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REVIEW ARTICLE

Atherogenic indices in clinical practice and biomedical research: A short review

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ABSTRACT

Cardiovascular diseases (CVD) represent a major cause of mortality and morbidity worldwide. To date, many physicians still requesting traditional lipid profile tests (TG, TC, HDL-C, and LDL-C) to confirm the clinical diagnosis related to CVD. However, using these tests may be inadequate for predicting CVD risk, especially in intermediate risk. For better clinical practice, laboratory diagnostic alternatives should frequently be evaluated and developed by physicians and laboratory scientists. In this review, we sought to focus on the benefits of lipid ratios (CRI-, CRI-II, AIP, AC, and CHOLindex) in supporting clinical diagnosis and how they can be calculated. A literature search in reputed databases (PubMed and Scopus) was performed to attain this aim, and peer-reviewed research articles were included to conduct this review. Short theoretical and practical notes about each index were accordingly included, along with calculation formulas. Thus, the current article can assist new researchers, and young physicians review what supports their knowledge in managing early CVDs.

Keywords atherogenic coefficient, atherogenic Index of plasma, coronary artery disease, dyslipidemia, lipid ratios

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INTRODUCTION

Cardiovascular diseases (CVDs) remain the leading causes of mortality and morbidity worldwide.[1] Most CVDs such as coronary artery disease (CAD), stroke, myocardial infarction (MI), and peripheral vascular disease (PVD) are developed and frequently attributed to a single risk factor called "dyslipidemia".[2,3] Dyslipidemia can be defined as an elevation in plasma lipids (low-density lipoproteins cholesterol, LDL-C; triglycerides, TGs; or both) or low levels of high-density lipoprotein cholesterol (HDL-C).[4] Genetics, lifestyle, certain disorders (such as thyroid dysfunction and kidney disease), and drugs are major contributors to cause dyslipidemia.[5] In addition to its high prevalence in economically advanced societies, dyslipidemia has been recently reported to find its way in semi-urban populations.[6]

However, early diagnosis of dyslipidemia before the onset of CVD is a helpful cardiovascular preventive measure. In the evaluation of dyslipidemia, lipid profiles (total cholesterol, TC; LDL-C; HDL-C; and TGs) are mostly considered, with emphasis majorly on LDC-C as "bad cholesterol".[7–9] Apart from their efficiency in diagnosis, using LDL-C alone, or HDL-C alone in predicting CVD risk may be inadequate especially in intermediate-risk when a someone have one or more risk factors (elevated blood lipids, high plasma glucose level, high blood pressure and overweight) that exceed desirable levels or a positive family history.[10–12] Thus, suggesting novel biomarkers or more accurate indices by physicians and biomedical scientists is always needed for best clinical practices. Over the past two decades, many reports showed that in cases when the traditional lipid profiles remain normal, several lipid ratios (atherogenic indices) can be diagnostic alternatives that have been shown in predicting the risk of CVD events and the efficacy of therapy.[13] Among them, atherogenic index of plasma (AIP),[14–17] Castelli's risk index I (CRI-I) and II (CRI-II),[18] atherogenic coefficient (AC),[9,19,20] and cholesterol index (CHOLindex).[21,22] In this review, the benefits of these indices (ratios) in diagnosing CVD were highlighted and how to calculate each index.

LIPID RATIOS (ATHEROGENIC INDICES)

Atherogenic index of plasma

Atherogenic index of plasma (AIP) is an unconventional lipid ratio representing the logarithm of the molar ratio of TGs to HDL-C (Figure 1).[23,24] Accumulated evidence showed that AIP is an important predictive index with a positive correlation with CVD. In 2010, Onat et al. prospectively evaluated 2676 middle-aged Turkey adults with clinical and laboratory investigations during about 8 years' follow-up and found that AIP is a strong risk factor for CAD in that population.[23] Moreover, Wang et al. (2021) tested the correlation between AIP and SYNTAX (angiographic grading tool to assess the complexity of CAD) score in the Chinese population.[25] They concluded that AIP is an independent risk factor for CAD and may assist in CAD prevention. In addition to many reports which have assessed the AIP in different populations to predict CVD in those populations,[13,16,17,26–28] some researchers suggest a positive correlation with other certain conditions such as acquired premature ejaculation and its severity.[29] Accordingly, evidence supports that AIP is now ready to be considered in clinical practice and for research purposes and further evaluated.

Castelli's risk indexes (I & II)

Castelli's risk indexes (also called cardiac risk indexes) are two lipid ratios, the CRI-I is the ratio of TC to HDL-C (Figure 2), while the CRI-II is the ratio of LDL-C to HDL-C (Figure 3), with notable positive associations with CVD risk.[9,18,30] They were reported by

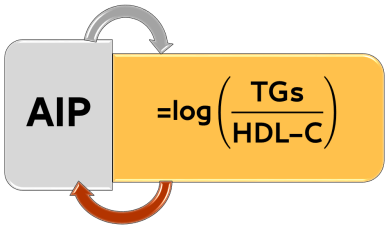

Figure 1 **The mathematical equation to calculate the AIP.**

William Castelli, at the end of the past century.[18] Later, many reports assessed and confirmed their positive correlation with CVD[18,24,31–33] and some other conditions such as chronic obstructive pulmonary disease (COPD, negative correlation)[34] and erectile dysfunction.[35] CRI-I has been particularly shown to reflect coronary plaques formation and the thickness of intima-media in the carotid arteries of young adults.[36,37] Therefore, physicians should consider CRI-I and II, in clinical practice to predict or assess atherosclerosis and CVD and for further evaluation.

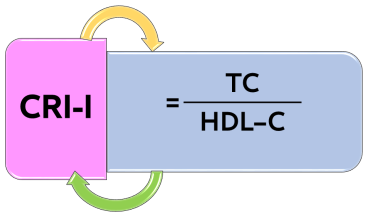

Figure 2 **Mathematical equation to calculate CRI-I.**

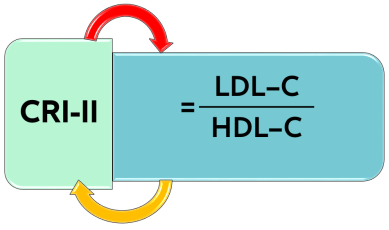

Figure 3 **Mathematical equation to calculate CRI-II.**

Atherogenic coefficient

Atherogenic coefficient (AC) is the ratio of non-HDL cholesterols to HDL-C (Figure 4).[9,19] It is a diagnostic alternative, which has been used in predicting the risk of developing CV events.[38,39] In this context, it could be a useful tool for CVD specialists to predict a patient's atherogenic status and for further assessment of this index.

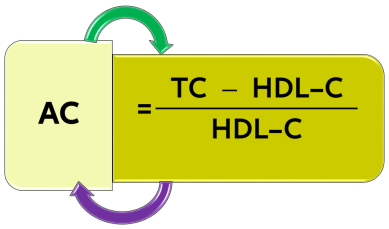

Figure 4 **The mathematical equation to calculate AC.**

Cholesterol index (CHOLindex)

Cholesterol index (CHOLindex) is a simple index that predicts the probability of developing CAD with greater accuracy than the other indices.[21,22] It can be calculated based on LDL-C and HDL-C in individuals with plasma TGs less than 400 mg/dL (Figure 5).[22] In cases when TGs concentration is higher than or equal to 400 mg/dL, the very-low-density lipoprotein cholesterol (VLDL-C) (i.e. $TGs_{(mg)}/5$) should also be included (Figure 6).[22]

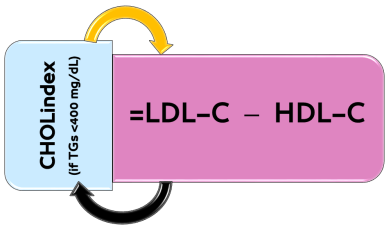

Figure 5 **Mathematical equation to calculate CHOLindex if the plasma TGs <400 mg/dL.**

All atherogenic indices can be easily calculated using simple mathematical formulas, which can be applied automatically within automated analytical devices, with no additional costs are required to be paid for calculating them.

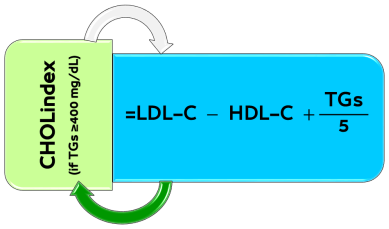

Figure 6 **Mathematical equation to calculate CHOLindex if the plasma TGs ≥400 mg/dL.**

NORMAL RANGES

In view of limited uses in clinical practices, the normal ranges of atherogenic indices cannot easily set. However, each index range in healthy individuals and patients without CVD in previous reports, based on country and sample size, is listed in (Table 1).

Table 1 **Atherogenic indices in healthy and non-cardiovascular disease patients.**

Index	Lab. Findings			Reference
	Country	No.	Ranges	
AIP	Brazil	197	-0.001±0.30	[19]
	Croatia	95	-0.005±0.269	[34]
	India	100	0.26±0.14	[40]
	Nigeria	699	0.06±0.002	[9]
		41	-0.79±0.15	[30]
	Turkey	51	0.28±0.26	[33]
		48	0.35±0.35	[29]
		32	0.54±0.22	[32]
		32	0.62±0.64	[41]
		19	0.52(0.20–0.59)*	[31]
CRI-I	Croatia	95	4.15(3.41–5.04)*	[34]
	India	100	3.04±0.65	[42]
	Italy	56	4.33(0.14)‡	[20]
	Mexico	49	Men 4.2(3.56–5.13)†	[42]
		81	Women 3.6(3.02–4.27)†	[42]
	Nigeria	699	3.76±0.10	[9]
		41	2.18±0.19	[30]
	Turkey	127	4.7±1.1	[22]
		48	3.19±2.42	[29]
		19	4.27(3.41–5.20)*	[31]
		32	4.4±0.91	[32]
		51	3.7(2.4–5.9)*	[33]
		32	2.26±1.54	[41]
CRI-II	Croatia	95	2.66(2.00–3.53)*	[34]
	India	100	1.68±0.56	[42]
	Italy	56	2.73(0.11)‡	[20]

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Table 1 continued

	Nigeria	699	2.32±0.09	[9]
		41	1.12±0.18	[30]
	Turkey	127	2.9±0.8	[22]
		51	2.3(1.1–4.5)*	[33]
		48	1.83±1.54	[29]
		32	2.9±0.72	[32]
		32	2.46±0.86	[41]
		19	2.80(2.18–3.52)*	[31]
AC	Brazil	197	3.25±1.36	[19]
	Croatia	95	3.15(2.41-4.04)*	[34]
	India	100	2.04±0.65	[42]
	Nigeria	699	2.76±0.10	[9]
		41	1.18±0.19	[30]
	Turkey	51	2.7(1.4–4.9)*	[33]
		48	2.49±2.04	[29]
		32	3.4±0.91	[32]
		32	1.27±1.54	[41]
		19	3.27(2.41–4.20)*	[31]
CHOLindex (mmol/L)	Nigeria	699	0.78±0.04	[9]

(*) = Mean(95% CI), (‡) = Mean(SE), (†) = Median (IQR), all other values are presented as Mean±SD.

CONCLUSIONS

Unconventional lipid ratios and indices (AIP, CRI-I, CRI-II, AC, and CHOLindex) are positively associated with CVD. Accordingly, these ratios can assist in predicting various CVD events. CHOLindex, based on the available literature, maybe the more accurate index when compared with the others. All atherogenic indices can be easily calculated using simple mathematical formulas, which can be applied automatically within automated analytical devices with no additional costs.

ABBREVIATIONS

AC, atherogenic coefficient; AIP, atherogenic index of plasma; CAD, coronary artery disease; CHOLindex, cholesterol index; COPD, chronic obstructive pulmonary disease; CRI-I, Castelli's risk index I; CRI-II, Castelli's risk index II; CVD, cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; PVD, peripheral vascular disease; SD, standard deviation; SE, standard error; TC, total cholesterol; TG, triglycerides; VLDL, very-low density lipoprotein cholesterol.

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DECLARATIONS

Authors' contributions

Conceptualization: HAA. Data curation, formal analysis, funding acquisition, investigation: N/A. Methodology, project administration: HAA. Resources: HAA. Supervision: HAA. Validation: ZSA & SAA. Writing-original draft, review & editing: HAA, ZSA &SAA. All the authors reviewed and approved the final draft submitted to this journal.

Competing interests

The authors have no conflict of interest.

Ethical approvals

Not applicable.

Data availability

Not applicable.

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