Journal of Clinical and Nursing Research, 2025, Volume 9, Issue 11
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

The Impact of Metabolic Syndrome on Coronary Artery Disease in Middle-Aged and Older Women

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Abstract: *Objective:* This study aims to assess the influence of Metabolic Syndrome (MS) on the risk and severity of Coronary Artery Disease (CAD) in middle-aged and elderly women (40–75 years old), to inform evidence-based prevention and management strategies for this population. *Methods:* A retrospective study enrolled 200 middle-aged and elderly female patients (aged 40–75 years) who underwent coronary angiography (CAG) at our hospital between January 2024 and March 2025. Participants were divided into an MS group (n = 88) and a non-MS group (n = 112) based on meeting MS diagnostic criteria. General clinical data including age, body mass index [BMI], blood pressure, blood glucose, blood lipids, and more were collected for both groups. The severity of coronary artery lesions was quantified using the Gensini score. Differences in the positive rate of coronary artery lesions, the number of diseased vessel segments, and Gensini scores between the two groups were compared. *Results:* Patients in the MS group exhibited a significantly higher prevalence of coronary artery lesions (79.55% vs. 48.21%, $p < 0.001$), a greater proportion of multivessel disease (46.59% vs. 18.75%, $p < 0.05$), and higher Gensini scores (25.72 ± 14.28 vs. 16.35 ± 9.86, $p < 0.05$) compared to the non-MS group. *Conclusion:* Metabolic syndrome is a significant risk factor for coronary artery disease in middle-aged and elderly women, substantially increasing both the incidence and severity of coronary lesions. Clinical efforts should focus on enhancing screening and comprehensive intervention for metabolic syndrome in this population to reduce the risk of coronary heart disease.

Keywords: Metabolic syndrome; Middle-aged and elderly women; CAD; Gensini score; Risk factors

Online publication: Dec 9, 2025

1. Introduction

Coronary atherosclerotic heart disease (CHD) ranks among the leading cardiovascular diseases causing death and disability in middle-aged and elderly populations worldwide. Women experience a significant increase in cardiovascular disease risk following menopause due to the loss of estrogen's protective effects [1]. According to the China Cardiovascular Health and Disease Report 2023, the prevalence of CHD among Chinese women aged 50 and above reaches 12.3%, representing a 3- to 4-fold increase compared to premenopausal women, with poorer prognosis [2]. Metabolic syndrome (MS) is a cluster of metabolic disorders characterized by central obesity,

hypertension, hyperglycemia, and dyslipidemia. Its core pathophysiological mechanism is insulin resistance, which increases cardiovascular disease risk by damaging vascular endothelium, promoting inflammation, and accelerating atherosclerosis (AS) progression [3]. Existing research has confirmed the strong association between MS and coronary artery disease in men, hypertensive patients, and diabetic patients. However, studies targeting the specific population of middle-aged and elderly women aged 40–75 remain insufficient. On one hand, these women often have comorbidities such as osteoporosis and osteoarthritis, which may mask MS-related symptoms. On the other hand, postmenopausal hormonal changes may interact synergistically with MS components, exacerbating coronary artery damage [4]. Furthermore, clinical practice still prioritizes MS screening in men over women, resulting in delayed detection of coronary artery disease in middle-aged and elderly women. This study examined 200 middle-aged and elderly women aged 40–75 who underwent coronary angiography (CAG). By comparing coronary lesion characteristics between metabolic syndrome (MS) and non-MS groups, this study analyzed the impact of MS on the occurrence and severity of coronary lesions in this population. Our aim is to provide data support for early prevention, risk stratification, and clinical intervention strategies for coronary heart disease in middle-aged and elderly women.

2. Materials and methods

2.1. General data

A retrospective study included 200 middle-aged and elderly female patients aged 40–75 years (mean 56.45 ± 7.32 years) who underwent coronary angiography (CAG) at our hospital's Department of Cardiology between January 2024 and March 2025 due to "chest pain, chest tightness" or "suspected coronary heart disease".

2.1.1. Inclusion criteria

First-time admission of middle-aged and elderly female patients aged 40–75 years with suspected coronary heart disease; Underwent CAG with confirmed coronary artery lesions; Complete clinical data (including demographic characteristics, laboratory tests, imaging records, and more.); No prior primary or secondary prevention interventions for coronary heart disease; No history of coronary intervention or coronary artery bypass grafting.

2.1.2. Exclusion criteria

Active severe infection; severe hepatic impairment (Child-Pugh Class C) or severe renal impairment (estimated glomerular filtration rate < 30 mL/min/1.73 m^2); diagnosis of any malignant tumor or autoimmune disease; a history of major surgery or significant trauma within the preceding 3 months; or poorly controlled thyroid dysfunction.

2.2. Methods

Diagnosis of metabolic syndrome followed the criteria recommended by the Diabetes Branch of the Chinese Medical Association (2019 edition) [5].

(1) Overweight and/or obesity

Body mass index (BMI) ≥25 kg/m^2

(2) Hyperglycemia

Fasting plasma glucose (FPG) ≥ 6.1 mmol/L (110 mg/dL), and/or 2-hour postprandial glucose ≥ 7.8

mmol/L (140 mg/dL), and/or diagnosed diabetes mellitus under treatment

(3) Hypertension

Systolic/diastolic blood pressure ≥ 140/90 mmHg, and/or diagnosed hypertension under treatment

(4) Dyslipidemia

Fasting triglycerides (TG) ≥ 1.7 mmol/L, and/or HDL-cholesterol (HDL-C) < 0.9 mmol/L (males) or < 1.0 mmol/L (females).

Presence of three or all four criteria confirms MS diagnosis. Participants not meeting these criteria were assigned to the non-MS group.

2.3. Observation indicators

2.3.1. General clinical data

Data on patient age, height, weight, waist circumference, and past medical history (including hypertension, diabetes, and hyperlipidemia) as well as medication history (including antihypertensive, antidiabetic, and statin medications) were retrieved from the electronic medical record system.

2.3.2. Laboratory testing

All patients underwent venous blood sampling the morning after admission (fasting ≥ 8 hours) to measure the following parameters:

(1) Fasting plasma glucose (FPG)

(2) Lipid profile

Total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C)

(3) Hepatic and renal function

Alanine aminotransferase (ALT), serum creatinine (Scr), with estimated glomerular filtration rate (eGFR) calculated using the CKD-EPI equation

(4) Thyroid function

2.3.3. Coronary Artery Disease assessment (CAG and Gensini score)

All patients underwent coronary angiography (CAG) performed by experienced interventional cardiologists using the Judkins technique with multi-position imaging. Two independent interventional cardiologists (blinded assessment) evaluated coronary artery lesions based on angiographic findings: Single-vessel disease (≥ 50% stenosis in one coronary artery), two-vessel disease (≥ 50% stenosis in two coronary arteries), multivessel disease (≥ 50% stenosis in three or more coronary arteries). Left main coronary artery disease was classified as two-vessel disease.

The severity of coronary lesions was quantified using the Gensini scoring system, with the following criteria: Scoring based on the degree of coronary stenosis: ≤ 25% stenosis = 1 point; 26–50% stenosis = 2 points; 51–75% stenosis = 4 points; 76–90% stenosis = 8 points; 91–99% stenosis = 16 points; ≥ 100% stenosis = 32 points [6]. Weighting by coronary territory: Left Main (LM) × 5; Left Anterior Descending (LAD) proximal segment × 2.5, mid-segment × 1.5, distal segment × 1; Left Circumflex (LCX) proximal segment × 2.5, distal segment × 1; Right Coronary Artery (RCA) proximal segment × 1.5, mid-segment × 1, distal segment × 1; collateral circulation vessels ×1; Total Gensini score = sum of stenosis severity scores × corresponding weight scores. Higher scores indicate more severe coronary artery disease.

2.4. Statistical methods

Data analysis was performed using SPSS 27.0 statistical software. For continuous variables meeting normal distribution, results were expressed as mean ± standard deviation ($\bar{x} \pm s$), with intergroup comparisons conducted using independent samples *t*-tests. Non-normally distributed continuous variables were presented as median with interquartile range [M (Q1, Q3)], and the Mann-Whitney U test was used for between-group comparisons. Categorical data were expressed as counts and percentages [n (%)], and group differences were assessed using the Chi-square or Fisher's exact test, as appropriate. A two-sided *p*-value of less than 0.05 was considered statistically significant.

3. Results

3.1. Comparison of general clinical characteristics between groups

There was no statistically significant difference in age between the two groups ($p > 0.05$). The MS group exhibited significantly higher BMI, waist circumference, SBP, DBP, FPG, TG, LDL-C, and prevalence rates of hypertension, diabetes, and hyperlipidemia compared to the non-MS group, while HDL-C was significantly lower in the MS group ($p < 0.05$). See **Table 1** for details.

Table 1. Comparison of general clinical data between the two patient groups

Indicator	MS group (n = 86)	Non-MS group (n = 94)	t/χ^2	p
Age (years)	62.87 ± 7.54	62.03 ± 7.11	0.89	0.436
BMI (kg/m^2)	28.63 ± 3.15	24.02 ± 2.87	10.52	< 0.05
Waist Circumference (cm)	88.56 ± 6.32	76.24 ± 5.89	14.03	< 0.05
SBP (mmHg)	145.27 ± 12.36	128.45 ± 10.78	9.86	< 0.05
DBP (mmHg)	88.45 ± 9.62	80.13 ± 8.54	6.89	< 0.05
FPG (mmol/L)	7.89 ± 1.63	5.32 ± 0.87	13.52	< 0.05
TC (mmol/L)	5.63 ± 1.02	5.21 ± 0.98	2.98	< 0.05
TG (mmol/L)	2.56 ± 0.98	1.45 ± 0.62	9.65	< 0.05
LDL-C (mmol/L)	3.62 ± 0.85	3.15 ± 0.76	4.12	< 0.05
HDL-C (mmol/L)	1.02 ± 0.21	1.35 ± 0.28	9.23	< 0.05
Hypertension [n (%)]	74 (84.09)	45 (40.18)	38.56	< 0.05
Diabetes [n (%)]	58 (65.91)	16 (14.29)	55.82	< 0.05
Hyperlipidemia [n (%)]	70 (79.55)	38 (33.93)	45.28	< 0.05

3.2. Comparison of coronary artery lesions between the two groups

The coronary artery lesion positivity rate in the MS group (79.55%) was significantly higher than that in the non-MS group (48.21%), with a statistically significant difference ($p < 0.05$). Regarding the number of diseased vessels, the proportion of single-vessel disease in the MS group (26.14%) did not differ significantly from that in the non-MS group (29.46%) ($p > 0.05$). However, the proportions of two-vessel disease (27.27%) and multivessel disease (46.59%) were significantly higher than those in the non-MS group (19.64% and 18.75%), with statistically significant differences ($p < 0.05$). The Gensini score in the MS group (25.72 ± 14.28 points) was

significantly higher than that in the non-MS group (16.35 ± 9.86 points), with statistically significant differences ($p < 0.05$). See **Table 2** for details.

Table 2. Comparison of coronary artery lesions between the two groups

Indicator	Group	MS group (n = 88)	Non-MS group (n = 112)	χ^2/t	p
Positive coronary lesions [n (%)]		70 (79.55)	54 (48.21)	19.02	< 0.05
Number of Lesions [n (%)]	Single-vessel disease	23 (26.14)	33 (29.46)	0.28	0.596
	Two-vessel disease	24 (27.27)	22 (19.64)	2.35	0.125
	Multivessel disease	23 (46.59)	21 (18.75)	13.28	< 0.05
Gensini score (points)	Gensini score (points)	25.72 ± 14.28	16.35 ± 9.86	5.48	< 0.05

4. Discussion

Middle-aged and elderly women (40–75 years old) in the perimenopausal and postmenopausal stages exhibit physiological characteristics that amplify the impact of metabolic syndrome (MS) on coronary artery disease: Estrogen exerts cardiovascular protective effects by activating estrogen receptor alpha (ERα) to promote nitric oxide (NO) synthesis and suppress inflammatory factor expression. Postmenopausal estrogen levels plummet, eliminating this protective effect. This leads to increased vascular endothelial sensitivity to MS components (such as hyperglycemia and hypertension), accelerating atherosclerosis (AS) progression [7]. Middle-aged and elderly women often exhibit "sarcopenic obesity", characterized by reduced muscle mass and fat accumulation (especially visceral fat), which further exacerbates insulin resistance (IR) and dyslipidemia. This creates a vicious cycle of "obesity-IR-metabolic abnormalities", increasing the risk of coronary artery disease [8]. Middle-aged and elderly women often present with atypical symptoms of coronary heart disease (e.g., chest tightness and fatigue rather than typical chest pain) and frequently have comorbidities like musculoskeletal or respiratory diseases. These conditions can mask MS-related symptoms, leading to delayed screening for MS and coronary lesions and missed opportunities for early intervention [9].

This study systematically analyzed the impact of MS on coronary artery disease in 200 middle-aged and elderly women aged 40–75 years. Results showed that the MS group exhibited significantly higher rates of positive coronary artery disease, multivessel disease, and Gensini scores compared to the non-MS group, consistent with findings from domestic and international studies [10]. Based on these results and pathophysiological mechanisms, the influence of MS on coronary artery disease in middle-aged and elderly women is analyzed as follows:

(1) The core characteristic of MS is the "cluster of metabolic abnormalities". Its components do not act independently but synergistically exacerbate coronary atherosclerosis through a cascade reaction involving "insulin resistance-inflammatory response-vascular endothelial injury". Insulin resistance (IR) serves as the core driver. In middle-aged and elderly women, postmenopausal decline in estrogen levels can induce IR by reducing insulin sensitivity. Under IR conditions, insulin's protective effects on vascular endothelium (e.g., promoting nitric oxide NO release) diminish. Concurrently, it stimulates excessive LDL-C synthesis in the liver and inhibits HDL-C-mediated cholesterol reverse transport, leading to lipid

deposition in coronary intima. Furthermore, IR activates the renin-angiotensin-aldosterone system (RAAS), elevating blood pressure and causing additional damage to the vascular endothelium. In this study, the MS group exhibited significantly elevated FPG and LDL-C levels alongside markedly reduced HDL-C, confirming the metabolic dysregulation associated with IR.

(2) Central obesity is a prerequisite for diagnosing metabolic syndrome (MS). Adipose tissue (particularly visceral fat) secretes inflammatory mediators such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6). These activate the nuclear factor-κB (NF-κB) pathway, promoting inflammatory cell infiltration and foam cell formation within the coronary artery intima. In this study, the MS group exhibited significantly higher BMI and waist circumference than the non-MS group, with a 46.59% prevalence of multivessel disease. This suggests obesity-related inflammation may be a key contributor to multivessel coronary artery disease. Hypertension can disrupt the coronary endothelial barrier through mechanical stress, facilitating lipid entry into the intima. Hyperglycemia, through non-enzymatic glycation, generates advanced glycation end products (AGEs), which activate the AGE receptor (RAGE), exacerbating endothelial cell apoptosis and smooth muscle cell proliferation.

Based on the study's results, the following measures are recommended to prevent and manage metabolic syndrome (MS) and coronary artery disease in middle-aged and older women: For women aged 40 and above, routinely monitor waist circumference, blood pressure, fasting plasma glucose (FPG), and lipid profiles (triglycerides, HDL-C) to identify MS patients early, particularly high-risk individuals with concomitant hypertension or diabetes. Reduce BMI to < 24 kg/m^2 and waist circumference to < 80 cm through dietary control (low-calorie, high-fiber diet) and exercise (≥ 150 min of moderate-intensity aerobic activity weekly). Target SBP < 130 mmHg and DBP < 80 mmHg, prioritizing ACEI/ARB agents for their dual antihypertensive and insulin resistance-improving effects; target FPG < 7.0 mmol/L, using metformin or SGLT2 inhibitors (e.g., dapagliflozin) as needed, with the latter reducing cardiovascular event risk; Target LDL-C < 2.6 mmol/L (high-risk individuals < 1.8 mmol/L), prioritizing statins with ezetimibe combination if necessary; For MS patients, especially those with multiple abnormalities (≥ 3 components), conduct regular coronary risk assessments such as coronary CTA, exercise stress testing to detect coronary lesions early and prevent progression to severe coronary artery disease.

The study's findings are limited by its single-center, retrospective design and relatively small sample size of 200 cases, potentially introducing selection bias; results require validation through multicenter, large-sample prospective studies. Insulin resistance-related indicators including fasting insulin and HOMA-IR were not measured, preventing direct quantification of the association between IR severity and coronary artery lesions. The impact of hormone replacement therapy (HRT) was not considered; some patients may have received HRT, and its effects on MS and coronary artery lesions require further analysis.

5. Conclusion

In summary, metabolic syndrome is a significant risk factor for coronary artery lesions in middle-aged and elderly women aged 40–75 years, substantially increasing the risk and severity of coronary artery lesions. Furthermore, the greater the number of MS components present, the more severe the coronary artery lesions. In clinical practice, screening for MS in middle-aged and elderly women should be strengthened. Early comprehensive intervention targeting MS components (controlling weight, blood pressure, blood glucose, and blood lipids) can reduce the risk of coronary artery disease and improve patient prognosis.

Disclosure statement

The author declares no conflict of interest.

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