INTRODUCTION

There is increasing and consistent evidence that inflammation is closely related to the occurrence and development of cancer.1-3 Numerous studies have suggested that activation of inflammation is a crucial mechanism that underlies the initiation and progression of thyroid cancer.4,5 Papillary thyroid carcinoma (PTC) is the most common histological type of differentiated thyroid malignancy. Systemic inflammatory markers, which include systemic inflammation response index,6 C-reactive protein,7 neutrophil-(NEU)-to-lymphocyte (LYM) ratio (NLR),8-10 platelet-lymphocyte ratio (PLR),11 lymphocyte-to-monocyte ratio (LMR),12,13 mean platelet volume (MPV),14 and red cell distribution width (RDW)15 have recently been shown to be independent prognostic factors in patients with PTC.

Abstract

Background: Papillary thyroid carcinoma (PTC) is considered to be an inflammatory disease. This study aimed to investigate the association of monocyte to high-density lipoprotein cholesterol ratio (MHR) with PTC.

Methods: Clinical parameters from 300 patients with PTC and 552 patients with benign thyroid nodule were compared. Serum renal function and liver enzymes, fasting plasma glucose, lipid profile, and blood cell count were measured.

Results: Patients with PTC had a higher MONO (p < 0.001) and MHR (p < 0.001). There was a step-wise increase in the prevalence of PTC (p = 0.003) with the tertile of MHR. Logistic regression analysis revealed that MHR could be considered an independent risk factor (p < 0.001) in the case-control study and the cohort study. Pearson correlation analysis and simple linear regression analysis indicated that MHR was positively associated with neutrophil (NEU) and lymphocyte (LYM) count as well as neutrophil-to-lymphocyte ratio (NLR). Area under the curve (AUC) was 0.711. The optimal cutoff of MHR was 0.33 × 10^9/mmol.

Conclusion: This study identifies novel evidence that patients with PTC have a higher MHR. MHR is an independent risk factor for PTC. These findings support the application of MHR to predict, diagnose, and evaluate the occurrence of PTC.

KEYWORDS
high-density lipoprotein cholesterol, inflammation, monocyte, monocyte to high-density lipoprotein cholesterol ratio, papillary thyroid carcinoma

1 | INTRODUCTION

There is increasing and consistent evidence that inflammation is closely related to the occurrence and development of cancer.1-3 Numerous studies have suggested that activation of inflammation is a crucial mechanism that underlies the initiation and progression of thyroid cancer.4,5 Papillary thyroid carcinoma (PTC) is the most
Monocyte (MONO) to high-density lipoprotein cholesterol (HDL-C) ratio (MHR) is obtained by dividing the MONO count by HDL-C. Monocytes are essential immune system cells that have unique roles during the inflammatory response while HDL-C has several biological activities including inhibition of the proliferation, differentiation, and activation of monocytes, and anti-inflammatory and anti-oxidative roles. HDL-C, alone or with the ratio of uric acid (UA), is associated with metabolic syndrome, type 2 diabetes mellitus, thyroiditis, and liver steatosis. MHR is a new biomarker of inflammation and oxidative stress and is being increasingly recognized as a novel clinically relevant biomarker of pathological inflammation and a new predictor and prognostic factor in cardiovascular disease, peripheral artery disease, metabolic syndrome, diabetic nephropathy, and multiple sclerosis.

Papillary thyroid carcinoma is also associated with increased inflammatory burden. There are no data about the relationship between MHR and PTC. Therefore, our study aimed to investigate this association.

2 METHODS

2.1 Study design and population

The study was carried out from January 2018 to December 2020 and involved 372 patients with PTC and 651 people with benign thyroid nodule (BTN) who were recruited from the inpatient departments of Shanghai Fifth People’s Hospital, Fudan University. Diagnosis of PTC and BTN was based on pathology. Retrospective analysis of parameters was performed according to the process described in Figure 1. Subjects were excluded from the study if they had any of the following: history of acute infectious disease, abnormal liver or renal function, leukopenia, or any treatment with immunosuppressive agents. Finally, data from 300 patients with PTC and 552 patients with BTN were analyzed.

The study protocol was approved by the medical ethics committee of Shanghai Fifth People’s Hospital, Fudan University (NO.2018–114). Informed consent was obtained from all patients and subjects.

2.2 Data collection

Patient age and medical history, including medication, and body mass index (BMI) were recorded. After a 12-h overnight fast, blood was obtained for assessment of renal function, liver enzymes, fasting plasma glucose (FPG), lipid profile, and blood cell count.

2.3 Laboratory data

Serum alanine aminotransferase (ALT), urea nitrogen (UN), UA, creatinine (Crea), total cholesterol (TC), HDL-C, low-density lipoprotein

---

**FIGURE 1** Flow chart of the study. BTN, benign thyroid nodule; PTC, papillary thyroid carcinoma; MHR, monocyte to HDL cholesterol ratio.
cholesterol (LDL-C), and FPG were analyzed using an automatic analyzer (Cobas702; Roche Corporation). NEU, LYM, MONO, and C-reactive protein (CRP) were analyzed using an automatic blood cell analyzer (Sysmex XN9000). NLR is the ratio of NEU (×10⁹/L) to LYM (×10⁹/L). LMR is the ratio of LYM (×10⁹/L) to MONO (×10⁹/L). MHR (×10⁹/mmol) is the ratio of MONO (×10⁹/L) to HDL-C (mmol/L).

2.4  |  Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) Version 22.0. Normally distributed continuous variables are expressed as mean ± standard deviation and were analyzed by Student t or ANOVA test. Non-normally distributed variables are expressed as median and interquartile range (IQR) and were analyzed by nonparametric test (Mann-Whitney or Kruskal-Wallis). Categorical variables are presented as frequencies and proportions, analyzed by chi-square test. Pearson correlation analysis and simple linear regression analysis were used to evaluate the association of parameters with MHR. Binary logistic regression analysis was performed to evaluate the association of serum MHR with PTC after adjusting for other clinical and biochemical variables. A p value < 0.05 was regarded as statistically significant.

3  |  RESULTS

3.1  |  Demographics of women with PTC and healthy controls in the case-control study

The clinical characteristics of the PTC group (n = 300) and BTN group (n = 552) are shown in Table 1. Compared with the BTN group, ALT (14.0 [11.0, 17.0] vs. 16.0 [11.0, 21.5] U/L, p = 0.004), MONO (0.40 ± 0.14 vs. 0.44 ± 0.16 × 10⁹/L, p < 0.001), and MHR (0.32 ± 0.15 vs. 0.37 ± 0.18 × 10⁹/mmol, p < 0.001) were significantly increased in the PTC group, while age (54 ± 13 vs. 49 ± 12 years, p < 0.001) and HDL-C (1.39 ± 0.38 vs. 1.32 ± 0.36 mmol/L, p = 0.017) were significantly decreased (Table 1). There was no significant difference in gender, smoke, BMI, UN, UA, Crea, TC, LDL-C, FPG, NEU, LYM, NLR, LMR, or CRP between the two groups (p > 0.05, Table 1).

| Variables         | Total   | BNT group | PTC group | p     |
|-------------------|---------|-----------|-----------|-------|
| n (Male/Female)   | 852 (211:641) | 552 (126:426) | 300 (85:215) | 0.081 |
| Smoke, n (%)      | 191 (22.4%) | 123 (22.3%) | 68 (22.7%) | 0.932 |
| Age (years)       | 52 ± 13 | 54 ± 13 | 49 ± 12 | <0.001 |
| BMI (kg/m²)       | 23.6 ± 2.8 | 23.6 ± 2.9 | 23.7 ± 2.6 | 0.685 |
| ALT (U/L)         | 16.0 [11.0, 23.0] | 14.0 [11.0, 17.0] | 16.0 [11.0, 21.5] | 0.004 |
| UN (mmol/L)       | 4.83 ± 1.32 | 4.86 ± 1.36 | 4.76 ± 1.24 | 0.297 |
| UA (µmol/L)       | 282 ± 80 | 281 ± 81 | 284 ± 78 | 0.549 |
| Crea (µmol/L)     | 61.5 ± 13.2 | 61.6 ± 13.6 | 61.3 ± 12.5 | 0.753 |
| TC (mmol/L)       | 4.59 ± 0.96 | 4.60 ± 0.92 | 4.56 ± 1.03 | 0.588 |
| HDL-C (mmol/L)    | 1.37 ± 0.37 | 1.39 ± 0.38 | 1.32 ± 0.36 | 0.017 |
| LDL-C (mmol/L)    | 2.96 ± 0.85 | 2.97 ± 0.82 | 2.93 ± 0.89 | 0.567 |
| FPG (mmol/L)      | 4.87 (4.56, 5.30) | 5.06 (4.57, 5.60) | 4.72 (4.60, 5.01) | 0.530 |
| NEU (×10⁹/L)      | 4.40 ± 1.37 | 4.38 ± 1.38 | 4.43 ± 1.34 | 0.573 |
| LYMPH (×10⁹/L)    | 1.63 ± 0.53 | 1.61 ± 0.53 | 1.67 ± 0.55 | 0.129 |
| MONO (×10⁹/L)     | 0.42 ± 0.15 | 0.40 ± 0.14 | 0.44 ± 0.16 | <0.001 |
| NLR               | 3.03 ± 1.59 | 3.07 ± 1.69 | 2.95 ± 1.39 | 0.281 |
| LMR               | 4.33 ± 1.94 | 4.43 ± 2.02 | 4.16 ± 1.79 | 0.050 |
| MHR (×10⁹/mmol)   | 0.34 ± 0.17 | 0.32 ± 0.15 | 0.37 ± 0.18 | <0.001 |
| CRP (mg/L)        | 4.0 (2.0, 9.0) | 4.0 (2.0, 8.5) | 5.0 (2.0, 10.5) | 0.058 |

Note: Data of normal distribution are expressed as mean ± standard deviation and analyzed by student t test. Non-normally distributed variables are expressed as median and interquartile range (IQR), and analyzed by nonparametric test (Mann-Whitney). Categorical variables are expressed as frequencies and proportions, and analyzed by using chi-square test. Bold indicates statistical significance (p < 0.05).

Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; BTN, benign thyroid nodule; Crea, creatinine; CRP, C-reactive protein; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LMR, lymphocyte-to-monocyte ratio; LYM, lymphocyte; MHR, monocyte to HDL cholesterol ratio; MONO, monocyte; NEU, neutrophil; NLR, neutrophil-to-lymphocyte ratio; PTC, papillary thyroid carcinoma; TC, total cholesterol; UA, uric acid; UN, urea nitrogen.
### Table 2 Comparison of parameters among three groups categorized by tertile of MHR in the cohort study

| Variables     | Lowest group | Middle group | Highest group | p   |
|---------------|--------------|--------------|---------------|-----|
| MHR (×10^7/mmol) | below 0.24   | 0.24–0.37    | above 0.37    |     |
| n (Male/Female) | 270 (21:249) | 294 (74:220) | 288 (116:172) | <0.001 |
| Smoke, n (%)    | 70 (25.9%)   | 61 (20.7%)   | 60 (20.8%)    | 0.247 |
| Age (years)     | 52 ± 13      | 53 ± 12      | 51 ± 13       | 1.000 |
| BMI (kg/m²)     | 23.3 ± 2.8   | 23.7 ± 2.7   | 24.0 ± 2.7    | 0.152 |
| ALT (U/L)       | 14.0 (11.0, 16.0) | 11.0 (10.0, 16.0) | 16.5 (12.0, 23.8) | <0.001 |
| HDL-C (mmol/L)  | 1.65 ± 0.36  | 1.37 ± 0.28  | 1.09 ± 0.25   | <0.001 |
| LDL-C (mmol/L)  | 3.29 ± 1.73  | 3.42 ± 1.35  | 4.70 ± 1.53   | <0.001 |
| NLR             | 2.83 ± 1.73  | 3.02 ± 1.56  | 3.22 ± 1.48   | 0.010 |
| LMR             | 5.58 ± 2.20  | 4.21 ± 1.53  | 3.29 ± 1.30   | <0.001 |
| CRP (mg/L)      | 4.0 (2.0, 8.0) | 4.0 (2.0, 7.0) | 4.0 (1.4, 11.0) | 0.042 |

Note: Data of normal distribution are expressed as means ± standard deviation and analyzed by student t test. Non-normally distributed variables are expressed as median and interquartile range (IQR), and analyzed by nonparametric test (Kruskal-Wallis H). Categorical variables are expressed as frequencies and proportions, and analyzed by chi-square test. Bold indicates statistical significance (p < 0.05).

Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; Crea, creatinine; CRP, C-reactive protein; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LMR, lymphocyte-to-monocyte ratio; LYM, lymphocyte; MHR, monocyte to HDL cholesterol ratio; MONO, monocyte; NEU, neutrophil; NLR, neutrophil-to-lymphocyte ratio; TC, total cholesterol; UA, uric acid; UN, urea nitrogen.

### 3.2 Comparison of clinical parameters among three groups categorized by tertile of MHR in the cohort study

Subjects were divided into three groups according to tertile of MHR: lowest (below 0.24), middle (0.24–0.37), or highest (above 0.37). There was a step-wise increase in the prevalence of PTC (30.4% vs. 32.3% vs. 42.7%, p = 0.003; Figure 2), and increased level of ALT (14.0 [11.0, 16.0] vs. 11.0 [10.0, 16.0] vs. 16.5 [12.0, 23.8] U/L, p < 0.001), UA (258 ± 68 vs. 281 ± 83 vs. 306 ± 79 µmol/L, p = 0.001), Crea (57.2 ± 10.5 vs. 62.2 ± 13.9 vs. 61.5 ± 13.2 µmol/L, p < 0.001), NEU (3.72 ± 1.30 vs. 4.39 ± 1.29 vs. 5.04 ± 1.18 × 10^9/L, p < 0.001), LYM (1.51 ± 0.50 vs. 1.63 ± 0.51 vs. 1.75 ± 0.57 × 10^9/L, p < 0.001), MONO (0.29 ± 0.08 vs. 0.40 ± 0.08 vs. 0.56 ± 0.13 × 10^9/L, p < 0.001), NLR (2.83 ± 1.73 vs. 3.02 ± 1.56 vs. 3.22 ± 1.48, p = 0.010), and CRP (4.0 [2.0, 8.0] vs. 4.0 [2.0, 7.0] vs. 4.0 [1.4, 11.0] mg/L, p = 0.042) with MHR tertile and a step-wise decrease in TC (4.75 ± 0.92 vs. 4.60 ± 0.95 vs. 4.42 ± 0.98 mmol/L, p < 0.001), HDL-C (1.65 ± 0.36 vs. 1.37 ± 0.28 vs. 1.18 ± 0.13, p < 0.001).

**Figure 2** Prevalence of PTC among three groups categorized by tertile of MHR. PTC, papillary thyroid carcinoma; MHR, monocyte to HDL cholesterol ratio.
vs. $1.09 \pm 0.25 \text{ mmol/L}, p < 0.001$, and LMR ($5.58 \pm 2.20$ vs. $4.21 \pm 1.53$ vs. $3.29 \pm 1.30, p < 0.001$; Table 2).

### 3.3 | Monocyte to high-density lipoprotein cholesterol ratio was an independent risk factor for PTC

To determine independent risk factors for PTC in the case-control study, age, ALT, and MHR, were entered into a binary logistic regression model (enter method). Age ($\beta$ [SE] = $-0.027$ [0.006], OR [95% CI] = 0.973 [0.962, 0.985], $p < 0.001$), ALT ($\beta$ [SE] = $0.011$ [0.006], OR [95% CI] = 1.011 [1.000, 1.023], $p < 0.001$), and MHR ($\beta$ [SE] = $0.036$ [0.360], OR [95% CI] = 4.882 [2.037, 11.700], $p < 0.001$) were independently associated with PTC.

### Table 3

| Variables                  | $\beta$ (SE) | OR (95% CI)       | $p$   |
|----------------------------|--------------|-------------------|-------|
| Age (years)                | $-0.027$ (0.006) | 0.973 (0.962, 0.985) | $<0.001$ |
| ALT (U/L)                  | $0.011$ (0.006)  | 1.011 (1.000, 1.023) | $0.049$  |
| MHR ($\times 10^9$/mmol)  | $0.036$ (0.360) | 4.882 (2.037, 11.700) | $<0.001$ |
| Age (years)                | $-0.028$ (0.006) | 0.973 (0.961, 0.984) | $<0.001$ |
| ALT (U/L)                  | $0.011$ (0.006)  | 1.011 (1.000, 1.023) | $0.050$  |
| HDL-C (mmol/L)             | $-0.340$ (0.206) | 0.712 (0.475, 1.066) | $0.099$  |
| MONO ($\times 10^9$/L)    | $1.511$ (0.497)  | 4.531 (1.711, 12.001) | $0.002$  |

Note: Data are presented as regression coefficient (standard error), odds ratio (95% confidence interval) and $p$ value. Logistic regression analysis (enter method) was used to determine the risk factors for development of PTC in the case-control study. Bold indicates statistical significance ($p < 0.05$).

Abbreviations: ALT, alanine aminotransferase; HDL-C, high-density lipoprotein cholesterol; MHR, monocyte to HDL cholesterol ratio; MONO, monocyte; PTC, papillary thyroid carcinoma.

### Table 4

| Variables                  | $\beta$ (SE) | OR (95% CI)       | $p$   |
|----------------------------|--------------|-------------------|-------|
| Gender                     | $0.195$ (0.041) | 1.216 (0.554, 2.670) | 0.626  |
| ALT (U/L)                  | $-0.010$ (0.011) | 0.990 (0.968, 1.013) | 0.394  |
| Crea ($\mu$mol/L)          | $-0.024$ (0.014) | 0.976 (0.949, 1.004) | 0.095  |
| TC (mmol/L)                | $0.026$ (0.149)  | 1.026 (0.766, 1.375) | 0.861  |
| NEU ($\times 10^9$/L)     | $-0.079$ (0.109) | 0.924 (0.746, 1.144) | 0.468  |
| LYM ($\times 10^9$/L)     | $-0.396$ (0.303) | 0.673 (0.371, 1.219) | 0.191  |
| CRP (mg/L)                 | $-0.001$ (0.013) | 0.999 (0.973, 1.025) | 0.916  |
| MHR ($\times 10^9$/mmol)  | $3.740$ (0.892)  | 41.102 (7.335, 241.672) | $<0.001$ |
| Gender                     | $0.253$ (0.228)  | 1.288 (0.824, 2.014) | 0.268  |
| ALT (U/L)                  | $-0.011$ (0.006) | 1.011 (1.000, 1.023) | 0.058  |
| Crea ($\mu$mol/L)          | $-0.012$ (0.007) | 0.988 (0.974, 1.002) | 0.096  |
| TC (mmol/L)                | $-0.002$ (0.081) | 0.998 (0.851, 1.171) | 0.983  |
| NEU ($\times 10^9$/L)     | $-0.084$ (0.064) | 0.919 (0.810, 1.043) | 0.190  |
| LYM ($\times 10^9$/L)     | $0.029$ (0.142)  | 1.030 (0.780, 1.360) | 0.835  |
| HDL-C (mmol/L)             | $-0.311$ (0.220) | 0.733 (0.476, 1.129) | 0.159  |
| MONO ($\times 10^9$/L)    | $1.912$ (0.592)  | 6.766 (2.120, 21.590) | $0.001$ |

Note: Data are presented as regression coefficient (standard error), odds ratio (95% confidence interval) and $p$ value. Logistic regression analysis (enter method) was used to determine the risk factors for development of PTC in the cohort study. Bold indicates statistical significance ($p < 0.05$).

Abbreviations: ALT, alanine aminotransferase; Crea, creatinine; CRP, C-reactive protein; HDL-C, high-density lipoprotein cholesterol; LYM, lymphocyte; MONO, monocyte; NEU, neutrophil; PTC, papillary thyroid carcinoma; TC, total cholesterol; UA, uric acid.
To determine independent risk factors for development of PTC in the cohort study, gender, ALT, Crea, TC, NEU, LYM, CRP, and MHR were entered into a binary logistic regression model (enter method). MHR ($\beta$ [SE] = 3.740 [0.892], OR [95% CI] = 41.102 [7.335, 241.672], $p < 0.001$) was independently associated with PTC (Table 4). Then, gender, ALT, Crea, TC, NEU, LYM, HDL-C, and MOHO were entered into a binary logistic regression model (enter method). MONO ($\beta$ [SE] = 1.912 [0.592], OR [95% CI] = 6.766 [2.120, 21.590], $p < 0.001$) was independently associated with PTC (Table 4).

3.4 Correlation of MHR with other inflammatory parameters

Pearson correlation analysis revealed that MHR was positively correlated with NEU ($r = 0.402, p < 0.001$, Figure 3A), LYM ($r = 0.193$, $p < 0.001$, Figure 3B), and NLR ($r = 0.097, p = 0.004$, Figure 3C).

Simple linear regression analysis revealed that MHR was also positively associated with NEU ($R^2 = 0.160, p < 0.001$, Figure 4A), LYM ($R^2 = 0.036, p < 0.001$, Figure 4B), and NLR ($R^2 = 0.008, p = 0.004$, Figure 4C).
3.5 | The accuracy of MHR for the diagnosis of PTC

The area under the ROC curve (AUC) of MHR was 0.711 (95% CI: 0.668–0.754, \( p < 0.001 \)). The sensitivity, specificity, and cutoff values of PFR were evaluated. The cutoff value with the highest Youden index (0.346) was defined as the optimization. The optimal value of MHR as an indicator for monitoring the development of PTC was \( 0.33 \times 10^9 / \text{mmol} \), which yielded a sensitivity of 64.0% and a specificity of 70.4% (Figure 5).

4 | DISCUSSION

Papillary thyroid carcinoma is related to inflammatory factors, but its pathogenesis has not been fully elucidated. We innovatively analyzed the relationship between MHR and PTC. The present study revealed novel evidence that MHR is closely related to PTC and an independent risk factor for PTC.

Monocyte is involved in the occurrence of PTC. Park et al.\(^3\) found that thyroid tumors had a high infiltration with inflammatory MONO, while blood and bone marrow were unaffected in a mouse model. In human PTC, the abundance and proportion of MONO were significantly increased, and MONO appeared to play a tumor-promoting role.\(^3\) The present study revealed that the level of MONO in the peripheral blood of PTC patients was significantly increased and MONO was an independent risk factor for PTC.

Monocyte to high-density lipoprotein cholesterol ratio is a new biomarker of inflammation and oxidative stress.\(^2\)\(^3\)\(^4\) Combining two indicators of opposite changes, MHR is a valuable marker in systemic inflammatory diseases. It is being increasingly recognized as a novel clinically relevant biomarker of pathological inflammation and a new predictor and prognostic factor in cardiovascular disease, cerebrovascular disease, peripheral artery disease, metabolic syndrome, diabetic nephropathy, and multiple sclerosis.\(^2\)\(^3\)\(^-\)\(^3\)\(^1\) Nonetheless rarely has MHR been studied in thyroid disease. One large-scale study reported that MHR level was significantly increased in patients with thyroid nodules; MHR was significantly associated with the presence of thyroid nodule and strongly associated with the presence and size of thyroid nodule irrespective of gender.\(^3\)\(^4\) There has been no report of a correlation between MHR and PTC. Our study confirmed our hypothesis that MHR was significantly increased in and closely related to PTC and an independent risk factor for PTC.

Although NEU, LYM, and NLR are classic inflammatory indicators, studies have suggested that they are associated with the incidence of PTC.\(^8\)\(^-\)\(^1\)\(^1\) In our study, NEU, LYM, and NLR were significantly higher in the lowest tertile of MHR group compared with the highest. MHR was positively correlated with NEU, LYM, and NLR. We speculated that MHR might participate in the pathogenesis of PTC by affecting inflammation.

This study has some limitations. The cross-sectional method prevented exploration of a causal relationship between MHR and PTC. Future longitudinal studies may provide clarification.

In summary, this study identifies novel evidence that patients with PTC have a higher MHR. MHR is an independent risk factor for PTC. These findings support the application of MHR to predict, diagnose, and evaluate the occurrence of PTC.

ACKNOWLEDGEMENTS

The authors appreciate the time and effort of all participants.
CONFLICT OF INTEREST
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

DATA AVAILABILITY STATEMENT
Data sharing is not applicable to this article as no datasets were generated or analyzed during the study.

ORCID
Heyuan Ding https://orcid.org/0000-0002-1574-8690

REFERENCES
1. Coussens LM, Werb Z. Inflammation and cancer. Nature. 2002;420(6917):860-867.
2. Murata M. Inflammation and cancer. Environ Health Prev Med. 2018;23(1):50.
3. Diakos CI, Charles KA, McMillan DC, Clarke SJ. Cancer-related inflammation and treatment effectiveness. Lancet Oncol. 2014;15(1):e493-e503.
4. Guarino V, Castellone MD, Avilla E, Melillo RM. Thyroid cancer and inflammation. Mol Cell Endocrinol. 2010;321(1):94-102.
5. Pagano L, Mele C, Sama MT, et al. Thyroid cancer phenotypes in relation to inflammation and autoimmunity. Front Biosci. 2018;23:2267-2282.
6. Xie H, Wei B, Shen H, Gao Y, Wang L, Liu H. BRAF mutation in papillary thyroid carcinoma (PTC) and its association with clinicopathological features and systemic inflammation response index (SIRI). Am J Transl Res. 2018;10(10):2726-2736.
7. Stanciu AE, Serdarevic N, Hurduc AE, Stanciu MM. IL-4, IL-10 and endocrine Hashimoto's thyroiditis. Scand J Clin Lab Invest. 2015;75(7):539-548.
8. Kim JY, Park T, Jeong SH, et al. Prognostic importance of baseline neutrophil to lymphocyte ratio in patients with advanced papillary thyroid carcinomas. Endocrine. 2014;46(3):526-531.
9. Manatakos DK, Tseleni-Balafouta S, Balalis D, et al. Association of baseline neutrophil-to-lymphocyte ratio with clinicopathological characteristics of papillary thyroid carcinoma. Int J Endocrinol. 2017;2017:8471235.
10. Sit M, Aktas G, Erkol H, Yaman S, Keyif F, Savli H. Neutrophil to lymphocyte ratio is useful in differentiation of malign and benign thyroid nodules. P R Health Sci J. 2019;38(1):60-63.
11. Ozmen S, Timur O, Calik I, et al. Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) may be superior to C-reactive protein (CRP) for predicting the occurrence of differentiated thyroid cancer. Endocr Regul. 2017;51(3):131-136.
12. Song L, Zhu J, Li Z, Wei T, Gong R, Lei J. The prognostic value of the lymphocyte-to-monocyte ratio for high-risk papillary thyroid carcinoma. Cancer Manag Res. 2019;11:8451-8462.
13. Kim K, Pak K, Kim U, et al. Lymphocyte-to-monocyte ratio prior to radiiodine ablation in low- and intermediate-risk, papillary thyroid cancer. Endocrine. 2020;70(2):364-371.
14. Sit M, Aktas G, Ozer B, et al. Mean platelet volume: an overlooked herald of malignant thyroid nodules. Acta Clin Croat. 2019;58(3):417-420.
15. Aktas G, Sit M, Karagoz I, et al. Could red cell distribution width be a marker of thyroid cancer? J Coll Physicians Surg Pak. 2017;27(9):556-558.
16. Puhm F, Afoynyshkin T, Resch U, et al. Mitochondria are a subset of extracellular vesicles released by activated monocytes and induce type I IFN and TNF responses in endothelial cells. Circ Res. 2019;125(1):43-52.
17. Ganjali S, Mottazi AA, Banach M, Kovanen PT, Stein EA, Sahhebkar A. HDL abnormalities in familial hypercholesterolemia: focus on biological functions. Prog Lipid Res. 2017;67:16-26.
18. Gomaraschi M, Basilio N, Sisto F, et al. High-density lipoproteins attenuate interleukin-6 production in endothelial cells exposed to pro-inflammatory stimuli. Biochim Biophys Acta. 2005;1736(2):136-143.
19. Kocak MZ, Aktas G, Erkus E, Sincer I, Atak B, Duman T. Serum uric acid to HDL-cholesterol ratio is a strong predictor of metabolic syndrome in type 2 diabetes mellitus. Rev Assoc Med Bras (1992). 2019;65(1):9-15.
20. Aktas G, Kocak MZ, Bilgin S, Atak BM, Duman TT, Kurtkulagi O. Uric acid to HDL cholesterol ratio is a strong predictor of diabetic control in men with type 2 diabetes mellitus. Aging Male. 2020;23(5):1098-1102.
21. Kurtkulagi O, Tel BMA, Kahveci G, et al. Hashimoto's thyroiditis is associated with elevated serum uric acid to high density lipoprotein-cholesterol ratio. Rom J Intern Med. 2021. [Epub ahead of print].
22. Zhang YN, Wang QQ, Chen YS, Shen C, Xu CF. Association between serum uric acid to HDL-cholesterol ratio and nonalcoholic fatty liver disease in lean chinese adults. Int J Endocrinol. 2020;2020:5953461.
23. Canpolat U, Çetin EH, Çetin S, et al. Association of monocyte-to-HDL cholesterol ratio with slow coronary flow is linked to systemic inflammation. Clin Appl Thromb Hemost. 2016;22(5):476-482.
24. Ganjali S, Gotto AM Jr, Ruscica M, et al. Monocyte-to-HDL-cholesterol ratio as a prognostic marker in cardiovascular diseases. J Cell Physiol. 2018;233(12):9237-9246.
25. Akboga MK, Balci KG, Maden O, et al. Usefulness of monocyte to HDL-cholesterol ratio to predict high SYNTAX score in patients with stable coronary artery disease. Biomark Med. 2016;10(4):375-383.
26. Ekizler FA, Cay S, Açıar B, et al. Monocyte to high-density lipoprotein cholesterol ratio predicts adverse cardiac events in patients with hypertrophic cardiomyopathy. Biomark Med. 2019;13(14):1175-1186.
27. Bolayar A, Gökke SF, Cüddem B, et al. Monocyte/high-density lipoprotein ratio predicts the mortality in ischemic stroke patients. Neurolog Neurochir Pol. 2018;52(2):150-155.
28. Selvaggio S, Abate A, Brugaletta G, et al. Platelet-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio and monocyte-to-HDL cholesterol ratio as markers of peripheral artery disease in elderly patients. Int J Mol Med. 2020;46(3):1210-1216.
29. Dincgez Cakmak B, Dondar B, Ketenci Gencer F, Aydin BB, Yildiz DE. TWEAK and monocyte to HDL ratio as a predictor of metabolic syndrome in patients with polycystic ovary syndrome. Gynecol Endocrinol. 2019;35(1):66-71.
30. Onalan E. The relationship between monocyte to high-density lipoprotein cholesterol ratio and diabetic nephropathy. Pak J Med Sci. 2019;35(4):1081-1086.
31. Ulusoy EK, Bolättürk ÖF, Gölf MF. Relation between the novel marker monocyte to high-density lipoprotein cholesterol ratio and severity in multiple sclerosis. Ann Indian Acad Neurol. 2020;23(3):275-279.
32. Park S, Zhu J, Altan-Bonnet G, Cheng SY. Monocyte recruitment and activated inflammation are associated with thyroid carcinogenesis in a mouse model. Am J Cancer Res. 2019;9(7):1439-1453.
33. Xie Z, Li X, He Y, et al. Immune cell confrontation in the papillary thyroid carcinoma microenvironment. Front Endocrinol. 2020;11:570604.
34. Liu XZ, Wang JM, Ji YX, Zhao DB. Monocyte-to-high-density lipoprotein cholesterol ratio is associated with the presence and size of thyroid nodule irrespective of the gender. Lipids Health Dis. 2020;19(1):36.

How to cite this article: Xu H, Pang Y, Li X, Zha B, He T, Ding H. Monocyte to high-density lipoprotein cholesterol ratio as an independent risk factor for papillary thyroid carcinoma. J Clin Lab Anal. 2021;35:e24014. https://doi.org/10.1002/jcla.24014