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Association of atherogenic indices and triglyceride-total cholesterol-body weight index (TCBI) with severity of stenosis in patients undergoing angiography: a case-control study

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Abstract

Objectives Coronary artery disease, caused by atherosclerosis, necessitates assessing plaque formation risk using indices like the atherogenic index of plasma (AIP), Castelli's risk indexes (CRI-I and CRI-II), the atherogenic coefficient (AC), and the triglyceride-total cholesterol-body weight index (TCBI). Although TCBI primarily assesses mortality risk, its relationship with stenosis severity is unclear. Utilizing data from a prior study, a case-control analysis was conducted on 1,187 subjects, which included 781 patients who underwent coronary angiography and 406 healthy controls. The indices were compared across varying degrees of arterial blockages.

Results AIP significantly correlated with stenosis severity in women, increasing the risk of three-vessel stenosis by 2.5 times. AC raised the risk of single-vessel stenosis in men by 2.7 times. CRI-I and CRI-II showed a positive relationship with arterial stenosis in women, with CRI-I increasing the risk of two and three-vessel blockages by 21.9% and 22.4%, respectively. A one-unit increase in CRI-II raised the risk by 33.1% for two arteries and 25.3% for three. In conclusion, AIP, CRI-I, and CRI-II in women, along with AC in men, correlated with arterial stenosis severity, while TCBI did not. Further research is needed to determine which index is most effective in predicting CAD risk.

Keywords Coronary artery disease, Atherosclerosis, Atherogenic indexes, Nutritional index, Angiography

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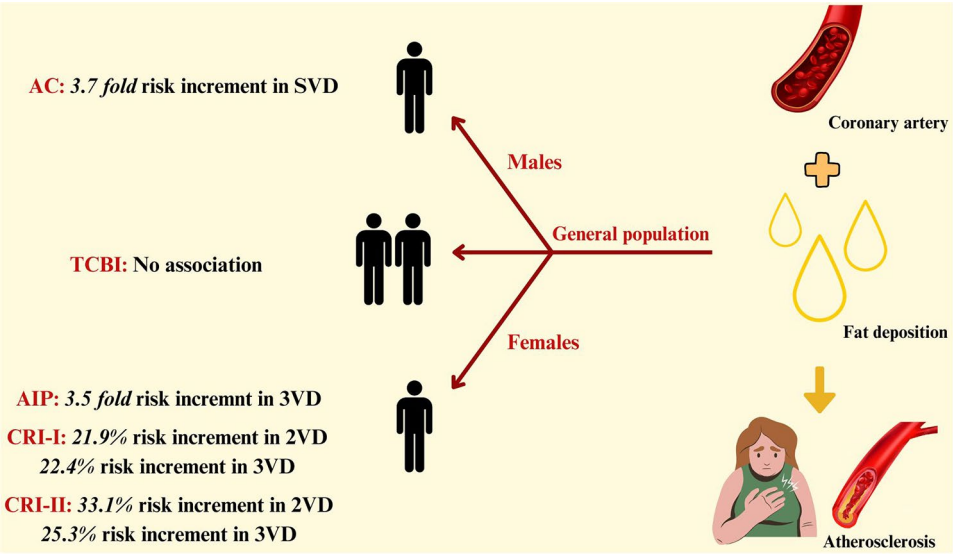
Graphical Abstract



Introduction

Coronary artery disease (CAD) results from atherosclerosis in the coronary arteries, which are responsible for supplying blood to the heart. The accumulation of plaques in these arteries leads to narrowing and reducing blood flow. In Iran, the prevalence of CAD and related risk factors is notably higher compared to Western countries, with an estimated prevalence of 31.7% in a northeastern city [1, 2]. Several population-based studies in Iran have identified elevated levels of triglycerides (TG), total cholesterol (TC), and low-density lipoprotein (LDL), along with decreased levels of high-density lipoprotein (HDL), as significant risk factors for developing CAD. Specifically, 61% of CAD cases exhibited TC levels exceeding 200 mg/dL, 32% had TG levels above 200 mg/dL, 47.5% had LDL levels greater than 130 mg/dL, and 5.4% had HDL levels below 35 mg/dL [3]. In recent years, atherogenic indices, or lipid ratios, have become valuable tools for diagnosing and understanding CVD risk prediction [4]. Among these, the atherogenic index of plasma (AIP)—based on the ratio of TG to HDL—has emerged as a significant indicator of cardio-metabolic abnormalities and insulin resistance [5–8]. Additionally, Castelli's risk index I (CRI-I) and II (CRI-II) are lipid-based indices used to predict atherogenicity and CVD risk, utilizing HDL, LDL, and TC measurements [4, 9]. CRI-I, in particular, provides insights into plaque development and intima-media thickness [10, 11]. Another notable CVD risk predictor is the atherogenic coefficient (AC) derived from TC, HDL, and LDL measurements [12, 13].

Recently, a newly developed index known as TCBI has emerged as a straightforward yet effective prognostic indicator for CVD [14]. A study by Maruyama et al. demonstrated that a low TCBI significantly predicts major adverse cardiac and cerebrovascular events (MACCEs) in patients with CAD [15]. Additional studies have further validated the promising predictive capability of this index in CVD patients [16–19], and a recent investigation highlighted its utility in accurate risk stratification for those with aortic stenosis [20]. However, the relationship between TCBI and the severity of stenosis remains unclear.

Generally, TCBI is compared with other nutritional indexes [21–23]. In our previous research, we evaluated the effectiveness of TCBI in predicting CVD risk compared to various atherogenic indices in a cohort study of the general population. We discovered a significant association between TCBI and CVD mortality. Notably, TCBI outperformed indices such as AIP and AC [24]. Since TCBI was initially developed for risk assessment in CVD patients [14], we aimed to fill this research gap by examining the relationship between TCBI and atherogenic indices with stenosis severity. This study used a case-control design involving CAD patients undergoing angiography, with findings compared to a healthy control group.

Methods

Participants and sampling

This case-control study was conducted between 2011 and 2012 at Ghaem Medical Educational Hospital in Mashhad, Iran. A total of 1,187 participants — comprising 610 men and 577 women — were candidates for angiography. Following the angiographic procedures, participants were categorized into four groups: those with

significant angiographic findings in one, two, or three vessels (defined as ≥ 50% occlusion in at least one coronary artery) and those with routine angiography results (defined as < 50% obstruction in the coronary arteries).

Multi-stage cluster sampling was utilized as the randomization technique. All patients were referred to a cardiologist for angiography and were evaluated based on established inclusion and exclusion criteria. The inclusion criteria required participants to have significant angiographic findings in one, two, or three vessels, defined as a ≥ 50% occlusion in at least one coronary artery. The exclusion criteria included any hospitalization for illness in the previous five years, signs of infection or systemic conditions, pregnancy, alcohol use, a history of acute myocardial infarction, systemic inflammatory disorders, congestive heart failure, cancer, and liver dysfunction. As a result, 781 patients (480 men and 301 women) undergoing coronary angiography were included in the case group.

In addition, 406 healthy controls (130 men and 276 women) were selected from individuals visiting the clinic for routine check-ups or pre-employment medical assessments. The inclusion criteria for the healthy control group required participants to be adults (≥ 18 years old), able to comprehend the study procedures and provide informed consent, physically capable and willing to give written consent, in good health according to the examination, without symptoms of heart disease, not pregnant or breastfeeding, and with no history of hospitalization for any illness in the past five years.

Sample size calculation

The following formula (Daniel, 1999) was used to determine the sample size [25]:

$$\mathrm{N} = \left(Z_{\alpha} + Z_{1-\beta}\right)^2 \left({S_1}^2 + {S_2}^2\right) / d^2$$

Here, Z_{α} = 2.81 for a significance level of 0.01, and Z_{β} = 1.28 corresponds to a test power of 90%. The symbols S_1 and S_2 represent the standard deviations of groups 1 (cases) and 2 (controls), respectively. Using this formula, a minimum sample size of 80 was established. An additional 30% ($N = 24$) was included to account for potential non-responders to account for potential non-responders. Consequently, the total number of samples required for recruitment was 104 ($N = 80 + 24 = 104$) per group. However, to enhance validity, facilitate subgroup analysis, and address sampling probabilities, the sample size for the case group was increased to 781. In contrast, that for the control group was raised to 406.

Calculation of indices

Participants' demographic characteristics were assessed using self-administered questionnaires, and blood samples in fasting state were collected to evaluate their lipid profile levels, including HDL, LDL, TG, and TC. To ensure accurate weight measurements, individuals were instructed to wear minimal clothing and empty their bladders beforehand. They stood on a calibrated digital or mechanical scale, and their weight was recorded in kilograms.

We calculated AIP, AC, CRI-I, CRI-II, and TCBI using specific formulas below, based on their validity and predictive capacity for CVD and its risk factors in the Iranian population [24, 26].

$$\mathrm{AIP} = \log\left(\frac{TG\left(\frac{mg}{dl}\right)}{HDL\left(\frac{mg}{dl}\right)}\right) \quad [27]$$

$$\mathrm{AC} = \frac{\mathrm{TC} - HDL\left(\frac{mg}{dl}\right)}{LDL\left(\frac{mg}{dl}\right)} \quad [12]$$

$$\mathrm{CRI\text{ - }I} = \frac{TC\left(\frac{mg}{dl}\right)}{HDL\left(\frac{mg}{dl}\right)} \quad [28]$$

$$\mathrm{CRI\text{ - }II} = \frac{LDL\left(\frac{mg}{dl}\right)}{HDL\left(\frac{mg}{dl}\right)} \quad [28]$$

$$\mathrm{TCBI} = TG\left(\frac{mg}{dl}\right) \times TC\left(\frac{mg}{dl}\right) \times \text{Body weight}\ (kg) \quad [29]$$

Statistical analysis

SPSS software (version 21, Chicago, IL, USA) was utilized for statistical analysis. Data normality was assessed using the Kolmogorov-Smirnov test. Mean ± standard deviation (SD) was used to present quantitative variables, while qualitative variables, were shown as frequency and percentage. Mean values of different groups were compared using analysis of variance (ANOVA) and chi-square, was used for categorical parameters.

Participants diagnosed with CAD were classified based on the severity of stenosis into three groups: single-vessel disease (SVD), two-vessel disease (2VD), and three-vessel disease (3VD). Following this classification, the TCBI and atherogenic indices values for these groups were compared to those of a healthy control group using multinomial logistic regression. Data was adjustment for age, smoking, HTN and diabetes. PRISM software (Version 10.4.1) was utilized for visualization of the findings. A P value < 0.05 was considered statistically significant.

Results

Table 1 presents the demographic data of the study participants. A total of 1,187 individuals were included in the study, comprising 610 men and 577 women. The mean ages for women were higher than for men across the analyzed cases. Among men in the 3VD group, the highest mean age was 60.02 ± 9.8 years, whereas women in the same group had a mean age of 62.03 ± 10.75 years. Women in all groups were primarily non-smokers. Among individuals with 3VD, 46.7% of men and 57.7% of women were also diagnosed with diabetes. Additionally, these individuals had elevated fasting blood glucose (FBG) values, with men averaging 138.27 ± 74.86 mg/dl and women averaging 147.02 ± 68.55 mg/dl. The study indicated that the mean weight of men increased with worsening stenosis severity. Furthermore, in men, AC in SVD and CRI-II in control groups were highest. It is noteworthy that the FBG levels in individuals with 3VD were significantly higher compared to those in other groups. Interestingly, women with 2VD and 3VD exhibited significantly higher CRI-I, CRI-II, and AIP (P-value < 0.05). We also observed a significant increase in TG levels among patients with 3VD.

According to the Multinomial logistic regression model demonstrated in Fig. 1, there was no association between TCBI, AC, CRI-I, and CRI-II with the severity of stenosis in men. However, we have found an association between AC and SVD in men, increasing the risk of SVD by 3.741 times compared to the control group [OR: 3.741, 95% CI: 1.395–10.056, P-value = 0.009]. The results indicated that AIP, CRI-I, and CRI-II significantly correlate with the severity of stenosis in women. In this case, AIP raised the risk of three-vessel stenosis by 2.5 times [OR: 3.537, 95% CI: 1.218–3.497, P-value = 0.020]; and a one-unit increase in CRI-I and CRI-II could raise the risk of two vessel stenosis by 21.9% [OR: 1.219, 95% CI: 1.008–1.473, P-value = 0.041] and 33.1% [OR: 1.331, 95% CI: 1.064–1.666, P-value = 0.012] in women, respectively. Moreover, the risk of three-vessel stenosis in women can increase by 22.4% [OR: 1.224, 95% CI: 1.026–1.459, P-value = 0.024] and 25.3% [OR: 1.253, 95% CI: 1.005–1.562, P-value = 0.045] when CRI-I and CRI-II are raised by 1 unit, respectively. However, there was no association between TCBI and AC with the severity of stenosis in women.

Discussion

The current case-control study aimed to compare atherogenic indices and TCBI between healthy individuals and patients undergoing angiography with varying degrees of stenosis severity. Our results showed that, except for TCBI, other indicators such as AIP, AC, CRI-I, and CRI-II were significantly higher in cases than in the healthy control group. It is important to note that, apart from AC, the remaining indices (AIP, CRI-I, CRI-II) showed significant differences from the control group in women with more than one vessel blockage. AC showed a substantial difference from the control group, only in men with one vessel blockage.

Our findings indicate that the AIP (Log [TG/HDL]), with odds of 3.537, shows a stronger association with the development of CAD than other atherogenic indices. A meta-analysis with 40,902 participants showed that an increase in one unit of AIP was associated with a 2.1-fold increase in the odds of developing CAD [29]. Confirming our findings, it has been shown that AIP was more robust than CRI-I, CRI-II, and AC for determining the CVD risk in schizophrenia patients [30]. The imbalance of plasma lipids leads to dyslipidemia, which is characterized by elevated levels of LDL-C, TG, and TC alongside decreased levels of HDL-C [31]. One possible reason AIP was significantly different from the control group only in the most severe form of CAD (participants with three-vessel blockage) could be that AIP, unlike CRI-I and CRI-II, includes TG as a part of its formula. Studies have shown that even when LDL is normal, hypertriglyceridemia can be an essential risk factor for carotid stenosis progression [32]. Notably, the association between the AIP and the severity of stenosis in our study was observed exclusively in women. This finding aligns with research conducted by Fernandez-Macías et al., who studied 340 healthy women and demonstrated the prognostic significance of AIP as an indicator of CVD [6]. Similarly, Koleva et al. reported elevated AIP values in women with metabolic syndrome [33]. Additionally, AIP has been recognized as a significant predictor of CVD in women with polycystic ovary syndrome, which is an independent risk factor for CVD often linked to insulin resistance [34, 35]. In our study, the women who participated had a mean age of over 50. Aging, especially during menopause, typically results in a decline in estrogen levels, which plays a protective role against the occurrence of CVD [36–38]. Furthermore, age and postmenopausal status can alter lipid profiles, affecting cardiovascular health. Notably, LDL, TC, and the ratio of TC to HDL were significantly higher in postmenopausal women [39].

CRI-I and CRI-II were calculated using TC/HDL (CRI-I) and LDL/HDL (CRI-II) ratios. Changes in both indices indicated dyslipidemia, which can be associated with the pathogenesis of CAD [40]. As part of the CRI-II formula, LDL plays a crucial role in the incidence of CAD, as highlighted in the Framingham Heart Study [41]. Our findings revealed that CRI-II exhibited more substantial effects across various degrees of vessel stenosis in women than CRI-I. In a study by Doganay et al., which investigated the severity of ischemia in patients suspected of having CAD, it was noted that CRI-II was correlated with the severity of ischemia in these individuals [42]. Additionally, CRI-II

Table 1 Demographic characteristics of study participants by health status: healthy controls and patients with one, two, or three vessel blockages

Variables		Males (*N*: 610)				*P*-value	Females (*N*: 577)				*P*-value
		Control	SVD	2VD	3VD		Control	SVD	2VD	3VD	
N (%)		130 (21.3%)	121 (19.8%)	134 (22%)	225 (36.9%)		276 (47.8%)	90 (15.6%)	81 (14%)	130 (22.5%)	
Age		53.52 ± 13.31	55.14 ± 10.95	56.69 ± 9.91	60.02 ± 9.8[abc]	**< 0.001**	53.77 ± 10.44	57.79 ± 11.11	61.21 ± 10.01	62.03 ± 10.75[ab]	**< 0.001**
Marital status	Single	4 (3.1%)	1 (0.8%)	0	1 (0.4%)	0.18	3 (1.1%)	1 (1.1%)	0	4 (3.1%)	0.47
	Married	121 (93.1%)	115 (95%)	127 (94.8%)	216 (96%)		236 (85.5%)	72 (80%)	72 (88.9%)	107 (82.3%)	
	Divorced	1 (0.8%)	0	0	0		5 (1.8%)	2 (2.2%)	1 (1.2%)	0	
	Widow	4 (3.1%)	5 (4.1%)	7 (5.2%)	8 (3.6%)		32 (11.6%)	15 (16.7%)	8 (9.9%)	19 (14.6%)	
Smoking habits	Non-smoker	79 (60.8%)	59 (48.8%)	72 (53.7%)	125 (55.6%)	0.077	213 (77.2%)	62 (68.9%)	57 (70.4%)	92 (70.8%)	**0.013**
	Current smoker	24 (18.5%)	42 (34.7%)	41 (30.6%)	53 (23.6%)		38 (13.8%)	10 (11.1%)	19 (23.5%)	24 (18.5%)	
	Ex-smoker	27 (20.8%)	20 (16.5%)	21 (15.7%)	47 (20.9%)		25 (9.1%)	18 (20%)	5 (6.2%)	14 (10.8%)	
HTN	Yes	41 (31.5%)	48 (39.7%)	62 (46.3%)	97 (43.1%)	0.077	115 (41.7%)	43 (47.8%)	42 (51.9%)	63 (48.5%)	0.34
	No	89 (68.5%)	73 (60.3%)	72 (53.7%)	128 (56.9%)		161 (58.3%)	47 (52.2%)	39 (48.1%)	67 (51.5%)	
DM	Yes	14 (10.8%)	42 (34.7%)	55 (41%)	105 (46.7%)	**< 0.001**	51 (18.5%)	43 (47.8%)	36 (44.4%)	75 (57.7%)	**< 0.001**
	No	116 (89.2%)	79 (65.3%)	79 (59%)	120 (53.3%)		225 (81.5%)	47 (52.2%)	45 (55.6%)	55 (42.3%)	
Weight, kg		69.56 ± 11.39	74.16 ± 14.09[a]	73.77 ± 13.63[a]	73.03 ± 12.24[a]	**0.015**	67.43 ± 13.56	66.96 ± 12.12	65.71 ± 11.88	64.89 ± 12.80	0.28
FBG, mg/dl		110.63 ± 42.21	116.07 ± 37.37[a]	122.77 ± 45.31[ab]	138.27 ± 74.86[abc]	**< 0.001**	118.15 ± 48.65	136.76 ± 55.82[a]	135.27 ± 70.45[a]	147.02 ± 68.55[abc]	**< 0.001**
TC, mg/dl		167.35 ± 47.57	165.06 ± 39.97	168.77 ± 37.98	168.67 ± 42.22	0.87	168.53 ± 41.93	166.73 ± 43.82	173 ± 42.10	172.78 ± 51.61	0.64
TG, mg/dl		135.18 ± 85.55	149.92 ± 70.94	155 ± 91.15	145.09 ± 74.24	0.22	139.5 ± 63.55	144.3 ± 69.1	147.17 ± 56.8	159.11 ± 65.74[abc]	**0.04**
LDL, mg/dl		100.39 ± 38.13	91.65 ± 32.58	98 ± 31.17	99.40 ± 31.36	0.16	96.43 ± 33.73	94.4 ± 31.3	107.43 ± 51.91	99.47 ± 32.61	0.072
HDL, mg/dl		39.73 ± 10.53	41.62 ± 13.62	40.21 ± 9.05	40.17 ± 14.67	0.65	43.77 ± 11.87	43.28 ± 20.92	40.61 ± 10.2	42.1 ± 20.4	0.39
AIP		0.49 ± 0.23	0.53 ± 0.2	0.54 ± 0.24	0.53 ± 0.21	0.2	0.48 ± 0.22	0.5 ± 0.22	0.54 ± 0.2[a]	0.57 ± 0.22[bc]	**0.001**
AC		1.30 ± 0.3	1.42 ± 0.44	1.35 ± 0.26	1.32 ± 0.25[b]	**0.006**	1.33 ± 0.29	1.33 ± 0.19	1.28 ± 0.19	1.34 ± 0.34	0.41
TCBI		1771.31 ± 2022.36	1982.46 ± 1513.78	2083.53 ± 1794.14	1903.01 ± 1441.36	0.48	1670.34 ± 1171.50	1709.70 ± 1321.22	1746.92 ± 1130.70	1865.99 ± 1320.64	0.51
CRI-I		4.39 ± 1.49	4.15 ± 1	4.32 ± 1.05	4.37 ± 1.08	0.32	4.03 ± 1.31	4.14 ± 1.13	4.41 ± 1.23[ab]	4.42 ± 1.35[ab]	**0.013**
CRI-II		2.63 ± 1.14	2.32 ± 0.81[a]	2.50 ± 0.78[b]	2.59 ± 0.89[b]	**0.025**	2.31 ± 1.01	2.4 ± 0.94	2.74 ± 1.65[ab]	2.59 ± 1.09[ab]	**0.008**

Abbreviations: HTN (Hypertension), DM (Diabetes Mellitus), FBG (Fasting Blood Glucose), TC (Total Cholesterol), TG (Triglycerides), LDL (Low-Density Lipoprotein), HDL (High-Density Lipoprotein), TCBI (Triglyceride-Total Cholesterol-Body Weight Index), AIP (Atherogenic Index of Plasma), AC (Atherogenic Coefficient), CRI-I (Castelli's Risk Index – I), CRI-II (Castelli's Risk Index – II)

Derived from ANOVA test. Continuous variables are presented as mean ± standard deviation, while categorical variables are presented as number (percentage)

a: healthy vs. SVD, 2VD, 3VD; b: SVD vs. 2VD, 3VD and c: 2VD vs. 3VD

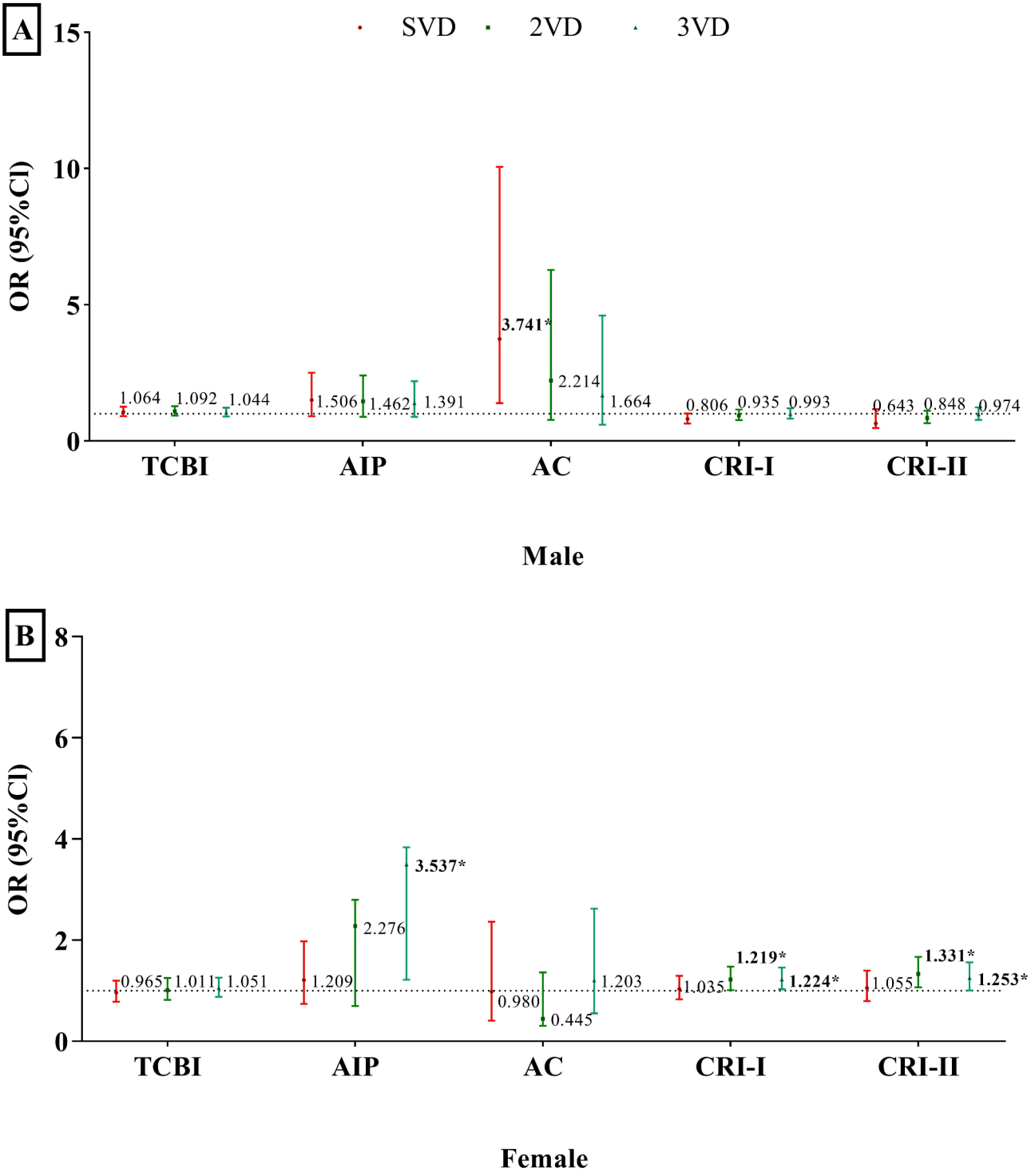


Fig. 1 Association between TCBI, Atherogenic indices, and stenosis severity compared to the healthy control group: Results stratified by sex (**A**: Male, **B**: Female). Definitions: SVD (Single-vessel disease), 2VD (Two-vessel disease), 3VD (Three-vessel disease). Multinomial logistic regression has been done; *P-value < 0.05

has a significant association with insulin resistance [43], a well-known risk factor for CVD, and a component of metabolic syndrome [44]. A case-control study by Rahamon et al. involving 11 patients with gestational diabetes mellitus and 29 non-GDM patients found that both CRI-I and CRI-II were significantly elevated in the GDM group, placing them at a higher risk for CVD [45]. Furthermore, another study showed that CRI-I and CRI-II levels were

higher in women with metabolic syndrome [33]. Fujihara et al. demonstrated that CRI-II is a valuable predictor of vulnerable CAD [46]. It is also an independent predictor of coronary slow flow, where atherosclerosis, inflammation, and endothelial dysfunction contribute to its pathogenesis [47]. In our study, women's average age was higher than men's. This is noteworthy because hypercholesterolemia is more common among women than men in the 50 to 64 age group, with a significant increase linked to aging [48]. This observation may help explain why the association was primarily observed in women.

The AC is a lipid indicator derived from dividing non-HDL cholesterol by HDL-C, and it has practical applications in clinical settings [49, 50]. Our findings indicate that AC is associated with a 2.7-fold increased risk in men with single-vessel stenosis. Bhardwaj et al. conducted a case-control study involving 60 CAD patients with confirmed angiographic results and 60 healthy participants, reporting that AC accounts for a 16% risk of CAD in both men and women [12]. Additionally, Sujatha et al. demonstrated that an increase in AC correlates with a higher stroke incidence than control groups [51]. Conversely to our findings, Celik et al. reported that AC exhibits the highest sensitivity among atherogenic indices (74%), serving as a protective factor in patients undergoing coronary artery bypass graft surgery, reducing the risk by 70.2% [52]. Unlike our study, this research did not analyze all CVD risk factors and treated the population without differentiation by gender [52]. Elevated AC raised the risk of metabolic syndrome by 98% [53], which is linked to the development of CVD and atherosclerosis [54].

Our findings indicate that most atherogenic indices are more strongly associated with the severity of stenosis in women than men. This discrepancy may be attributed to gender differences in lipid profile status. Hormonal variations between men and women could also play a significant role in these differences. For instance, one study found that women in the follicular phase exhibited the lowest levels of TC and LDL. In contrast, these parameters peaked during the ovulatory phase [55]—additionally, disparities in fat distribution patterns between genders further influence lipid profiles [56]. Research has shown that fat distribution is a crucial factor affecting TG, HDL, and the apoproteins B (Apo-B) and A1 levels in men and women [57]. This is primarily related to the waist-to-hip ratio (WHR), which is connected to unfavorable levels of TG and HDL [58], as well as differences in body fat percentage and subcutaneous versus visceral adipose tissue between the genders [59].

TCBI is a simple nutritional assessment tool designed for CVD patients, incorporating TG, TC, and body weight [14]. The existing literature predominantly emphasizes the prognostic role of TCBI concerning MACCEs, such as mortality or stroke [14, 15, 17, 60–62] events in the CVDs patients. For instance, even a Japanese study conducted on patients with aortic stenosis undergoing transcatheter aortic valve implantation focused on MACCEs, such as mortality, as the primary endpoint rather than evaluating the severity of stenosis [20]. The lack of association observed in our research between TCBI and stenosis severity suggests that while TCBI may be effective for long-term prognostication of adverse events, it may not directly correlate with specific structural or anatomical conditions like stenosis severity. Supporting the utility of TCBI in large cohort studies and MACCE predictions, our previous research demonstrated TCBI's capacity for predicting mortality [24]. TG is an essential part of the TCBI formula. Although it is involved in the development of atherosclerosis, its association with this condition diminishes when other risk factors are considered, especially cholesterol-related lipoproteins like HDL and LDL [63–65]. As a result, TG may not be a reliable predictor of atherosclerosis risk or plaque formation. In contrast, LDL and its associated protein, apo-B, show a stronger correlation with significant cardiovascular events [66, 67]. This could explain why the TCBI, unlike other atherogenic indices, was not linked to the severity of stenosis in patients undergoing angiography in this Iranian population.

Strengths and limitations

It is the first to examine the relationship between atherogenic indices and TCBI with stenosis levels in angiography patients compared to a control group. Additionally, it uniquely assesses the severity of arterial blockage. The data was also analyzed by sex to offer deeper insights into the correlations between CAD indicators and artery stenosis. However, unlike previous studies that considered medication effects, our research lacked access to patients' medication information, which may have influenced the results. The single-center design limits generalizability, and its observational nature restricts causal inferences. Therefore, larger multi-center cohort studies are needed to confirm these findings, and employing machine learning methods may be advantageous [68].

Conclusion

The study demonstrated significant correlations between TCBI and atherogenic indices with arterial stenosis in men and women. In women, the AIP, CRI-I, and CRI-II were linked to stenosis in two or three arteries. Additionally, the AC correlated with one artery stenosis in the men. Conversely, TCBI did not indicate any significant relationship with coronary artery stenosis within the study group. It is suggested that AIP, CRI-I, and CRI-II can be used for risk assessment in the CAD population of women, while AC can be used in the CAD population

of men. Furthermore, prospectively conducting the study and establishing causality could provide valuable insights into the significance of these findings and underscore the clinical relevance of these indicators in healthcare settings.

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Author contributions
M.I. and F.K. wrote and edited the final main manuscript. M.I. also prepared a graphical abstract. H.M., A.R., S.H.H.Sh., and M.N. participated in data collection. A.Sh. and M.M. diagnosed CVD patients. S.D. performed statistical analysis and designed the study. All authors read and approved the final manuscript.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethical Approval and Consent to participate
This study was approved by the Ethics Committee of the Mashhad University of Medical Sciences (MUMS) and the Institutional Review Board of Mashhad University Medical Center (IR.MUMS.MEDICAL.REC.1403.006). Informed consent was obtained from all subjects. Also, the study was conducted according to the Helsinki Declaration.

Consent for publication
It is not applicable to the Consent of Image Publication for this manuscript. The figures were designed only in this manuscript for presenting the results of the current paper.

Competing interests
The authors declare no competing interests.

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