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Evaluate the Potential Role of MPO, MCP-1, and Hcy levels in the Pathogenicity of Atherosclerosis

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Abstract: Atherosclerosis (AS) is a chronic inflammatory disorder causing cardiovascular illnesses, Responsible for rising death rates worldwide. This study aimed to investigates the diagnostic potential of Hcy, MCP-1, and MPO biomarkers. In this study, 90 participants were enrolled, aged 20 to 75, including 60 AS patients divided into two groups: 30 pre-catheterization (Pre-Cath) patients and 30 post-catheterizations (Post-Cath) patients, along with 30 healthy controls. Results revealed significantly elevated levels of Hcy, MCP-1, and MPO in AS patients compared to controls. Higher WHR was significantly correlated with increased levels of Hcy, reinforcing the association between central obesity and vascular inflammation. Notably, MCP-1 and MPO levels were higher in patients with a WHR > 0.9, especially in a group Pre-Cath patients, emphasizing its role in endothelial dysfunction in obese individuals. Correlation analysis demonstrated that there were many correlations between the parameters, such as association between Hcy and MPO, highlighting their role in vascular inflammation. Higher MCP-1 levels were observed in patients (≤50), particularly in the Post-Cath patients group. In contrast, MPO levels were markedly higher in patients (>50), particularly in Post-Cath cases, highlighting its relevance linking aging to sustained inflammation. These biomarkers play important roles in the diagnosis, onset, and progression of AS, so they can be used to help develop early diagnostic and therapeutic approaches to prevent disease progression.

Keywords*: Hcy, MCP-1, MPO, catheterization, Atherosclerosis.*

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Introduction

Atherosclerosis (AS) represents a chronic inflammatory process driven by deposition of cholesterol rich lipoproteins and inflammatory activation in the vessel wall to produce atheromatous plaques (1). Such plaques cause arteries to thicken and narrow, which can trigger dangerous cardiovascular incidents such as heart attacks and strokes (2, 3). AS pathogenesis comprises cellular lipid metabolism coupled to local inflammation; a critical driver of global morbidity and mortality due to cardiovascular disease (CVD) (4, 5). The development of AS starts with damage to endothelial cells, followed by accumulation of lipoproteins and an inflammatory process that leads to fibrous plaques forming on the arterial wall (6). Accumulation of low-density lipoprotein (LDL) cholesterol in the arterial wall promotes infiltration of immune cells and formation of lipid laden foam cells, they help to form a lipid-rich necrotic center in the plaque (7, 8). It goes beyond to involving the

migration of vascular smooth muscle cells (SMCs) into the intima layer, proliferation and contributing to the synthesis of extra cellular matrix (ECM) proteins that forms a fibrous cap which stabilizes the plaque (9). Nonetheless, damage and rupture of this cap can lead to thrombosis (10). SMCs phenotypic switching is prominently involved in AS, with SMCs derived cells displaying tumor like behaviors like genomic instability and resistance to cell death (11). Risk factors for AS include age, hypertension, high cholesterol, smoking, diabetes, obesity and chronic inflammation due to other conditions (12, 13). Smoking stimulates the intracellular formation of reactive oxygen species (ROS) and diminishes intracellular antioxidant systems, resulting in oxidative stress (14). Chronic hypertension is a major contributor to various CVD (15). Diagnosing AS involves different techniques and strategies, all playing a role in aiding in the complete understanding of the pathology (16). These techniques go all the way from biochemical markers and imaging variants to clinical assessments.

Understanding the molecular basis of factors implicated in the AS initiation and progression helps in developing early diagnostic and therapeutic approaches to prevent disease progression. Our research focuses on finding the potential relationship between the products of some AS-related genes, e.g. Homocysteine (Hcy), Monocyte Chemoattractant Protein-1 (MCP-1) and Myeloperoxidase (MPO) their association with AS pathogenicity. Hcy, an amino acid formed during methionine metabolism, is a major factor contributing to atherogenesis (17). Hyperhomocysteinemia (high concentrations of Hcy) is involved in common CVD as AS, through the adverse action of this compound on the vascular system (18). Through the actions of endothelial dysfunction, oxidative stress, stimulation and promotion of thrombogenesis Hcy promotes AS (19). Hcy is known to disrupt endothelium-dependent vasodilation by promoting a nitric oxide-deficient state (20). Such impairment is associated with elevated oxidative, and inflammatory stress, which inflammation through cytokines such as IL-1β and Tumor Necrosis Factor-alpha (TNF-α) is increased by high levels of Hcy producing reactive oxygen species (ROS), Interferon-gamma (INF-γ) and (TNF-α) are the primary pro-inflammatory cytokines that induce the erosion of the fibrous cap of atherosclerotic plaques, hence heightening the risk of rupture (21, 22). In this context, MCP-1 plays a complex role in the development and progression of AS (23). Monocyte recruitment and regulation to sites of inflammation is a key process in atherogenesis, one in which MCP-1 participates (24). MCP-1 produced by classical Myosin Heavy Chain 11 (Myh11) and SMCs is atheroprotective, influencing monocyte levels early in the disease and contributing to plaque stability (25). In contrast, MCP-1 from Lectin, Galactoside-Binding, Soluble 3 (Lgals3) transitioned vascular SMCs exacerbates plaque pathogenesis in late-stage disease by influencing inflammatory cell populations, leading to increased plaque instability (26). Finally, Neutrophils and macrophages secrete MPO, an enzyme that facilitates the formation and then the expansion of the atheromatous plaque by oxidizing lipoprotein particles (especially LDL) that play a central role during plaque genesis (27). This enzyme's activity is linked to plaque instability and rupture, making it a potential target for

therapeutic intervention (28). MPO is the only human enzyme capable of producing hypochlorous acid (HOCl) at physiological chloride concentrations, which oxidizes LDL particles (29). Oxidized LDL is recognized by scavenger receptors on endothelial cells and macrophages, leading to endothelial dysfunction and foam cell formation, key processes in AS progression (30). In hypoxic conditions, MPO catalyzes the formation of HOCl, exacerbating oxidative stress and inflammation, contributing to promoting atherosclerotic plaque formation (31). Due to the lack of studies on these biomarkers, the study aimed to enhance understanding of AS pathogenicity by investigating the roles of the biomarkers Hcy, MCP-1 and MPO, in the initiation and progression of AS, thereby aiding in the development of early diagnostic and therapeutic strategies to impede disease progression.

Ethics approval and consent to participate

This study was conducted in compliance with the Declaration of Helsinki. The research received approval from the University of Baghdad Ethics Committee and the Baghdad Health Directorate (Date: September 23, 2024, NO: EC-40). Informed permission was acquired from all participants in the study.

Materials and methods

Sample collection

A total of 90 Iraqis were included in this trial; 60 were randomly selected and diagnosed with AS while attending the Ibn Al-Bitar Specialized Cardiac Surgery Center in Baghdad. Patients with AS in this study were categorized into two groups: the Pre-Cath group (30 patients) and the Post-Cath group (30 patients). Moreover, 30 ostensibly healthy individuals took part in this investigation. The study prolonged the duration from August 2024 to February 2025. The ages of AS patients and healthy individuals varied from 20 to 75 years. All participants in the study completed a questionnaire inquiring about sex, age, weight, height, waist circumference, hip circumference, smoking status, duration of illness, presence of chronic hypertension, family medical history, type of treatment received, and whether they had undergone catheterization or open-heart surgery. Individuals with other chronic diseases were excluded from the study.

The waist-to-hip ratio measurement

The waist-to-hip ratio (WHR) quantifies the distribution of body fat in the waist and hip areas. The computation is predicated on the hips, which constitute the predominant segment of the buttocks, and the waist circumference. The formula is articulated as WHR = waist circumference/hip circumference. The optimal waist-to-hip ratio (WHR) is below 0.9 for males and below 0.8 for females (32). Patients with AS exhibited an increased WHR of 0.98.

Blood samples collection

Venous blood samples were collected from both the patients and control groups, with 6 ml of blood extracted from each individual via venipuncture. Four milliliters were gradually injected into the disposable serum tubes containing the separation gel. Blood in gel-containing tubes was let to coagulate at ambient temperature for 10-15 minutes, followed by centrifugation at 3000 rpm for approximately 10-15 minutes. The serum was subsequently aliquoted into several Eppendorf tubes in identical volumes and preserved at -20°C for use in serological assays (ELISA).

Enzyme-linked immunosorbent assay

This assay utilizes the "Double Antibody Sandwich" technique (ELISA Kits, ELK Biotechnology, U.S.A). It measures the concentrations of Hcy, MCP-1 and MPO in the samples. This is accomplished by measuring the optical density (O.D.) of the samples and contrasting them with a derived standard curve. All standards, samples, and reagents were prepared according to the test preparation guidelines in the kit brochure to ensure precision and uniformity.

Statistical analysis

This study analyzed the outcomes of obtained data using the Statistical Package of Social Sciences (SPSS) version 23, employing One-Way ANOVA and Pearson's correlation coefficient. Data were presented as mean ± standard error, with significant differences observed at $p < 0.05$. Furthermore, a Receiver Operating Characteristic (ROC) curve analysis was conducted to determine sensitivity, specificity, and the Area Under the Curve (AUC) for each parameter examined, in order to assess their diagnostic accuracy for the disease.

Results

As shown in Table 1 and Figure 1, which present serum concentration levels of studied parameters in Post-Cath patients, Pre-Cath patients, and the control group. The results showed a significant increase in Hcy levels in Pre- Cath patients ($P < 0.001$), compared to the control group. Although Hcy levels decreased Post-Cath patients ($P < 0.001$), they remained higher than those observed in the control group. Besides, results showed MCP-1 levels increase in the Pre-Cath and Post-Cath patients ($p < 0.001$) compared to the control group, also the Post-Cath patients showed even higher levels ($p=0.05$) in compared with Pre-Cath patients. Furthermore, Pre-Cath Patients exhibited higher MPO levels ($P < 0.001$), compared to the control group. This elevation persisted Post-Cath patients ($P = 0.03$), compared to the Pre-Cath patients.

Parameter	Patients Groups	Concentration (Mean±S.E.)	P value
Hcy (ng/mL)	Control	229.15±14.44	<0.001**
	Pre-Cath AS patients	417.34±38.79	<0.001**
	Post-Cath AS patients	256.33±18.57	
MCP-1 (pg/mL)	Control	72.38±4.21	<0.001**
	Pre-Cath AS patients	121.31±10.30	0.05*
	Post-Cath AS patients	153.33±16.78	
MPO (ng/mL)	Control	11.02±0.99	<0.001**
	Pre-Cath AS patients	16.52±1.72	0.03*
	Post-Cath AS patients	21.07±1.73	

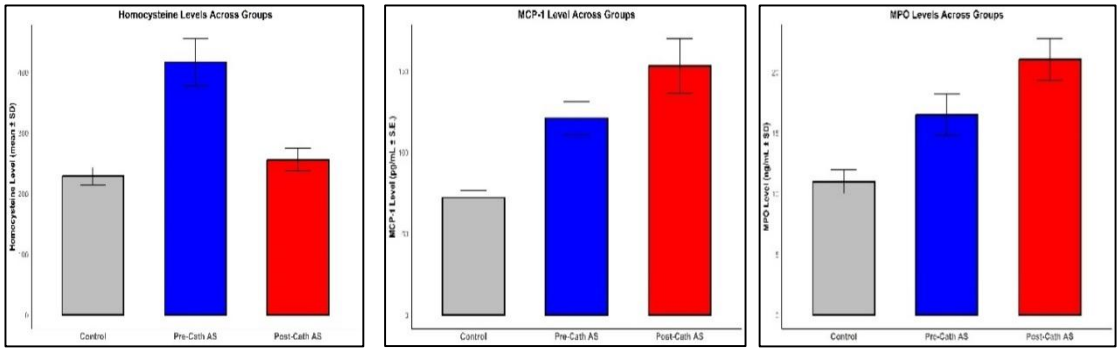


Figure (1): Serum levels of Hcy, MCP-1, MPO in AS Pre-Cath patients, Post-Cath patients and the control group.

In Table 2, analysis of ELISA results reveals significant differences in several biomarkers across different age groups. For Hcy, In Pre-Cath and Post- Cath patients, Hcy levels were significantly higher ($P < 0.001$), than those in the control group, particularly in Pre-Cath patients in the ≤50 years category ($P=0.006$) compared to Patients >50 years. Besides, MCP-1 levels were significantly increased in Pre- and Post-Cath patients, patients groups in both age categories ($P < 0.001$) compared to the control group, while no significant differences were found between the two age categories in the Pre-Cath patients group. The Post-Cath patients group showed significantly higher MCP-1 levels in the age categories ≤50 years ($P = 0.01$). Finally, In Pre-Cath and Post-Cath patients, MPO levels were higher ($P < 0.001$), compared to the control group. While, Post-Cath patients exhibited no significant difference in MPO levels compared to the control group. These results emphasize the importance of monitoring Hcy, MCP-1 and MPO as potential indicators of disease progression and inflammatory response in cardiovascular patients.

Table (2): The distribution of (Hcy, MCP-1 and MPO) serum level according to age in the studied groups.

Parameter	Groups	Age groups (Yrs.)	Concentration (Mean±S.E.)	P value
Hcy (ng/mL)	Control	≤50	218.50±17.11	<0.001**
		>50	258.42±25.66	
	Pre-Cath AS patients	≤50	547.00±152.46	
		>50	377.88±18.82	
	Post-Cath AS patients	≤50	255.66±57.83	
		>50	256.50±19.01	
MCP-1 (pg/mL)	Control	≤50	69.82±4.51	<0.001**
		>50	79.44±9.89	
	Pre-Cath AS patients	≤50	124.36±22.43	
		>50	120.38±11.85	
	Post-Cath AS patients	≤50	211.42±44.49	
		>50	138.80±17.04	
MPO (ng/mL)	Control	≤50	11.23±1.21	0.001**
		>50	10.46±1.80	
	Pre-Cath AS patients	≤50	20.11±5.24	
		>50	15.43±1.60	
	Post-Cath AS patients	≤50	18.81±2.49	
		>50	21.63±2.08	

Present study results have uncovered, Hcy concentration in the Pre-Cath and Post-Cath patients in both categories WHR ≤0.9 and WHR >0.9 shows a significant difference (p <0.001) comparison to control group. In context, The MCP-1 concentrations in the Pre- and Post-Cath patients in both categories WHR are significantly different (p<0.001) comparison to control group. Between Pre-Cath, there is a substantial difference in MCP-1 concentrations (p=0.01), in WHR ≤0.9 in comparison to WHR >0.9 patients. Likewise, Post-Cath patients also demonstrate substantial differences (p=0.01) in MCP-1 concentrations in WHR ≤0.9 when comparison to those with WHR >0.9. Finally, MPO levels in the Pre- and Post-Cath, patients in both categories WHR showed a significant difference (p<0.001) comparison to control group. For Pre-Cath patients, MPO serum levels are elevated in WHR ≤0.9 comparison to patients with WHR >0.9, but these differences are not a significant. as shown in Table **3**.

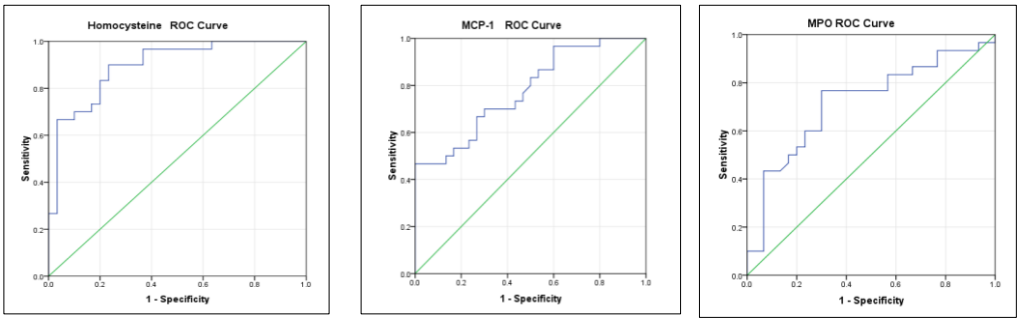
Table (3): Serum level according to WHR in in the studied group groups.

Parameter	Groups	Waist/hip Ratio	Concentration (Mean±S.E.)	P value
Hcy (ng/mL)	Control	≤0.9	219.27±20.32	<0.001**
		>0.9	242.07±20.45	
	Pre-Cath AS patients	≤0.9	514.28±136.83	
		>0.9	382.09±18.49	
	Post-Cath AS patients	≤0.9	237.91±68.27	
		>0.9	259.17±19.31	
MCP-1 (pg/mL)	Control	≤0.9	68.11±6.15	<0.001**
		>0.9	77.98±5.33	
	Pre-Cath AS patients	≤0.9	161.59±18.74	
		>0.9	106.66±10.90	
	Post-Cath AS patients	≤0.9	106.43±9.17	
		>0.9	160.54±18.96	
MPO (ng/mL)	Control	≤0.9	11.51±1.30	001**
		>0.9	10.39±1.58	
	Pre-Cath AS patients	≤0.9	19.78±5.25	
		>0.9	15.34±1.40	
	Post-Cath AS patients	≤0.9	18.91±4.92	
		>0.9	21.40±1.88	

This study evaluates the diagnostic performance of three immunological markers Hcy, MCP-1, and MPO in relation to AS. With an AUC of 0.9, a sensitivity of 90%, and a specificity of 77%, Hcy displayed the best diagnostic accuracy with a very significant (P <0.001). The MCP-1 has an AUC of 0.78, sensitivity of 50%, and specificity of 100%, with a strong statistical significance of (P < 0.001). MPO exhibited an AUC of 0.72, a sensitivity of 77%, and a specificity of 70%, with a statistically significant (P =0.004). These results imply that Hcy is the main immunological marker for AS; MCP-1 and MPO could therefore enhance its diagnostic relevance. Table 4 and Figure.3, illustrate the results.

Table (4): ROC curve results for the studied parameters in AS patients and control groups.

Parameter	AUC	cutoff	Sensitivity	Specificity	P Value
Hcy	0.9	278.9	90%	77%	<0.001**
MCP-1	0.78	109.14	50%	100%	<0.001**
MPO	0.72	13.47	77%	70%	0.004**



Figure(3): The ROC Curve of Hcy, MCP-1, and MPO biomarkers in AS patients and control groups.

The table 5 presents the results of Pearson correlation analysis between various parameters, including Hcy, MCP-1, MPO, Age, and WHR. The study found a notable positive association between Hcy and MCP-1 levels, implying a quite modest link between these two biomarkers. A stronger correlation was observed between Hcy and MPO levels (P = 0.003), indicating a more pronounced association. Additionally, MCP-1 and MPO levels had a modest but noteworthy connection (P = 0.005). However, Age and WHR showed a stronger and significant connection (P = 0.001), implying a noteworthy link between these two factors.

Table (5): Correlation of studied parameters

Parameter	Pearson Correlation	P-value
Hcy and MCP-1 level	0.242*	0.021
Hcy and MPO level	0.305**	0.003
Hcy and Age	0.041	0.702
Hcy and WHR	0.071	0.505
MCP-1 and MPO level	0.295**	0.005
and Age MCP-1	0.216	0.041
MCP-1 and WHR	0.189	0.074
MPO and Age	0.142	0.183
MPO and WHR	0.05	0.638
Age and WHR	0.418**	0.001

Overall, these results reveal generally that Hcy, MCP-1, and MPO levels are connected; Hcy and MPO exhibit the best association. Additionally, age and WHR demonstrate a significant relationship.

Discussion

The results in table 1 and Figure 1, showed a significant increase in Hcy levels in Pre-Cath patients, while these levels decreased Post-Cath, but remained higher than the normal values observed in the control group. Considered as a main risk factor for AS, Hcy causes oxidative stress by increasing the synthesis of free radicals, therefore severely harming endothelial cells and promoting the growth of atherosclerotic plaques (33). It also helps to lower nitric oxide (NO) generation, which causes poor vasodilation and faster arterial stiffness (34). Moreover, Hcy intensifies the accumulation of oxidized lipids and lipoproteins inside artery walls and triggers inflammatory reactions (33). Comparatively to the control group, Pre-Cath and Post-Cath patients had much higher MCP-1 levels. The results also showed that MCP-1 levels in Post-Cath patients were even higher than those in Pre-Cath patients, reflecting the role of inflammation in the persistent vascular damage (35). Key inflammatory cytokine MCP-1 is essential in attracting monocytes to blood vessel walls, so enabling immune cell invasion and the development of atherosclerotic plaques (36). As it stimulates macrophages to absorb oxidized lipoproteins, which causes plaque development and arterial blockage, it also encourages foam cell production (37). Furthermore involved in vascular remodeling following catheterization is MCP-1, whose higher levels following the operation are linked to more severe inflammatory reactions and higher risk of restenosis (38).

Similarly, the study revealed a significant increase in MPO levels in Pre-Cath patients compared to the control group, and this elevation persisted after catheterization, with even higher levels than before the procedure. Key enzyme released by neutrophils, MPO has several pathogenic activities including producing strong oxidative species such HOCl, which damages endothelial cells and lipoproteins (39). MPO also enhances LDL oxidation, contributing to plaque instability and increasing the risk of rupture (40). Furthermore, increased MPO levels after the procedure exacerbate inflammation, which may heighten the likelihood of complications such as recurrent arterial stenosis (41). These results indicate increased Hcy, MCP-1, and MPO are associated with AS, therefore highlighting the crucial part oxidative stress and inflammation play in the development of illness.

The ELISA study showed notable variations in biomarker levels between various age groups, therefore suggesting the influence of age on AS pathogenesis. In Pre-Cath and Post-Cath patients had noticeably higher Hcy levels than the control group; Pre-Cath patients aged ≤50 years showed the greatest rise. This implies that younger individuals might be more sensitive to the negative consequences of Hcy on vascular integrity or more prone to metabolic dysregulation (42). Key causes of oxidative stress, endothelial dysfunction, and inflammatory activation all of which hasten the course of AS are increased Hcy (33). Although Hcy levels decreased following catheterization, they remained above normal values in the control group, reinforcing its role in persistent vascular dysfunction (43). Similarly, Reflecting

its important function in monocyte recruitment, plaque development, and chronic inflammation, MCP-1 levels were significantly raised in Pre-Cath and Post-Cath patients across all age categories relative to the control group (44). On the Pre-Cath patients, however, age groups showed no statistically significant variations; on the Post-Cath patients, aged ≤50 years showed noticeably greater MCP-1 levels. This result implies that younger patients may have more marked inflammatory response after catheterization, therefore raising their risk of restenosis (45).

The sustained elevation of MCP-1 Post-Cath patients indicates persistent immune activation, necessitating targeted anti-inflammatory strategies to mitigate long-term complications in this patient group (35). The study confirmed the importance of MPO in generating oxidative stress and endothelial damage by showing a notable rise in Pre-Cath and Post-Cath patients over the control group (29). However, while MPO levels remained elevated in Pre-Cath patients, no significant difference was observed between Post-Cath patients and the control group, suggesting a possible reduction in neutrophil activity or oxidative burden following intervention (39). Given that MPO contributes to LDL oxidation, plaque instability, and vascular inflammation, its reduction after catheterization may indicate a partial improvement in oxidative stress (27). These results show generally the complicated interaction in AS between oxidative stress, inflammation, and endothelial dysfunction. Particularly in Hcy and MCP-1 levels, age-related variations point to younger patients perhaps having a more marked inflammatory and metabolic response, which could affect the course of disease and results following treatments (46).

Further investigation on the possible influence of central adiposity on inflammation and AS by means of biomarkers levels using WHR Analysis of the investigated Biomarkers (Hcy, MCP-1 and MPO) in AS Patients WHR ≤0.9 and >0.9. Hcy levels exhibited a considerable disparity among patient groups (Pre-Cath and Post-Cath) within both WHR categories (≤0.9 and >0.9) in comparison to the control group. This indicates that people with AS exhibit elevated Hcy levels compared to healthy persons, correlating with an augmented risk of endothelial injury and the advancement of AS (33). Pre-Cath and Post-Cath patients' MCP-1 levels were noticeably higher than those of the control group, therefore supporting their function in inflammation linked to AS (47). MCP-1 levels were notably higher in those with WHR ≤0.9 among Pre-Cath patients, suggesting that patients with peripheral obesity may have an enhanced inflammatory response, whereas central obesity (WHR >0.9) appears to lower inflammation levels, maybe due to a less pro-inflammatory fat distribution than peripheral fat (48). The same trend was observed in Post-Cath patients, indicating that the relationship between WHR and MCP-1 levels persists even after medical intervention (catheterization) (49). In Pre-Cath and Post-Cath patients had much higher MPO levels than the control group, so verifying its importance in the development of AS and vascular injury. Among Pre-Cath patients, MPO levels were elevated in those with WHR ≤0.9, suggesting that the impact of fat distribution on MPO might be less pronounced, as MPO primarily enhances oxidative stress and immune response (50).

The ROC analysis results showed that Hcy is the most accurate marker for

diagnosing AS. In contrast, MCP-1 exhibited high specificity but lower sensitivity, indicating its role as a complementary marker rather than a primary one. MPO demonstrated moderate accuracy, reflecting its role in the inflammatory and oxidative processes associated with the disease (51).

The Pearson correlation analysis results reveal a substantial positive correlation between Hcy and MCP-1 levels, indicating that increased Hcy levels may be marginally associated with raised MCP-1, an inflammatory protein involved in CVD, especially AS (52). Additionally, a strong correlation was observed between Hcy and MPO, indicating that higher Hcy levels are more distinctly associated with increased MPO levels, an inflammatory enzyme critical in the pathological processes related to AS and oxidative damage (33). This strong association may reflect a synergistic effect between Hcy and oxidative stress in exacerbating CVD (53). The moderate connection between MCP-1 and MPO indicates a potential interaction between these two inflammatory proteins in the inflammatory processes related to CVD (54). The largest correlation found in this study was between age and WHR, meaning that increasing age is clearly linked with higher WHR, a fundamental indication of fat distribution and a main risk factor for metabolic and CVD (55, 56). These results highlight the biological relationships between Hcy and inflammatory markers such MPO and MCP-1, so supporting the function of Hcy in aggravating inflammation and AS. Furthermore, the great link between age and WHR emphasizes the relevance of aging as a risk factor related with central obesity, which in turn is a major predictor of CVD (57).

References

1. Gusev E, Sarapultsev A. Atherosclerosis Gusev, E. and Sarapultsev, A. (2023). Atherosclerosis and inflammation: Insights from the theory of general pathological processes. International Journal of Molecular Sciences, 24(9), 7910.
2. Al-Kaabi, Z. I.; Mohammad, N. A. and Al-Ansari, A. B. (2015). Circulating human IL-10-secreting regulatory B cells in acute and chronic ischemic heart disease. Iraqi Journal of Biotechnology, 14.(1)
3. Al-Khayatt, M. A. and Yenzeel, J. H. (2023). Study of some hematological and physiological parameters and electrolytes in cardiomyopathy Iraqi patients. Iraqi Journal of Biotechnology, 22.(1)
4. Suleiman, A.; Muhsin, H.; Abdulkarrem, R. and Abed, F. (2019). Efficiency of primer design tools in evaluation of two molecular methods to detect two single nucleotide polymorphisms related with atherosclerosis. Malaysian Journal of Biochemistry and Molecular Biology, 2, 17–20.
5. Jabbar, E. A. K.; Al-Rumaidh, S. Z. and Jouda, J. (2021). Estimation of some biomarkers and cholesterol/HDL ratio to predict the risk of cardiovascular disease in rheumatoid arthritis. Ibn Al-Haitham Journal for Pure and Applied Sciences, 23–28.
6. Libby, P. (2021). Inflammation during the life cycle of the atherosclerotic plaque. Cardiovascular Research, 117(13), 2525–2536.
7. Al-Assaf, A. I. S. (2017). Platelet activity and some immunological findings in atherosclerosis and coronary heart disease. Ibn Al-Haitham Journal for Pure and Applied Sciences, 19(2), 1–10.
8. Mahmud, M. S. and Ashoor, L. S. (2022). Risk factors associated with coronary artery disease in Iraqi patients with non-alcoholic fatty liver. Iraqi Journal of Biotechnology, 21.(2)
9. Mohindra, R.; Agrawal, D. K. and Thankam, F. G. (2021). Altered vascular extracellular matrix in the pathogenesis of atherosclerosis. Journal of Cardiovascular Translational Research, 1–14.
10. Corti, A.; De Paolis, A.; Grossman, P.; Dinh, P. A.; Aikawa, E.; Weinbaum, S.; *et al*. (2022). The effect of plaque morphology, material composition, and microcalcifications on the risk of cap rupture: A structural analysis of vulnerable

atherosclerotic plaques. Frontiers in Cardiovascular Medicine, 9, 1019917.
11. Pan, H.; Ho, S. E.; Xue, C.; Cui, J.; Johanson, Q. S.; Sachs, N.; *et al*. (2024). Atherosclerosis is a smooth muscle cell–driven tumor-like disease. Circulation, 149(24), 1885–1898.
12. Sultan, N. S. and Al-Tai, A. F. (2018). Estimation of pentraxin-3 (PTX3) in rheumatoid arthritis male patients with and without type II diabetes mellitus in Iraq. Ibn Al-Haitham Journal for Pure and Applied Sciences, 31(3), 55–62.
13. Atheeb, A. K.; Hussein, S. Z. and Al-Mudhaffar, S. S. (2021). Oxidative stress status in sera of type 2 diabetic Iraqi patients with coronary artery diseases. International Journal of Drug Delivery Technology, 11(2), 291–297.
14. Shalash, W. K. and Kadri, Z. H. (2021). Evaluation of malondialdehyde, C-reactive protein, and DNA damage related with the smoking habit by comet assay in Iraq. International Journal of Drug Delivery Technology, 11(2), 298–302.
15. Mahmoud, E. A. (2022). Expression of vascular endothelial growth factor in the placenta of Iraqi women complicated with hypertensive disorder. International Journal of Drug Delivery Technology, 12(3), 977–980.
16. He, Z.; Luo, J.; Lv, M.; Li, Q.; Ke, W.; Niu, X.; *et al*. (2023). Characteristics and evaluation of atherosclerotic plaques: An overview of state-of-the-art techniques. Frontiers in Neurology, 14, 1159288.
17. Gospodarczyk, A.; Marczewski, K.; Gospodarczyk, N.; Widuch, M.; Tkocz, M. and Zalejska-Fiolka, J. (2022). Homocysteine and cardiovascular disease—A current review. Wiadomości Lekarskie, 75(11 Pt 2), 2862–2866.
18. Jiang, Q.; Wang, L.; Si, X.; Tian, J.-L.; Zhang, Y.; Gui, H.-L.; *et al*. (2021). Current progress on the mechanisms of hyperhomocysteinemia-induced vascular injury and use of natural polyphenol compounds. European Journal of Pharmacology, 905, 174168.
19. Jakubowski, H. and Witucki, Ł. (2025). Homocysteine metabolites, endothelial dysfunction, and cardiovascular disease. International Journal of Molecular Sciences, 26(2), 746.
20. DePace, N. L. and Colombo, J. (2019). Nitric oxide (Prong-2). In Clinical Autonomic and Mitochondrial Disorders: Diagnosis, Prevention, and Treatment for Mind-Body Wellness (pp. 71–138).
21. Ahmed, M. Q. and Hussein, T. A. (2023). The role of TNF-α and total IgE in pathogenicity of Iraqi fuel station workers with allergic rhinitis. Ibn Al-Haitham Journal for Pure and Applied Sciences, 36(1), 15–24.
22. Neamah, A. S.; Wadan, A.-H. S.; Lafta, F. M. and Elakwa, D. E.-S. (2024). The potential role of targeting the leptin receptor as a treatment for breast cancer in the context of hyperleptinemia: A literature review. Naunyn-Schmiedeberg's Archives of Pharmacology, 397(11), 1–16.
23. Xing, Y. and Lin, X. (2024). Challenges and advances in the management of inflammation in atherosclerosis. Journal of Advanced Research.
24. He, S.; Yao, L. and Li, J. (2023). Role of MCP-1/CCR2 axis in renal fibrosis: Mechanisms and therapeutic targeting. Medicine, 102(42), e35613.
25. Owsiany, K. M.; Deaton, R. A.; Soohoo, K. G.; Nguyen, A. T. and Owens, G. K. (2022). Dichotomous roles of smooth muscle cell–derived MCP-1 (monocyte chemoattractant protein 1) in development of atherosclerosis. Arteriosclerosis, Thrombosis, and Vascular Biology, 42(8), 942–956.
26. Di Gregoli, K.; Somerville, M.; Bianco, R.; Thomas, A. C.; Frankow, A. and Newby, A. C. (2020). Galectin-3 identifies a subset of macrophages with a potential beneficial role in atherosclerosis. Arteriosclerosis, Thrombosis, and Vascular Biology, 40(6), 1491–1509.
27. Tangeten, C.; Zouaoui Boudjeltia, K.; Delporte, C.; Van Antwerpen, P. and Korpak, K. (2022). Unexpected role of MPO-oxidized LDLs in atherosclerosis: In between inflammation and its resolution. Antioxidants, 11(5), 874.
28. Miceli, G.; Basso, M. G.; Pintus, C.; Pennacchio, A. R.; Cocciola, E. and Cuffaro, M.; *et al*. (2024). Molecular pathways of vulnerable carotid plaques at risk of ischemic stroke: A narrative review. International Journal of Molecular Sciences, 25(8), 4351.
29. Frangie, C. and Daher, J. (2022). Role of myeloperoxidase in inflammation and atherosclerosis. Biomedical Reports, 16(6), 53.
30. Babakr, A. T. (2024). Scavenger receptors: Different classes and their role in the uptake of oxidized low-density

lipoproteins. Biomedical Pharmacology Journal, 17.(2)

31. Zhang, J.; Han, Y.; Jia, R.; Zhu, Q.; Wang, X. and Liu, M.; *et al*. (2024). Exploring the role of myeloperoxidase in the atherosclerotic process in hypoxic mice based on the MAPK signaling pathway. Biochemical Pharmacology, 225, 116275.
32. Górnicka, M.; Szewczyk, K.; Białkowska, A.; Jancichova, K.; Habanova, M. and Górnicki, K.; *et al*. (2022). Anthropometric indices as predictive screening tools for obesity in adults: The need to define sex-specific cut-off points. Applied Sciences, 12(12), 6165.
33. Yuan, D.; Chu, J.; Lin, H.; Zhu, G.; Qian, J. and Yu, Y.; *et al*. (2023). Mechanism of homocysteine-mediated endothelial injury and its consequences for atherosclerosis. Frontiers in Cardiovascular Medicine, 9, 1109445.
34. Boutouyrie, P.; Chowienczyk, P.; Humphrey, J. D. and Mitchell, G. F. (2021). Arterial stiffness and cardiovascular risk in hypertension. Circulation Research, 128(7), 864–886.
35. Liu, Y.; Xu, K.; Xiang, Y.; Ma, B.; Li, H. and Li, Y.; *et al*. (2024). Role of MCP-1 as an inflammatory biomarker in nephropathy. Frontiers in Immunology, 14, 1303076.
36. Su, C.; Lu, Y.; Wang, Z.; Guo, J.; Hou, Y. and Wang, X.; *et al*. (2023). Atherosclerosis: The involvement of immunity, cytokines, and cells in pathogenesis, and potential novel therapeutics. Aging and Disease, 14(4), 1214.
37. Lorey, M. B.; Öörni, K. and Kovanen, P. T. (2022). Modified lipoproteins induce arterial wall inflammation during atherogenesis. Frontiers in Cardiovascular Medicine, 9, 841545.
38. Wang, X.; Gao, B. and Feng, Y. (2022). Recent advances in inhibiting atherosclerosis and restenosis: From pathogenic factors, therapeutic molecules to nano-delivery strategies. Journal of Materials Chemistry B, 10(11), 1685–1708.
39. Lin, W.; Chen, H.; Chen, X. and Guo, C. (2024). The roles of neutrophil-derived myeloperoxidase (MPO) in diseases: New progress. Antioxidants, 13(1), 132.
40. Amirfakhryan, H. and New, K. J. (2024). The role of myeloperoxidase as a biomarker in atherosclerotic cardiovascular disease. Cardiology Plus, 9(3), 195–209.
41. Cheng, D.; Talib, J.; Stanley, C. P.; Rashid, I.; Michaëlsson, E. and Lindstedt, E.-L.; *et al*. (2019). Inhibition of MPO (myeloperoxidase) attenuates endothelial dysfunction in mouse models of vascular inflammation and atherosclerosis. Arteriosclerosis, Thrombosis, and Vascular Biology, 39(7), 1448–1457.
42. Ungvari, A.; Gulej, R.; Csik, B.; Mukli, P.; Negri, S. and Tarantini, S.; *et al*. (2023). The role of a methionine-rich diet in unhealthy cerebrovascular and brain aging: Mechanisms and implications for cognitive impairment. Nutrients, 15(21), 4662.
43. Ullah, M.; Wahab, A.; Khan, S. U.; Zaman, U.; Rehman, K. U. and Hamayun, S.; *et al*. (2023). Stent as a novel technology for coronary artery disease and their clinical manifestation. Current Problems in Cardiology, 48(1), 101415.
44. Georgakis, M. K.; Van Der Laan, S. W.; Asare, Y.; Mekke, J. M.; Haitjema, S. and Schoneveld, A. H.; *et al*. (2021). Monocyte chemoattractant protein-1 levels in human atherosclerotic lesions associate with plaque vulnerability. Arteriosclerosis, Thrombosis, and Vascular Biology, 41(6), 2038–2048.
45. Ullrich, H.; Olschewski, M.; Muenzel, T. and Gori, T. (2021). Coronary in-stent restenosis: Predictors and treatment. Deutsches Ärzteblatt International, 118(38), 637.
46. Wacka, E.; Wawrzyniak-Gramacka, E.; Tylutka, A.; Morawin, B.; Gutowicz, M. and Zembron-Lacny, A. (2023). The role of inflammation in age-associated changes in the red blood system. International Journal of Molecular Sciences, 24(10), 8944.
47. Kong, P.; Cui, Z.-Y.; Huang, X.-F.; Zhang, D.-D.; Guo, R.-J. and Han, M. (2022). Inflammation and atherosclerosis: Signaling pathways and therapeutic intervention. Signal Transduction and Targeted Therapy, 7(1), 131.
48. Varra, F.-N.; Varras, M.; Varra, V.-K. and Theodosis-Nobelos, P. (2024). Molecular and pathophysiological relationship between obesity and chronic inflammation in metabolic dysfunctions and inflammation-mediating treatment options. Molecular Medicine Reports, 29(6), 95.
49. Blanco-Colio, L. M.; Méndez-Barbero, N.; Pello Lázaro, A. M.; Aceña, Á.; Tarín, N. and Cristóbal, C.; *et al*. (2021). MCP-1 predicts recurrent cardiovascular events in patients with persistent inflammation. Journal of Clinical Medicine, 10(5), 1137.
50. Wójcik, P.; Gęgotek, A.; Žarković, N. and Skrzydlewska, E. (2021). Oxidative stress

and lipid mediators modulate immune cell functions in autoimmune diseases. International Journal of Molecular Sciences, 22(2), 723.

51. Hayden, H.; Ibrahim, N.; Klopf, J.; Zagrapan, B.; Mauracher, L.-M. and Hell, L.; *et al*. (2021). ELISA detection of MPO-DNA complexes in human plasma is error-prone and yields limited information on neutrophil extracellular traps formed in vivo. PLoS One, 16(4), e0250265.
52. Deng, H.; Chen, Y.; Xing, J.; Zhang, N. and Xu, L. (2024). Systematic low-grade chronic inflammation and intrinsic mechanisms in polycystic ovary syndrome. Frontiers in Immunology, 15, 1470283.
53. Jin, P.; Ma, J.; Wu, P.; Bian, Y.; Ma, X. and Jia, S.; *et al*. (2025). Mutual mediation effects of homocysteine and PCSK9 on coronary lesion severity in patients with acute coronary syndrome: Interplay with inflammatory and lipid markers. Lipids in Health and Disease, 24(1), 19.
54. Singh, S.; Anshita, D. and Ravichandiran, V. (2021). MCP-1: Function, regulation, and involvement in disease. International Immunopharmacology, 101, 107598.
55. Kesztyüs, D.; Lampl, J. and Kesztyüs, T. (2021). The weight problem: Overview of the most common concepts for body mass and fat distribution and critical consideration of their usefulness for risk assessment and practice. International Journal of Environmental Research and Public Health, 18(21), 11070.
56. Shafeeq, N. K.; Hussein, T. A. and Abass, E. A. (2021). Metabolic syndrome. Ibn Al-Haitham Journal for Pure and Applied Sciences, 34(3), 26–38.
57. Majnarić, L. T.; Bosnić, Z.; Kurevija, T. and Wittlinger, T. (2021). Cardiovascular risk and aging: The need for a more comprehensive understanding. Journal of Geriatric Cardiology, 18(6), 462.