894	0.682	0.858 (0.835-0.881)

RDW, red blood cell distribution width; PDW, platelet distribution width; MPV, mean platelet volume; AUC, area under the curve; CI, confidence interval.

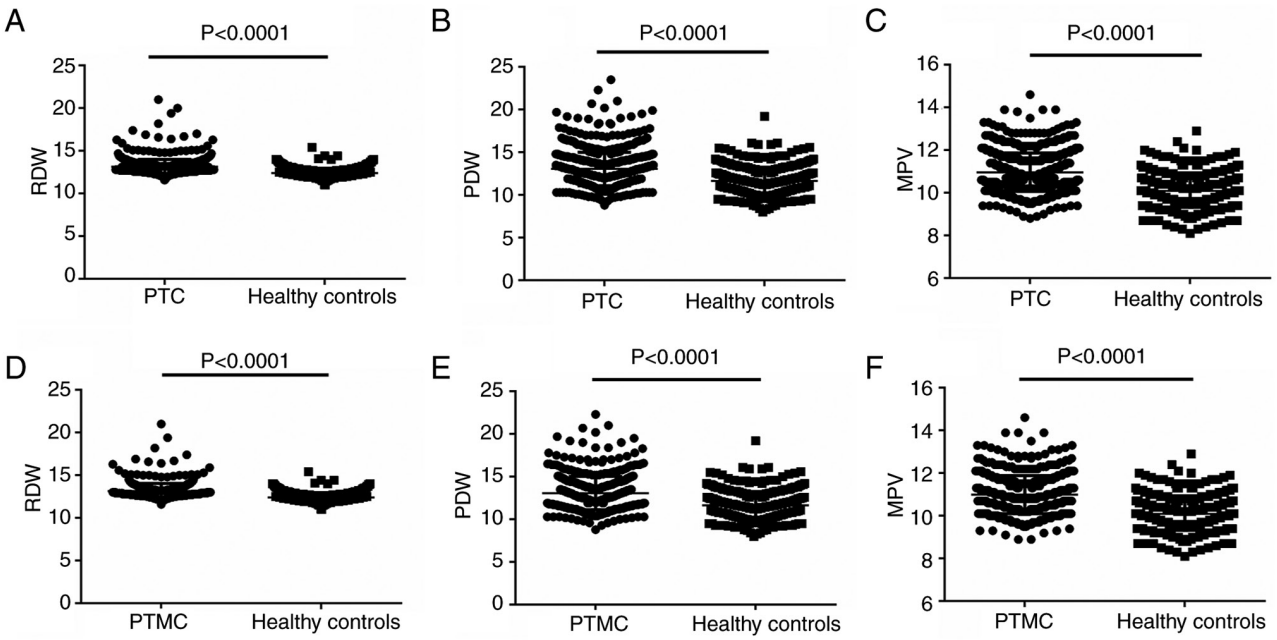

Figure 1. Differences in RDW, PDW and MPV levels between patients with PTC or PTMC and healthy controls. (A) RDW levels, (B) PDW levels and (C) MPV levels in patients with PTC and in healthy controls. (D) RDW levels, (E) PDW levels and (F) MPV levels in patients with PTMC and in healthy controls. PTC, papillary thyroid carcinoma; PTMC, papillary thyroid microcarcinoma; RDW, red blood cell distribution width; PDW, platelet distribution width; MPV, mean platelet volume.

0.702, respectively. When the optimal cut-off point was 12.15, PDW had SEN and SPE values of 0.652 and 0.662, respectively. RDW, MPV and PDW had AUC (95% CI) values of 0.808 (0.780-0.835), 0.771 (0.743-0.799) and 0.711 (0.681-0.742), respectively (Fig. 2A). When RDW and MPV were combined together, the AUC (95% CI) value was enhanced to 0.858 (0.835-0.881).

For PTMC, the diagnostic values of RDW, MPV and PDW for differentiating between the patients with PTMC and the healthy controls are shown in Table II and Fig. 2B. When the optimal cut-off point was 12.65, RDW had SEN and SPE values of 0.782 and 0.723, respectively. When the optimal cut-off point was 10.45, MPV had SEN and SPE values of 0.714 and 0.703, respectively. When the optimal cut-off point was 12.15, PDW had SEN and SPE values of 0.661 and 0.663, respectively. RDW, MPV and PDW had AUC (95% CI) values of 0.812 (0.783-0.840), 0.779 (0.749-0.808) and 0.718 (0.685-0.751), respectively. When RDW and MPV were combined together, the AUC (95% CI) value was enhanced to 0.858 (0.835-0.881).

Association between RDW, MPV, PDW and clinicopathological characteristics in patients with PTC or PTMC. The differences in the clinicopathological characteristics between higher and lower groups in patients with PTC based on RDW, PDW and MPV are summarized in Table III. A higher RDW value was significantly associated with being female (P=0.0003), deeper tumor infiltration (P=0.0472), and normal FT3 (P=0.0076) and FT4 (P=0.0490) levels. A higher PDW value was only significantly associated with an elevated TRAB level (P=0.0119). A higher MPV value was only significantly associated with an elevated TRAB level (P=0.0032).

The differences in the clinicopathological characteristics between higher and lower groups based on RDW, PDW and MPV in patients with PTMC are summarized in Table IV. A higher RDW value was only significantly associated with being female (0.0108). A higher PDW value was significantly associated with being female (P=0.0267) and an elevated TRAB level (P=0.0202). A higher MPV value was also significantly associated with elevated TRAB (P=0.0047).

Table II. Evaluation of diagnostic values (normal and papillary thyroid microcarcinoma).

Variables	Cut-off point	Sensitivity	Specificity	AUC (95% CI)
RDW	12.65	0.782	0.723	0.812 (0.783-0.840)
MPV	10.45	0.714	0.703	0.779 (0.749-0.808)
PDW	12.15	0.661	0.663	0.718 (0.685-0.751)
RDW + MPV		0.894	0.682	0.858 (0.835-0.881)

RDW, red blood cell distribution width; PDW, platelet distribution width; MPV, mean platelet volume; AUC, area under the curve; CI, confidence interval.

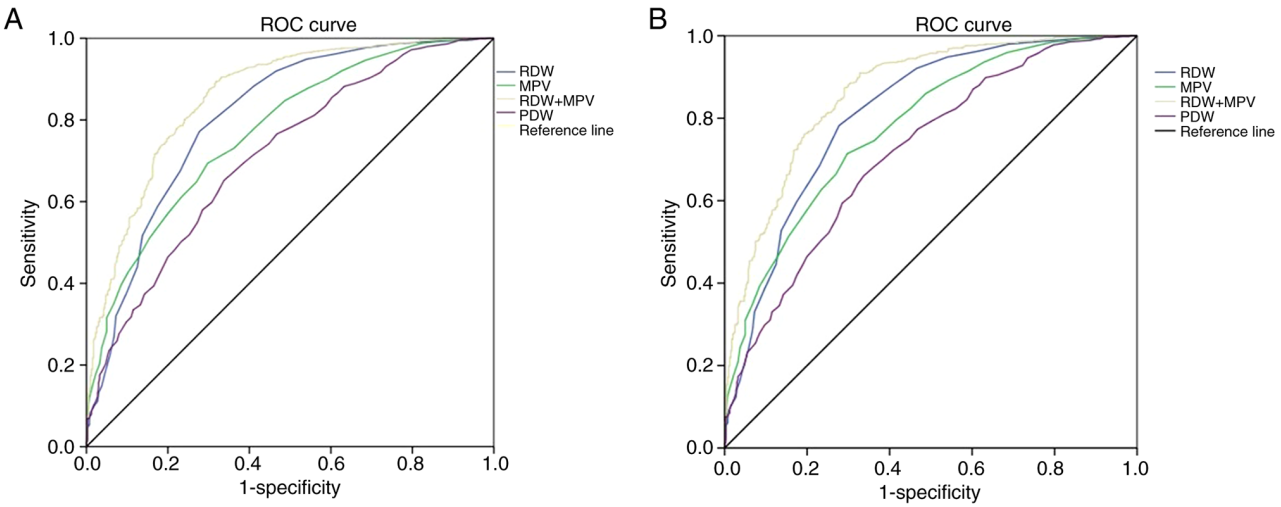

Figure 2. ROC curve analysis results of RDW, PDW and MPV for predicting the presence of PTC or PTMC. ROC curve of RDW, PDW and MPV for predicting the presence of (A) PTC and (B) PTMC. ROC, receiver operating characteristic; PTC, papillary thyroid carcinoma; PTMC, papillary thyroid microcarcinoma; RDW, red blood cell distribution width; PDW, platelet distribution width; MPV, mean platelet volume.

Discussion

Studies have suggested that cancer may be either causative or a result of chronic inflammation, which has moved the research focus towards the connection between inflammation and malignant tumors (18,19). Cancer-associated inflammatory changes have a significant effect on carcinogenesis and tumor progression (18,19). The potential mechanism behind this may involve the association between inflammation and malnutrition, immune dysfunction, angiogenesis, and activation of cytokines and platelets (20,21).

Tumor-infiltrating inflammatory cells mediate a series of processes that are associated with progression, invasion and metastasis (22). The immune regulatory cytokines that are secreted in a pro-inflammatory environment can also promote tumor growth and metastases (23). Certain evidence indicates that inflammation markers such as neutrophil/lymphocyte ratio and platelet/lymphocyte ratio play a vital role during the differential diagnosis of PTC (24). The associated inflammatory markers, such as lymphocyte-to-monocyte ratio and IL-6, have been shown to play an important role in PTC (25,26). As a simple index of the inflammatory system, blood parameters have been widely applied as the predictive markers for the prognosis of some types of malignancy, such as colorectal cancer, nasopharyngeal carcinoma and gastric cancer (27-29). In the last two decades, increasing evidence has suggested that a high RDW value increases the overall and disease-specific mortality rate in patients who have inflammatory bowel disease, acute myocardial infarction and prostate cancer (7,8,30,31). Studies have also shown that RDW can be applied as a diagnostic and prognostic biomarker in various types of solid cancer. For example, the RDW value was significantly higher in patients with breast cancer compared with that in patients with fibroadenomas, and it was also highly correlated with the size of the primary tumor and the number of metastatic axillary lymph nodes (9). Furthermore, RDW was reported to be associated with malnutrition, which has been proven to be associated with a lesser response to treatment, and a poorer prognosis and quality of life (32,33). Platelets regulate neoangiogenesis, diffusion and tumor cell growth (34). Nevertheless, the activation of platelets is more closely associated with their size rather than their count. MPV is an indicator of platelet activation, while PDW displays variation in platelet size, and both of these parameters have been applied to predict the prognosis of various cancer types, such as gastric and breast cancer (29,35).

As one of the cancer types with the most quickly changing basis of understanding in the past decade, thyroid carcinoma has undergone significant staging system revisions based on the eighth version of the AJCC Staging Guidelines (17).

Table III. Comparison of clinicopathological parameters of 780 patients with papillary thyroid carcinoma or papillary thyroid microcarcinoma between high and low groups in terms of RDW, PDW and MPV.

		RDW			PDW			MPV		
Characteristics	Cases, n	<13, n (%)	≥13, n (%)	P-value[a]	<12.8, n (%)	≥12.8, n (%)	P-value[a]	<10.9, n (%)	≥10.9, n (%)	P-value[a]
Sex				0.0003			0.2539			0.8810
Male	184	110 (29.3)	74 (18.3)		85 (21.9)	99 (25.3)		91 (23.8)	93 (23.4)	
Female	596	266 (70.7)	330 (81.7)		304 (78.1)	292 (74.7)		291 (76.2)	305 (76.6)	
Age, years				0.1170			0.3865			0.3137
<46	379	191 (50.8)	188 (46.5)		187 (48.1)	192 (49.1)		189 (49.5)	190 (47.7)	
≥46	401	185 (49.2)	216 (53.5)		202 (51.9)	199 (50.9)		193 (50.5)	208 (52.3)	
Depth of tumor				0.0472			0.5594			0.9308
T1	726	357 (94.9)	369 (91.3)		360 (92.5)	366 (93.6)		354 (92.7)	372 (93.5)	
T2 + T3 + T4	54	19 (5.1)	35 (8.7)		29 (7.5)	25 (6.4)		28 (7.3)	26 (6.5)	
Lymph node metastasis				0.0571			0.3860			0.1368
N0	584	270 (71.8)	314 (77.7)		286 (73.5)	298 (76.2)		277 (72.5)	307 (77.1)	
N1	196	106 (28.2)	90 (22.3)		103 (26.5)	93 (23.8)		105 (27.5)	91 (22.9)	
Number of foci				0.7183			0.2416			0.2107
Unifocal	497	242 (64.4)	255 (63.1)		240 (61.7)	257 (65.7)		235 (61.5)	262 (65.8)	
Multifocal	283	134 (35.6)	149 (36.9)		149 (38.3)	134 (34.3)		147 (38.5)	136 (34.2)	
pStage				0.9559			0.4087			0.3319
I	743	358 (95.2)	385 (95.3)		373 (95.9)	370 (94.6)		365 (95.5)	378 (95.0)	
II	37	18 (4.8)	19 (4.7)		16 (4.1)	21 (5.4)		17 (4.5)	20 (5.0)	
FT3				0.0076			0.9898			0.9187
≤6.01	756	358 (95.2)	398 (98.5)		377 (96.9)	379 (96.9)		370 (96.9)	386 (97.0)	
>6.01	24	18 (4.8)	6 (1.5)		12 (3.1)	12 (3.1)		12 (3.1)	12 (3.0)	
FT4				0.0490			0.7174			0.6361
≤19.05	746	354 (94.1)	392 (97.0)		371 (95.4)	375 (95.9)		364 (95.3)	382 (96.0)	
>19.05	34	22 (5.9)	12 (3.0)		18 (4.6)	16 (4.1)		18 (4.7)	16 (4.0)	
Anti-AG				0.1801			0.8986			0.8327
≤115	645	318 (84.6)	327 (80.9)		321 (82.5)	324 (82.9)		317 (83.0)	328 (82.4)	
>115	135	58 (15.4)	77 (19.1)		68 (17.5)	67 (17.1)		65 (17.0)	70 (17.6)	
Anti-TPO				0.4796			0.2596			0.6973
≤34	534	262 (69.7)	272 (67.3)		259 (66.6)	275 (70.3)		259 (67.8)	275 (69.1)	
>34	246	114 (30.3)	132 (32.7)		130 (33.4)	116 (29.7)		123 (32.2)	123 (30.9)	
Anti-TRAB				0.5152			0.0119			0.0032
≤1.22	764	367 (97.6)	397 (98.3)		386 (99.2)	378 (96.7)		380 (99.5)	384 (96.5)	
>1.22	16	9 (2.4)	7 (1.7)		3 (0.8)	13 (3.3)		2 (0.5)	14 (3.5)	

[a]Calculated by χ^2 test. RDW, red blood cell distribution width; PDW, platelet distribution width; MPV, mean platelet volume; FT3, free triiodothyronine; FT4, free thyroxine; AG, thyroglobulin antibodies; TPO, thyroperoxidase antibody; TRAB, thyrotropin receptor antibody; pStage, pathological stage.

Several studies have attempted to discover the possibility of preoperatively predicting malignancy (36,37), which is largely advocated to establish a tailored surgery, thus preventing a diagnostic thyroidectomy. Gambardella *et al* (38) analyzed the role of the neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio and the lymphocyte-to-monocyte ratio as prognostic factors of malignancy for indeterminate thyroid nodules, and found that the NLR is an easy and reproducible inflammatory biomarker that is able to improve the accuracy of preoperative prognostication for malignancies (38).

In the present study, the values of RDW, PDW and MPV in patients with PTC were identified as significantly higher than those in healthy controls through comparison between

Table IV. Comparison of clinicopathological parameters of 542 patients with PTMC between high and low groups in terms of RDW, PDW and MPV.

		RDW			PDW			MPV		
Characteristics[a]	Cases, n	<13, n (%)	≥13, n (%)	P-value[a]	<12.8, n (%)	≥12.8, n (%)	P-value[a]	<10.9, n (%)	≥10.9, n (%)	P-value[b]
Sex				0.0108			0.0267			0.3626
Male	122	70 (27.3)	52 (18.2)		50 (18.5)	72 (26.5)		55 (20.8)	67 (24.1)	
Female	420	186 (72.7)	234 (81.8)		220 (81.5)	200 (73.5)		209 (79.2)	211 (75.9)	
Age, years				0.6526			0.7274			0.6275
<46	257	124 (48.4)	133 (46.5)		126 (46.7)	131 (48.2)		128 (48.5)	129 (46.4)	
>46	285	132 (51.6)	153 (53.5)		144 (53.3)	141 (51.8)		136 (51.5)	149 (53.6)	
Lymph node metastasis				0.5393			0.1708			0.1634
N0	442	206 (80.5)	236 (82.5)		214 (79.3)	228 (83.8)		209 (79.2)	233 (83.8)	
N1	100	50 (19.5)	50 (17.5)		56 (20.7)	44 (16.2)		55 (20.8)	45 (16.2)	
Number of foci				0.6368			0.2546			0.1785
Unifocal	348	167 (65.2)	181 (63.3)		167 (61.9)	181 (66.5)		162 (61.4)	186 (66.9)	
Multifocal	194	89 (34.8)	105 (36.7)		103 (38.1)	91 (33.5)		102 (38.6)	92 (33.1)	
FT3				0.0514			0.2377			0.0654
≤6.01	530	247 (96.5)	283 (99.0)		262 (97.0)	268 (98.5)		255 (96.6)	275 (98.9)	
>6.01	12	9 (3.5)	3 (1.0)		8 (3.0)	4 (1.5)		9 (3.4)	3 (1.1)	
FT4				0.2438			0.1664			0.3033
≤19.05	522	244 (95.3)	278 (97.2)		257 (95.2)	265 (97.4)		252 (95.5)	270 (97.1)	
>19.05	20	12 (4.7)	8 (2.8)		13 (4.8)	7 (2.6)		12 (4.5)	8 (2.9)	
Anti-AG				0.3810			0.7050			0.9508
≤115	447	215 (84.0)	232 (81.1)		221 (81.9)	226 (83.1)		218 (82.6)	229 (82.4)	
>115	95	41 (16.0)	54 (18.9)		49 (18.1)	46 (16.9)		46 (17.4)	49 (17.6)	
Anti-TPO				0.9646			0.9533			0.4854
≤34	370	175 (68.4)	195 (68.2)		184 (68.1)	186 (68.4)		184 (69.7)	186 (66.9)	
>34	172	81 (31.6)	91 (31.8)		86 (31.9)	86 (31.6)		80 (30.3)	92 (33.1)	
Anti-TRAB				0.6961			0.0202			0.0047
≤1.22	530	251 (98.0)	279 (97.6)		268 (99.3)	262 (96.3)		263 (99.6)	267 (96.0)	
>1.22	12	5 (2.0)	7 (2.4)		2 (0.7)	10 (3.7)		1 (0.4)	11 (4.0)	

[a]PTMC is defined as a PTC ≤10 mm in maximal diameter, so all patients with PTMC are stage T1. Considering that the pStage of PTMC patients is consistent with lymph node metastasis, some characteristics (depth of tumor and pStage) are missing from Table IV compared with Table III. [b]Calculated by χ^2 test. RDW, red blood cell distribution width; PDW, platelet distribution width; MPV, mean platelet volume; FT3, free triiodothyronine; FT4, free thyroxine; AG, thyroglobulin antibodies; TPO, thyroperoxidase antibody; TRAB, thyrotropin receptor antibody; pStage, pathological stage.

the two groups. In order to verify whether the RDW, PDW and MPV values could be used as differential diagnosis indicators for PTMC, the patients with PTMC were also analyzed, and the differences between the patient and control were also significant. These results suggested that RDW, PDW and MPV could be applied as screening indicators for PTC or PTMC. Jin *et al* (37) reported that the PDW value was higher in patients with PTC than that in patients with benign thyroid nodules or healthy controls, which was consistent with the present result. The present study also showed that RDW, PDW and MPV alone had the ability to differentiate PTC or PTMC from healthy controls. In addition, combining the RDW and MPV values could enhance their diagnostic power, which suggests their ability to be clinically accessible indicators. Low levels of MPV and PDW were considered as indicators coexisting with Hashimoto's thyroiditis in patients with PTC (39). Young patients with PTC are more likely to suffer from Hashimoto's thyroiditis than elderly patients with PTC, who are considered to have a poor prognosis. Hashimoto's thyroiditis was associated with a smaller primary tumor and less lymph node involvement at presentation, and was also predictive of a lower rate of lymph node involvement and persistent disease at the end of follow-up, which indicated that Hashimoto's thyroiditis may have a protective effect on patients with PTC (40,41).

Decreased MPV and PDW were prognostic of coexistence with Hashimoto's thyroiditis in elderly patients with PTC, which indicated that lower MPV and PDW might be protective indicators for patients with PTC (39).

The associations between RDW, PDW and MPV, and clinicopathological features, were investigated in the present study. A higher RDW was significantly associated with the female sex and deeper tumor infiltration, but had no association with lymph node metastasis. High RDW level has a prognostic value for lower survival time in patients with gastric, lung, renal and hematological tumors (42,43). However, few studies have reported the association between RDW and the prognosis of PTC. This may be associated with the disease state of PTC, a relatively indolent malignancy (44,45), which is different from other malignant tumors.

Despite gaining some new data, the present study still has some limitations. Firstly, the main limitation of the study is the decision method for the cut-off values. The current literatures confirmed the optimal cut-off values for RDW, MPV and PDW by using ROC curves, median value or previous studies. Only the median values were applied as cut-off values for analysis, and the cutoff values according to ROC and previous studies were not used. Secondly, patients with PTC usually have long survival times; therefore, it is quite difficult to conduct a survival analysis and the standardization of follow-up is a major problem. Thirdly, the study is retrospective in nature and only conducted in a single center. Therefore, similar to most retrospectively designed studies, potential bias and inaccuracies are inevitable in the data collection process. Further prospective randomized controlled studies that include large cohorts and multiple centers are therefore needed to validate these findings in the future.

In summary, RDW, PDW and MPV, as available and convenient biomarkers with diagnostic capabilities, can differentiate patients with PTC or PTMC from healthy controls. In addition, combining the RDW and MPV values can increase this diagnostic power. To the best of our knowledge, this is the first study to verify the utility of preoperative RDW combined with MPV for the diagnosis of PTC or PTMC.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

JH, JW, QW, JZ and HS conceived and designed the experiments, analyzed and interpreted the data, and wrote the manuscript. JH, JW, QW, YL and TL performed the experiments, and collected and analyzed the data. JH, JW, JZ and HS confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Shandong Provincial Hospital Affiliated to Shandong First Medical University (Jinan, China; approval no. 2018-456), and each participant provided written informed consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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