

Evaluation of the C-Reactive Protein to HDL Cholesterol Ratio as a Marker of Cardiovascular and Renal Risk Among Type 2 Diabetic Patients

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Abstract

BACKGROUND/AIMS: Type 2 diabetes (T2D) is a metabolic disorder commonly accompanied by persistent low-grade inflammation, accelerated development of atherosclerosis, and gradual decline in renal function. The ratio of C-reactive protein (CRP) to high-density lipoprotein-cholesterol (HDL-C) has recently been proposed as a composite biomarker reflecting inflammatory activity and anti-atherogenic capacity. The present study aimed to investigate the relationship between the CRP/HDL-C ratio and the presence of coronary artery disease (CAD) as well as the stages of chronic kidney disease (CKD) in individuals with T2D.

MATERIALS AND METHODS: A total of 148 individuals with T2D were enrolled in this cross-sectional study: 56 patients without CAD and 92 patients with CAD confirmed by angiography; additionally, 44 healthy controls were included. Renal function and CKD staging were determined from the estimated glomerular filtration rate (eGFR) calculated using the CKD-epidemiology collaboration equation. Clinical characteristics and a broad range of biochemical, inflammatory, lipid, and renal markers were evaluated, and the CRP/HDL-C ratio was derived for each participant. Statistical analysis included intergroup comparisons, Spearman correlation testing, and receiver operating characteristic (ROC) curve analysis.

RESULTS: T2D patients, particularly those with CAD, had significantly higher CRP levels, CRP/HDL-C ratios, blood pressure, glucose levels, abnormal lipid levels, and lower eGFR than controls ($p < 0.001$). Progressive stages of CKD were associated with worsening renal function, elevated CRP levels, poor glycemic control, and dyslipidemia. The CRP/HDL-C ratio correlated positively with age, body mass index, fasting blood glucose, glycated hemoglobin, total cholesterol, triacylglycerols, low-density lipoprotein cholesterol, and blood pressure, and correlated negatively with eGFR and serum creatinine. ROC analysis demonstrated that the CRP/HDL-C ratio had good discriminatory ability for the presence of CAD (area under the curve 0.82; 95% confidence interval: 0.740-0.890), with an optimal cut-off value of 2.2, sensitivity of 78%, and specificity of 75%.

CONCLUSION: The CRP/HDL-C ratio is significantly associated with cardiovascular and renal complications in T2D. An elevated ratio reflects increased inflammatory burden, dyslipidemia, and renal impairment, supporting its potential role as a simple and accessible biomarker for cardio-renal risk assessment in patients with T2D.

Keywords: CRP/HDL-C ratio, diabetic nephropathy, chronic kidney disease, coronary artery disease

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INTRODUCTION

Type 2 diabetes (T2D) is a multifactorial metabolic condition defined not only by sustained hyperglycemia but also by ongoing low-grade systemic inflammation and enhanced atherogenesis. Individuals with T2D have a substantially increased risk of coronary artery disease (CAD) and chronic kidney disease (CKD), which are leading causes of cardiovascular morbidity and mortality worldwide.¹ The coexistence of coronary and renal complications reflects shared pathophysiological mechanisms, including endothelial dysfunction, oxidative stress, lipid abnormalities, and systemic inflammation. C-reactive protein (CRP) is a widely recognized biomarker of systemic inflammation and has been repeatedly linked to adverse cardiovascular outcomes as well as the progression of diabetic kidney disease. Elevated CRP levels promote endothelial dysfunction, increase vascular permeability, and contribute to atheromatous plaque instability.² However, inflammation in T2D is not solely defined by elevated pro-inflammatory markers; it is also characterized by qualitative and quantitative alterations in protective lipoproteins. High-density lipoprotein-cholesterol (HDL-C) is known to have anti-inflammatory and antioxidant properties and contributes to endothelial protection and vascular homeostasis. In the diabetic milieu, HDL undergoes structural and functional modifications, losing its anti-atherogenic properties. Reduced HDL concentrations, together with increased inflammatory burden, create a pro-atherogenic environment that accelerates both vascular and renal injury.³ The CRP to HDL-cholesterol ratio (CRP/HDL-C ratio) integrates these opposing biological processes into a single inflammatory index, reflecting the balance between systemic inflammation and anti-atherogenic capacity. Emerging evidence suggests that combined inflammatory-lipid indices may have superior predictive value compared to isolated biomarkers.⁴ However, data on the association between the CRP/HDL-C ratio and CAD and CKD stages in T2D remain limited. In addition to systemic inflammation, vascular-specific inflammatory pathways contribute to diabetic complications. The interplay between systemic inflammatory markers, lipid dysfunction, vascular inflammation, and renal impairment represents a critical yet insufficiently explored area in diabetic patients.⁵ Therefore, this study was designed to examine the relationship between the CRP/HDL-C ratio and the presence and extent of CAD and the severity across CKD stages, and to evaluate its potential role as a simple inflammatory index reflecting combined cardio-renal risk in patients with T2D.

We hypothesized that a higher CRP/HDL-C ratio would be significantly associated with both CAD and progressive renal dysfunction, thereby supporting its potential utility as an accessible, clinically relevant biomarker in routine clinical practice.

MATERIALS AND METHODS

Study Design and Participants

This cross-sectional study enrolled 192 individuals, including 148 patients with T2D and 44 apparently healthy participants who served as a control group (50% male, 50% female). The diagnosis of T2D was established in accordance with the criteria of the American Diabetes Association.⁶ All individuals with T2D had a documented disease duration and received regular clinical follow-up. Patients with T2D were stratified into two groups: those without documented CAD ($n=56$, 65% male, 35% female) and those with CAD confirmed by coronary angiography ($n=92$, 61%

male, 39% female). Patients with diabetic nephropathy were further categorized according to estimated glomerular filtration rate (eGFR) and staged for CKD using the CKD-epidemiology collaboration (CKD-EPI) equation as follows: stage II ($n=47$), stage IIIa ($n=40$), stage IIIb ($n=54$), and stage IV ($n=7$). The control group consisted of apparently healthy individuals with no history of diabetes, cardiovascular disease, or CKD. The control participants were not individually age-matched to the T2D groups. Inclusion criteria: age ≥ 18 years, diagnosed T2D, available complete biochemical and clinical data, for the CAD group: angiographically confirmed CAD. Exclusion criteria: acute inflammatory or infectious disease, malignancy, autoimmune disorders, severe hepatic dysfunction, acute coronary syndrome within the previous 3 months. For all participants, the following data were collected: age, sex, body weight, height, body mass index (BMI), glycemic control parameters, duration of diabetes, and smoking status. Blood pressure was assessed using standardized measurement procedures following a 10-minute resting period.

Laboratory Investigations

Venous blood samples were obtained following a 12-hour overnight fast. Serum concentrations of the following parameters were measured using standardized, automated photometric methods: fasting glucose, total cholesterol, triacylglycerols, HDL-C, low-density lipoprotein cholesterol (LDL-C), blood urea, and creatinine. CRP levels were determined using an immunoturbidimetric assay. Renal function was assessed using eGFR calculated from the CKD-EPI creatinine equation. CKD stages were defined according to KDIGO guidelines based on eGFR values. The CRP/HDL-C ratio was computed using the formula: $\text{CRP/HDL-C ratio} = \text{CRP (mg/L)} \text{ divided by } \text{HDL-C (mg/dL)}$. Prior to analysis, all values were standardized to ensure uniformity across measurements. For unit conversion of HDL-C from mmol/L to mg/dL, a conversion factor of 38.67 was applied (i.e., $\text{mmol/L} \times 38.67$).

Ethical Considerations

The study protocol was reviewed and approved by Ss. Cyril and Methodius University in Skopje Faculty of Medicine Ethics Committee for Human Research (approval no: 03-5602/11, date: 16.12.2022). All participants provided written informed consent prior to enrollment. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and its subsequent amendments.

Statistical Analysis

Statistical analysis was performed using MedCalc for Windows, version 23.1.7 (MedCalc Software, Ostend, Belgium). The normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed variables are presented as mean $\pm$ standard deviation, while non-normally distributed variables were analyzed using non-parametric methods. For comparisons between two groups, Student's t-test was applied to normally distributed variables, and the Mann-Whitney U test to non-normally distributed variables. For comparisons among more than two groups, one-way analysis of variance with appropriate post-hoc analysis was used for normally distributed variables, whereas the Kruskal-Wallis test was applied for non-normally distributed variables. Categorical variables were compared using the chi-square test. Correlations between continuous variables were assessed using Spearman's correlation analysis because several variables did not meet normality assumptions. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the discriminatory ability of the

CRP/HDL-C ratio for CAD. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Comparison of Clinical and Laboratory Characteristics in T2D Patients, with and without CAD, and in Healthy Controls

Patients with T2D differed significantly from healthy controls in several clinical and laboratory parameters, including glycemic control, blood pressure, lipid profile, inflammatory markers, and renal function. Overall comparisons among the three study groups revealed significant differences in CRP, the CRP/HDL-C ratio, eGFR, serum creatinine, fasting blood glucose, and lipid parameters (Table 1). Patients with CAD generally exhibited less favorable metabolic, inflammatory, and renal profiles than those without CAD; however,

the overall p-values presented in Table 1 reflect comparisons across all three groups.

Comparison of Clinical and Laboratory Characteristics in T2D Patients Stratified by CKD Stage and Healthy Controls

The data demonstrate that advancing CKD in patients with T2D is associated with worsening renal impairment, poorer glycemic control, worsening dyslipidemia, and heightened systemic inflammation. Serum creatinine, blood urea, eGFR, glycated hemoglobin (HbA1c), triacylglycerols, and CRP were strongly associated with CKD stage progression and may serve as useful indicators of disease severity. In contrast, BMI, duration of diabetes, and LDL cholesterol did not differ significantly across CKD stages, suggesting a weaker association with renal disease progression in this study population. Table 2 presents the results.

Table 1. Comparison of clinical and laboratory characteristics in T2D patients, with and without CAD, and in healthy controls

Clinical and laboratory characteristics	T2D patients without CAD n=56	T2D patients with CAD n=92	Healthy controls n=44	p-value
Age (years)	58.2±6.005	54.6±6.4	40.5±8.13	<0.001
Male/female (%)	65/35	61/39	50/50	/
BMI (kg/m ²)	28.93±0.67	27.8±0.74	26.5±0.68	0.029
Duration of T2D (years)	6.78±2.62	7.1±2.75	/	0.324
Smoking	68%	62%	54%	0.367
Alcohol	41%	37%	28%	0.325
Blood glucose (mmol/L)	7.46±1.6	7.61±1.45	4.73±0.8	<0.001
HbA1c (%)	7.45±1.45	6.46±1.5	4.36±0.5	<0.001
SBP (mm/Hg)	155.5±2.23	157.04±2.14	125±1.54	<0.001
DBP (mm/Hg)	87.7±0.95	91.93±1.06	87.7±0.95	0.0179
CRP (mg/L)	111.86±9.08	135.25±10.05	2.25±0.13	<0.001
Total cholesterol (mmol/L)	6.93±1.38	7.14±1.36	4.93±0.08	<0.001
Triacylglycerols (mmol/L)	5.02±2.2	5.08±3.02	4.08±1.23	<0.001
HDL-C (mg/dL)	41.04±19.4	27.6±19.5	67.3±11.3	<0.001
LDL-C (mmol/L)	4.7±1.54	4.54±2.14	3.3±0.08	<0.001
Blood urea (mmol/L)	7.83±2.78	8.4±3.1	4.4±2.1	<0.001
Serum creatinine (mmol/L)	128.5±5.2	135.5±3.07	66.7±2.08	<0.001
CRP/HDL-C ratio	2.1±1.7	2.34±0.34	0.009±0.003	<0.001
eGFR (mL/min per 1.73 m ²)	79.4±11.2	50.05±13.7	132.6±22.3	<0.001

Results are expressed as mean ± standard deviation.

T2D: Type 2 diabetes, HbA1c: Glycated Hemoglobin, BMI: Body mass index, eGFR: Estimated glomerular filtration rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, CRP: C-reactive protein, HDL-C: High-density lipoproteins-cholesterol, LDL-C: Low-density lipoproteins-cholesterol, CAD: Coronary artery disease.

Table 2. Comparison of clinical and laboratory characteristics in T2D patients stratified by CKD stage and healthy controls

	Stage II n=47	Stage IIIa n=40	Stage IIIb n=54	Stage IV n=7	Healthy subjects n=44	p-value
Age (years)	52.3±5.6	56.3±6.7	59.5±5.05	58.8±4.1	40.5±8.1	<0.01
BMI (kg/m ²)	28.4±4.2	29.1±6.6	29.5±5.1	32.4±5.04	22.3±2.4	0.39
Duration of T2D (years)	6.5±2.8	5.7±1.9	6.7±1.6	8.8±1.5	/	0.56
Blood glucose (mmol/L)	6.4±0.6	7.5±0.9	7.5±1.2	7.8±0.5	4.7±0.4	<0.001
HbA1c (%)	6.3±1.2	6.1±1.3	6.7±1.6	8.8±1.5	4.36±0.5	<0.001
Total cholesterol (mmol/L)	6.8±0.9	6.9±0.9	7.01±0.9	7.5±1.1	4.9±0.6	<0.001
Blood urea (mmol/L)	7.7±1.6	7.8±2.1	9.1±1.6	9.7±1.3	4.3±1.3	<0.001
Serum creatinine (mmol/L)	99.3±12.6	130.1±19.2	152.2±20.1	207.7±26.8	66.7±13.8	<0.001

Table 2. Continued

	Stage II n=47	Stage IIIa n=40	Stage IIIb n=54	Stage IV n=7	Healthy subjects n=44	p-value
Triacylglycerols (mmol/L)	4.72±1.2	5.28±1.02	5.08±1.3	5.6±1.5	5.4±2.1	0.15
HDL-C (mg/dL)	54.9±17.8	46.2±10.05	12.1±69.9	12.5±30.9	67.3±11.3	<0.001
LDL-C (mmol/L)	4.7±1.54	4.4±1.14	4.3±0.8	4.2±1.1	4.5±1.7	0.123
CRP (mg/L)	54.7±12.7	66.5±21.4	89.8±15.4	115.2±24.4	2.25±0.13	<0.001
CRP/HDL-C ratio	0.99±1.04	1.43±2.12	0.8±0.22	2.71±0.78	0.13±0.01	<0.001

Results are expressed as mean ± SD.

T2D: Type 2 diabetes, HbA1c: Glycated Hemoglobin, BMI: Body mass index, eGFR: Estimated glomerular filtration rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, CRP: C-reactive protein, HDL-C: High-density lipoproteins-cholesterol, LDL-C: Low-density lipoproteins-cholesterol, CKD: Chronic kidney disease, SD: Standard deviation.

Correlation of the CRP/HDL-C Ratio with Clinical and Laboratory Parameters in Study Subjects

Spearman correlation analysis demonstrated that the CRP/HDL-C ratio was positively correlated with several metabolic and cardiovascular risk factors. Specifically, higher CRP/HDL-C ratios were moderately correlated with age ($\rho=0.54$), BMI ($\rho=0.34$), total cholesterol ($\rho=0.51$), triglycerides ($\rho=0.54$), LDL-C ($\rho=0.42$), and blood pressure (systolic blood pressure: $\rho=0.55$; diastolic blood pressure: $\rho=0.51$). Strong positive correlations were observed with fasting blood glucose ($\rho=0.70$) and HbA1c ($\rho=0.71$), indicating that poorer glycemic control was associated with higher CRP/HDL-C ratios. Conversely, the CRP/HDL-C ratio was negatively correlated with blood urea ($\rho=-0.60$), serum creatinine ($\rho=-0.68$), and eGFR ($\rho=-0.78$), suggesting an association with declining renal function. The duration of T2D showed only a weak correlation ($\rho=0.02$), indicating that the CRP/HDL-C ratio may reflect the current metabolic and inflammatory status rather than disease duration. These findings support the potential value of the CRP/HDL-C ratio as an integrative marker linking metabolic dysregulation, cardiovascular risk, and renal impairment in patients with T2D. Table 3 presents the results.

Diagnostic Performance of the CRP/HDL-C Ratio for Discrimination of CAD

ROC curve analysis demonstrated that the CRP/HDL-C ratio had good discriminatory ability for detecting CAD. The area under the curve was 0.82 (95% confidence interval: 0.740-0.890; $p<0.0001$), with an optimal cut-off value of <2.2, yielding a sensitivity of 78% and a specificity of 75%. The positive and negative predictive values were 87% and 70%, respectively. These findings suggest that the CRP/HDL-C ratio may be a useful and accessible biomarker for identifying T2D patients with CAD. However, because ROC analysis was performed within the same cohort without external validation, these results should be considered exploratory and should be confirmed in independent populations (Table 4).

DISCUSSION

The study indicates a significant association of the CRP/HDL ratio with cardiovascular and renal complications in patients with T2D. Patients with T2D, particularly those with angiographically confirmed CAD, exhibited significantly higher CRP levels and CRP/HDL-C ratios, impaired renal function, poorer glycemic control, and more pronounced lipid abnormalities compared with patients with T2D without CAD and healthy controls. These findings support the hypothesis that the imbalance between systemic inflammation and protective HDL-C-mediated anti-atherogenic activity contributes to

Table 3. Correlation of the CRP/HDL-C ratio with clinical and laboratory parameters in study subjects

Clinical and laboratory parameters	CRP/HDL-C ratio
	Spearman ρ
Age (years)	0.54
Duration of T2D (years)	0.02
BMI (kg/m ²)	0.34
Glucose (mmol/L)	0.7
HbA1c (%)	0.71
Total cholesterol (mmol/L)	0.51
Triacylglycerols (mmol/L)	0.54
LDL-C (mmol/L)	0.42
Blood urea (mmol/L)	-0.6
Serum creatinine (μ mol/L)	-0.68
SBP (mm/Hg)	0.55
DBP (mm/Hg)	0.51
eGFR (mL/min per 1.73 m ²)	-0.78
HbA1c: Glycated Hemoglobin, BMI: Body mass index, eGFR: Estimated glomerular filtration rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HDL-C: High-density lipoproteins-cholesterol, LDL-C: Low-density lipoproteins-cholesterol. CRP: C-reactive protein.	

Table 4. Diagnostic performance of the CRP/HDL-C Ratio for discrimination of CAD

The area under the ROC curve (AUC)	0.82
95% confidence interval (95% CI)	0.740-0.890
Significance level p (area=0.5)	<0.0001
Youden index J	0.53
Optimal cut-off	< 2.2
Sensitivity %	78
Specificity %	75
NPV-negative predictive value %	70
PPV-positive predictive value %	87
CRP/HDL-C: C-reactive protein/high-density lipoprotein cholesterol, CAD: Coronary artery disease, ROC: Receiver operating characteristic.	

the progression of both macrovascular and renal complications in T2D.⁷ Inflammation is a key mechanism in the development of both atherosclerosis and diabetic nephropathy. CRP is a widely recognized marker of inflammation that has been linked to endothelial dysfunction, oxidative stress, instability of atherosclerotic plaques,

and vascular damage. Conversely, HDL-C exerts anti-inflammatory, antioxidant, and endothelial-protective effects. In patients with diabetes, HDL particles undergo structural and functional modifications, leading to reduced anti-atherogenic capacity. The CRP/HDL-C ratio therefore reflects the combined influence of increased inflammatory burden and impaired lipid-mediated vascular protection, making it a potentially valuable integrative biomarker of cardio-renal risk.⁴ In this study, the overall comparison demonstrated that CRP/HDL-C ratios differed significantly among the three study groups, with the highest values observed in patients with CAD. ROC analysis demonstrated that the CRP/HDL-C ratio had good discriminatory ability to identify CAD in patients with T2D. However, because the ROC analysis was performed within the same cohort and lacked external or internal validation, these findings should be interpreted cautiously. Future studies using independent cohorts and appropriate validation methods are required to confirm the clinical utility of this marker. Similar observations have been reported in previous studies, which have shown that combined inflammatory-lipid indices may predict cardiovascular events more accurately than isolated inflammatory or lipid parameters.^{4,8,9} The present study also demonstrated a significant association between the CRP/HDL-C ratio and renal dysfunction. Patients with more advanced stages of CKD exhibited higher CRP concentrations, worsening renal function parameters, and altered lipid profiles. Although the CRP/HDL-C ratio did not increase completely linearly across all CKD stages, the highest values were observed in advanced renal impairment, particularly stage IV CKD, suggesting that progressive renal dysfunction is accompanied by enhanced systemic inflammation and reduced anti-atherogenic protection. These results align with earlier research showing that persistent inflammation plays a major role in the development and progression of diabetic kidney disease as well as cardiovascular complications.^{9,10} Correlation analysis further supported the relationship between the CRP/HDL-C ratio and metabolic, cardiovascular, and renal abnormalities. Higher CRP/HDL-C ratios were positively correlated with age, BMI, blood pressure, fasting blood glucose, HbA1c, total cholesterol, triglycerides, and LDL-C levels, indicating that an increased inflammatory burden is closely associated with poorer metabolic control and a less favorable cardiovascular risk profile. In addition, the CRP/HDL-C ratio showed significant correlations with renal function parameters, including serum creatinine and eGFR, suggesting an association with renal dysfunction in patients with T2D. The weak correlation with diabetes duration indicates that the CRP/HDL-C ratio may reflect the current inflammatory and metabolic status rather than cumulative disease duration. The clinical implications of these findings are important. The CRP/HDL-C ratio is inexpensive, widely available, and easily calculated from routine laboratory parameters. Therefore, it may be used as a practical marker for early identification of T2D patients at increased risk of cardiovascular and renal complications. Incorporating this ratio into routine clinical assessment could improve risk stratification and facilitate earlier preventive interventions that target inflammation and dyslipidemia and provide cardio-renal protection.^{11,12}

Study Limitations

Several limitations of the present study should be considered. First, its cross-sectional design precludes causal inference. Second, the absence of an a priori sample size calculation represents another limitation of this study. Although significant associations were identified, the sample

size, particularly within advanced CKD stages, may have limited the statistical power. Future studies should include prospective sample size estimation and larger populations to validate these findings. Third, because this was a single-center study, the generalizability of the findings may be limited. Furthermore, multivariable regression analyses were not performed, thereby restricting the ability to determine independent predictive associations. An additional limitation is the age difference between the control group and the T2D mellitus (T2DM) groups. Although the control participants were healthy individuals without diabetes or cardiovascular disease, they were younger than the diabetic participants. Because age is an important determinant of inflammation, renal function, lipid metabolism, and cardiovascular risk, residual confounding by age cannot be excluded. Future studies with age-matched controls or analyses adjusted for age and other relevant confounders are needed to confirm these findings. Another limitation is that multiple comparisons were performed among several clinical and biochemical variables without formal adjustment for multiple testing. Therefore, the possibility of a type I error cannot be completely excluded, and the findings should be considered exploratory and should be confirmed in future studies using appropriate correction methods. Prospective, multicenter studies with larger cohorts are needed to validate the prognostic significance of the CRP/HDL-C ratio. In addition, studies incorporating multivariable regression analyses are warranted to determine whether the observed associations are independent of established cardiovascular and renal risk factors. Further research should evaluate whether interventions targeting systemic inflammation and improving HDL-C functionality can reduce cardio-renal risk in patients with T2D.

CONCLUSION

The CRP/HDL-C ratio is associated with cardiovascular and renal complications in patients with T2D. Its good discriminatory performance for CAD suggests potential utility as an accessible marker for cardio-renal risk assessment; however, further studies with external validation and adjusted analyses are required before clinical implementation.

MAIN POINTS

- The C-reactive protein/high-density lipoprotein-cholesterol (CRP/HDL-C) ratio was significantly higher in patients with T2D mellitus (T2DM) than in healthy controls and was highest in patients with coronary artery disease (CAD) and advanced chronic kidney disease (CKD).
- Higher CRP/HDL-C ratios were associated with poorer glycemic control, dyslipidemia, elevated blood pressure, and declining renal function.
- The CRP/HDL-C ratio demonstrated good discriminatory ability for identifying CAD, with an area under the curve of 0.82 (95% confidence interval: 0.740-0.890), a sensitivity of 78%, and a specificity of 75%.
- Progressive CKD stages in patients with T2DM were associated with increased systemic inflammation, worsening renal function, and adverse lipid profiles.
- The CRP/HDL-C ratio is a simple, inexpensive, and readily available biomarker that may help assess combined cardiovascular and renal risk in patients with T2DM.

ETHICS

Ethics Committee Approval: The study protocol was reviewed and approved by Ss. Cyril and Methodius University in Skopje Faculty of Medicine Ethics Committee for Human Research (approval no: 03-5602/11, date: 16.12.2022).

Informed Consent: All participants provided written informed consent prior to enrollment.

Footnotes

Authorship Contributions

Surgical and Medical Practices: I.K., Concept: I.K., Design: I.K., Data Collection and/or Processing: I.K., K.T.T., Analysis and/or Interpretation: S.C., S.T., Literature Search: I.K., Writing: I.K.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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Declaration on the Use of Artificial Intelligence (AI): No artificial intelligence tools were used in the preparation of this manuscript.

REFERENCES

- Garcia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, et al. Pathophysiology of type 2 diabetes mellitus. *Int J Mol Sci.* 2020; 21(17): 6275.
- Chen J, Yan L, He L, Wang W. Association between different dimensions of the C-reactive protein-triglyceride-glucose index and future cardiovascular disease risk in individuals with cardiovascular-kidney-metabolic syndrome stages 0-3: a nationwide cohort study. *Diabetol Metab Syndr.* 2025; 17(1): 299.
- Ménégaud L, Laubriet A, Crespy V, Leleu D, Pilot T, Van Dongen K, et al. Inflammation and oxidative stress markers in type 2 diabetes patients with Advanced Carotid atherosclerosis. *Cardiovasc Diabetol.* 2023; 22(1): 248.
- Gao Y, Wang M, Wang R, Jiang J, Hu Y, Wang W, et al. The predictive value of the hs-CRP/HDL-C ratio, an inflammation-lipid composite marker, for cardiovascular disease in middle-aged and elderly people: evidence from a large national cohort study. *Lipids Health Dis.* 2024; 23(1): 66.
- Oda Y, Nishi H, Nangaku M. Role of inflammation in progression of chronic kidney disease in type 2 diabetes mellitus: clinical implications. *Semin Nephrol.* 2023; 43(3): 151431.
- American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: standards of care in diabetes-2025. *Diabetes Care.* 2025; 48(1 Suppl 1): S27-49.
- Jiang Y, Yu J. Association between hs-CRP/HDL with type 2 diabetes mellitus in middle-aged and elderly people: a cross-sectional study from CHARLS. *Front Endocrinol (Lausanne).* 2025; 16: 1471292.
- Zhang Y, Chen G, Wang W, Jing Y. C-reactive protein to high-density lipoprotein cholesterol ratio: an independent risk factor for diabetic retinopathy in type 2 diabetes patients. *Front Nutr.* 2025; 12: 1537707.
- Sun H, Yang J, Ma L, Wu Y. Association between hs-CRP/HDL-C ratio and risk of prediabetes or diabetes: a cross-sectional study based on NHANES 2015-2023. *BMC Endocr Disord.* 2025; 25(1): 183.
- Wu T, Gu T, Wang Q, Li Y, Chen X, Shen S, et al. Correlation of CRP/HDL-C ratio with diabetic kidney disease in type 2 diabetes mellitus patients: evidence from the NHANES 2015-2020. *J Lab Med.* 2026; 50(3): 153-161.
- Han F, Guo H, Zhang H, Zheng Y. Hs-CRP/HDL-C can predict the risk of all cause mortality in cardiovascular-kidney-metabolic syndrome stage 1-4 patients. *Front Endocrinol (Lausanne).* 2025; 16: 1552219.
- Abbas AA. The link between chronic kidney disease and cardiovascular biomarkers: a comprehensive analysis. *IJCR.* 2025; 7(1): 21-6.