Asian Journal of Research in Biochemistry

Volume 14, Issue 2, Page 7-17, 2024; Article no.AJRB.113882
ISSN: 2582-0516

Role Played by Biochemical and Hematological Parameters in the Prediction of Cardiovascular Risk

W. K. T. Nuwanthika [a++], D. I. K. Welivitigoda [a++], S. P. N. N. Senadeera [b*], D. U. Kottahachchi [a], C. B. Ranaweera [a] and N. Wijesighe [c]

[a] Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, General Sir John Kotelawala Defence University, Sri Lanka.
[b] Department of Zoology and Environment Sciences, Faculty of Science, University of Colombo, Sri Lanka.
[c] Department of Clinical Sciences, Faculty of Medicine, General Sir John Kotelawala Defence University, Rathmalana, Sri Lanka.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJRB/2024/v14i2278

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/113882

Review Article

Received: 02/01/2024
Accepted: 06/03/2024
Published: 11/03/2024

ABSTRACT

Introduction: The term "cardiovascular diseases" (CVDs) refers to any disease affecting the heart or blood vessels. CVDs are the most common cause of death worldwide and the most responsible reason for 10% of deaths in the early 20th century. These CVDs can emerge as myocardial infarction or ischemic heart disease, stroke, and congestive heart failure. For diagnosing CVDs, physical, radiological investigations, and laboratory investigations for cardiac enzymes and lipid profile are used. In clinical practices, cardiovascular risk prediction models are very important in the

[++] Those authors contributed equally;
**Corresponding author: E-mail: nimeshans.zoology@stu.cmb.ac.lk, cbr2704@kdu.ac.lk, nadeesenadeera1997@gmail.com*

identification, prevention, and staging of the severity of CVDs. Framingham Risk Score-coronary heart disease, Framingham Risk Score-cardiovascular disease, QRESEARCH-cardiovascular risk algorithm, Joint British Society risk-calculator-3, WHO/ISH CVD risk prediction charts, and Atherosclerotic Cardiovascular Disease risk-estimator are some of the available CVD risk estimators. However, many of these estimators can be used only to evaluate individuals more than 40 years and to assess the risk for 10-years. Therefore, new risk estimators are needed to overcome the deficiencies of the available risk estimators. Research have been done in novel directions; on ratios of routinely performing hematological and biochemical laboratory parameters such as Neutrophil to Lymphocyte Ratio (NLR), Platelet to Lymphocyte Ratio (PLR), and Aspartate aminotransferase to Alanine aminotransferase ratio (AST/ALT). The outcomes indicate a relationship between the above-said ratios and the risk for CVDs.

Conclusion: On such grounds, this review describes the importance of developing a CVD risk estimator by amalgamating some of the biochemical and hematological parameters, including NLR, PLR, and AST/ALT ratios, aiming to overcome the existing shortcomings.

Keywords: Cardiovascular diseases (CVD); atherosclerotic cardiovascular disease (ASCVD); neutrophil-to-lymphocyte ratio (NLR); platelet-to-lymphocyte ratio (PLR); aspartate aminotransferase (AST) and alanine aminotransferase (ALT).

1. INTRODUCTION

"Cardiovascular disease" refers to any disease that affects the heart or blood vessels. It is frequently caused by atherosclerosis of arteries and an elevated risk of thrombosis [1]. This process can be associated with any artery in the body, including coronary, cerebral and renal arteries [2].

1.1 Occurrence of CVD

Cardiovascular disease (CVD) is a significant health issue in low- and middle-income countries. People in such countries face problems such as less access to adequate health care, and therefore, many people are diagnosed in the latter stages of the disease and tend to die younger. CVDs are the responsible reason for 10% of the deaths at the beginning of the 20th century. By 2001, it was 30%. About 80% of CVD deaths occurred in low- and middle-income countries. As WHO estimated, 17.9 million people died from CVDs worldwide in 2019. It represents 32% of global deaths. Of this, 85% were due to myocardial infarction and stroke [1]. According to the American College of Cardiology, the global prevalence of CVDs in 2015 was 422.7 million. The 12.6 million CVD deaths in 1990 rose to 17.9 million (8.5 million females and 9.4 million males) in 2015 [3]. In South Asia, some studies show a 73% rise in the prevalence of ischemic heart disease between 1990 and 2010. Furthermore, these studies have found that South Asian people encounter their first MI almost ten years earlier than other people [4]. A study conducted in 2016 on 'Risk estimates of cardiovascular diseases in a Sri Lankan community', revealed that CVD prevalence and mortality rate is almost 80% in developing countries [5].

2. TYPES OF CVDs

Cardiovascular diseases include coronary heart disease (CHD), heart failure (HF), atrial fibrillation, valvular disease, sudden cardiac death (SCD), sick sinus syndrome (SSS), cardiomyopathy and aortic aneurysms [6].

3. RISK FACTORS OF CVD

Risk factors for cardiovascular diseases can be categorized mainly as controllable and uncontrollable factors [1]. Tobacco use, unhealthy diet, physical inactivity, obesity, dyslipidemia, hypertension, diabetes mellitus, smoking, and alcohol consumption can be considered as the main controllable risk factors. Advanced age, gender, and family history are the major uncontrollable risk factors [7]. Reducing salt, saturated fat, and sugar in the diet, preventing, or reducing alcohol consumption and tobacco usage, regular healthy physical activities, and a healthy diet containing plenty of fibers, more fruits, and vegetables will reduce the risk for cardiovascular diseases. Reducing the stress level and drug treatment for hypertension, diabetes mellitus, and high blood lipid is necessary to reduce the cardiovascular risk [1].

4. DIAGNOSIS OF CVD

4.1 Physical and Radiological Examinations

Initially a general examination is done including the presence of conjunctival pallor, jaundice, cachexia and obesity. The arterial pulse is checked, and blood pressure and jugular venous pressure are measured. Further, inspection of the precordium and cardiac auscultation is done [8].

As radiological investigations, ideally chest X-ray is done to assess the heart size, lung fields and calcification of aorta. An electrocardiogram (ECG) is taken to see evidence of ischemia, arrhythmia and ventricular hypertrophy. An exercise electrocardiography is commonly done to demonstrate inducible ischemia. CT coronary angiography (CTCA) is a very sensitive and specific method for the detection of coronary artery diseases and cardiovascular magnetic resonance (CMR) also an imaging method that does not use harmful radiation [8].

4.2 Use of CVD Risk Estimating Tools

In clinical practice, the use of 'cardiovascular disease risk assessment models' are an important aspect in the identification, prevention and staging of the severity of CVDs. CVD risk assessment depends on risk factor profile, mean population CVD risk, mean population risk factor levels and relative risk of each risk factor [9]. Various CVD risk prediction models are in clinical practice such as, Framingham Risk Score-coronary heart disease (FRS-CHD), Framingham Risk Score- cardiovascular disease (FRS-CVD), QRISK2 (QRESEARCH cardiovascular risk algorithm), Joint British Society risk calculator 3 (JBS3), WHO/ISH CVD risk charts and Atherosclerotic Cardiovascular Disease (ASCVD) [10]. The above calculates the 10-year CVD risk of individuals and all the mentioned calculators give the risk in numeric values.

Age, gender, and ethnicity have been considered in every risk estimating tool. In most risk estimating tools, the smoking status, diabetic status of the individual, blood pressure (systolic and/or diastolic), and either one or more of the different serum cholesterol levels such as serum total cholesterol, HDL cholesterol, LDL cholesterol and cholesterol/HDL ratio, and treatment for hypertension are considered. The QRISK2 considers the presence of CKD, atrial fibrilization, rheumatoid arthritis, family history of CVD and body mass index (BMI) as additional factors [10-13].

The Atherosclerotic Cardiovascular Disease (ASCVD) Risk Estimator was developed by the American Heart Association and American College of Cardiology with the aim of reducing the 10-year predicted risk for ASCVD and aiding in the management of "ABCS", aspirin treatment in appropriate patients, blood pressure control, cholesterol management and cessation of smoking. This risk assessment tool has been developed based on "2013 ACC/AHA Guidelines on the assessment of cardiovascular risk". This tool can be used for primary prevention of the patients and adhere to the "ABCS" over time [14]. Age, sex, race, laboratory test results like total cholesterol (mg/dL), HDL cholesterol (mg/dL), HDL cholesterol (mg/dL), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), patient history like diabetes, smoking status, and treatment for hypertension, on statins, on aspirin therapy are used as parameters for the calculation.

Age, sex, systolic blood pressure, and smoking data are used in the Framingham Risk Score (FRS), Systematic Coronary Risk Evaluation (SCORE), and World Health Organization/International Society of Hypertension (WHO/ISH) models. The FRS model in the current investigation employs BMI rather than the ratio of total cholesterol to HDL cholesterol, but the SCORE and WHO/ISH models contain data on total cholesterol. This is because HDL cholesterol data were not gathered by the National Health and Morbidity Survey (NHMS). Diabetes is included by both the WHO/ISH and the FRS models [15].
Different guidelines recommend different risk scores such as the ASCVD risk score in ACC/AHA 2013 guidelines, the QRISK2 risk engine in NICE 2014 guidelines and the FRS CVD risk score in Canadian 2012 guidelines [10].

5. HEMATOLOGICAL PARAMETERS USED TO ACCESS THE CVD RISK

5.1 Full Blood Count Parameters

Although it is an inexpensive test, components of the test such as total and differential white blood cell counts support the diagnosis of bacterial, viral, and parasitic infections and inflammations. The platelet count shows an impact on hemostasis [16]. Studies have shown that there

is a strong association between hematological parameters and the risk of CVDs [17,18].

5.1.1 Absolute neutrophil count (ANC)

ANC > 7500 cells/ µL is termed as neutrophilia and it can be seen in inflammatory conditions and bacterial infections [19]. ANC < 2500 cells/ µL is termed as neutropenia and it can be seen in viral infections such as dengue fever [20]. In the study of "Neutrophilia predicts death and heart failure after myocardial infarction", which is a community-based study, they have concluded that the ANC is strongly associated with death and heart failure [21].

5.1.2 Absolute lymphocyte count (ALC)

ANC < 1500 cells/ µL is termed as lymphocytopenia [22,23] revealed that ALC less than or equal to 1500 cells/mm3 had a higher risk of mortality in heart failure and, lower groups had high mortality [22]. [24] revealed that low relative lymphocyte count is an independent marker of poor prognosis in elderly patients with chronic heart failure.

5.1.3 Platelet count

Studies have been conducted to investigate the relationship between platelet count with mortality, future CVD, and future cancer. Even higher platelet counts within the normal platelet count have been associated with an increased risk of CVD risk, whereas lower platelet counts have been associated with cancer [25]. Platelet count and mean platelet volume, which are directly related to platelet activation, are associated with the clinical outcome and mortality of stroke, myocardial infarction, and coronary artery disease [26].

5.1.4 Red cell distribution width (RDW)

The red blood cell distribution width (RDW) is a measurement of anisocytosis of red blood cells [27]. According to [28] revealed that interpretation of RDW can be used to distinguish between inflammatory non-inflammatory conditions [29]. revealed that RDW level may be a predictive biomarker of morbidity and mortality in CVDs.

5.2 Ratios

It is a valuable option to gain further information on systemic inflammation by using the indices of cell populations and differential count (DC). Initially, in the field of oncology, risk prediction through neutrophils-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were used [30].

5.2.1 Neutrophils-to-lymphocyte ratio (NLR)

NLR is a novel inflammatory marker for systemic inflammation, which is extensively used in cardiovascular diseases, infections, inflammatory diseases and in several types of cancers [31,32]. Studies have been conducted and revealed that NLR has a prognostic value in disease conditions including HF, AMI, CAD, infective endocarditis, and acute pulmonary embolism [30,33].

5.2.2 Platelets-to-lymphocytes ratio (PLR)

PLR has risen as an inflammatory marker, which reveals shifts in platelet and lymphocyte counts because of acute inflammatory and prothrombotic states. Firstly, PLR was used to predict the prognosis of neoplastic diseases as a systemic inflammatory biomarker [34]. PLR has also been identified as an independent prognostic factor in patients with acute heart failure (AHF) [35].

5.3 NLR and PLR in CVD

As atherosclerosis is the main underlying cause of cardiovascular diseases, which has an inflammatory origin, CVD also has a relation with biomarkers of inflammation. Pathogenesis of atherosclerosis is associated with almost all the cellular components of blood. Especially white blood cells (WBCs), such as neutrophils, lymphocytes, and monocytes play a main role. These cell counts are considered as better predictors of CVD risk than total WBC count alone [18]. Platelets and red blood cells (RBC) are also involved. Also red cell distribution width (RDW), which is commonly called as the measurement of the variability of size of circulating blood cells can be used as a predictor of CVD risk. Mainly WBCs provide a small progressive predictive value for the estimation of 10-year CVD risk [18].

In the findings of the post-hoc analysis of [30], it was indicated that both high NLR and PLR values are associated with CVD risk and these NLR and PLR should be used as biomarkers for CVD risk prediction. There is an urge to have risk stratification and prognostication in CVD to target for the prevention and follow up of the high-risk

individuals [36]. A systematic review and meta-analysis of observational studies were conducted by authors, which aimed to survey and predict the association between NLR and CVD risk. Finally, this survey concluded that high NLR is associated with coronary artery diseases (CAD), stroke and composite cardiovascular events. Therefore, NLR should be considered when assessing the cardiovascular risk in the population. [37] concluded that the WBCs are associated with increased CVD risk. Compared to age-sex matched controls, NLR and PLR values of heart failure (HF) patients were higher. In this study, it is proven that the HF patients have higher NLR values than the control. [38] similarly shown out that higher mortality and heart transplantation risk in HF patients is foreboded by higher NLR values. [39] investigated and proved that NLR is an important inflammatory marker and potential predictor of CVD risk. As platelets play a main role in atherosclerosis, an increased platelet activation is noticed and PLR which is a novel inflammatory marker is also associated. High PLR is reported as a predictor of long-term mortality in acute coronary syndrome (ACS).

[40] conducted a study using a population with 180 patients who underwent elective coronary angiography (CAG), where 100 patients had abnormal CAG and 80 patients had normal CAG. They concluded that the patients with abnormal CAG had significantly higher NLR and PLR compared to the patients with normal CAG. Moreover, they have suggested that NLR and PLR could be section of CVD evaluation before coronary angiography.

6. BIOCHEMICAL PARAMETERS USED TO ACCESS THE CVD RISK

6.1 Lipid Profile (Cholesterol)

Lipid profile is a major investigation done for assessing the risk for CVDs as dyslipidemia is a leading course for developing atherosclerotic plaques with or without the influence of genetic factors [41]. The potential role of lipid profile parameters in the progression of CVDs has been discussed in many studies. According to [9,42] high total cholesterol and triglyceride levels could interfere with the constriction and abstraction mechanism of cardiac blood vessels where lipid profile has a significant correlation with CVDs. Moreover, elevation in LDL cholesterol level leads to atherosclerosis due to the accumulation of LDL in the intima- media of the arteries and individuals who have a higher HDL cholesterol level have a comparatively lower risk for CVDs [9,42,43].

6.2 Liver Profile

As [44] revealed, there is an association between the non-alcoholic fatty liver disease (NAFLD) and CVDs. As the liver produces inflammatory cytokines, lipoproteins and several atherogenic factors, the changes in liver enzymes will directly or indirectly affect cardiovascular health [44,45]. Ndrepepa G et al,[46] revealed that CVD is the most common cause of death in patients with NAFLD [46]. Therefore, the liver profile is also done as a supportive investigation based on the clinical condition.

6.2.1 Aspartate aminotransferase (AST) and alanine aminotransferase (ALT)

Myocardial cells contain the highest concentration of AST, compared to skeletal muscles, kidneys, and liver [47]. Ndrepepa G, et al [46] reveals that AST may be a marker of structural CVDs, such as stress arising due to cardiac risk factors, reperfusion related injury and necrosis due to acute coronary syndrome [46]. ALT is mostly considered to be a liver specific enzyme, although it can be found in small concentrations in the brain, skeletal muscle, and intestinal tissue [47,48].

6.3 AST/ALT Ratio

The AST/ALT ratio can be used as a predictor of many clinical conditions as it is a non-invasive, non-expensive and simple indicator that can be derived from routine laboratory test results [49]. As AST is released from many tissues like liver and myocardium and ALT is released only by liver, myocardial damage can result in an elevation of AST/ALT ratio.

The study done by [50] using mice, revealed that mice with elevated AST/ALT ratio had a reduced ability to carry oxygen and elevated oxidative stress markers were also detected [50]. The same study implies that there can be a heart-liver interaction, so it is reasonable to suspect an elevated AST/ALT ratio in patients with heart diseases. Both these facts imply that death due to CVD can happen via oxidative stress. [50,51] highlighted that elevated AST/ALT ratio is significantly associated with a higher risk of developing CVDs.

The summary of the studies done to assess the association between hematological parameters and CVDs and the association between liver enzymes and CVDs are mentioned in Table 1.

7. TREATMENT AND MANAGEMENT

Apart from managing favorable lifestyle modification, lipid- lowering drugs, antihypertensives, antidiabetic drugs, antiplatelet

Table 1. Studies showing the associations among NLR, PLR, and AST/ALT ratio related to CVDs

Research group	Hematological parameter ratios used	Biochemical parameter ratios used	Country of the study conducted	Association / Other findings
Angkananard et al., 2018 [36]	NLR	-	Thailand	All CVD outcomes including CAD, ACS, stroke and composite Cardiovascular event (CVE) had an association with high NLR values.
Larmann et al., 2020 [30]	NLR, PLR	-	Germany	Both PLR and NLR were associated with preoperative cardiovascular adverse events in coronary heart disease patients. Both could be used as inexpensive and broadly available tools for preoperative risk assessment.
Sari et al., 2015 [40]	NLR, PLR	-	Turkey	To predict the severity of CAD in patients undergoing elective coronary angiography (CAG), NLR and PLR can be used as a part of cardiovascular examination before CAG.
Benites-Zapata et al., 2015 [38]	NLR	-	-	High NLR has been associated with increased mortality in patients with acute heart failure and in neoplastic diseases.
Ewid et al., 2020 [47]	-	AST/ALT ratio	Saudi Arabia	Functional status decline in HFrEF (heart failure patients with reduced ejection fraction) patients could be predicted by the elevation of AST/ALT ratio.
Weng et al., 2015 [52]	-	AST/ALT ratio	United Kingdom	In men, high AST/ALT ratio is associated with increased risk of developing CVD.
Liu et al., 2021 [50]	-	AST/ALT ratio	China	High AST/ALT ratio as an independent factor for both all-cause and cardiovascular mortality in patients with hypertension.
Yokoyama et al., 2016 [53]	-	AST/ALT ratio	Japan	Increased AST/ALT ratio positively correlates with NT-proBNP levels.
Lazo et al., 2011 [54]	-	AST/ALT ratio	United States	Elevated levels of liver transaminases were significantly correlated with the cardiac biomarkers; troponin T and NT-proBNP. Consequently, they concluded that liver transaminases could be used as predictors in patients at risk of CVD.

and anticoagulation therapies are the primary regimes for the prevention and treatment of CVDs [55,56]. Prevention of cardiac events is important to reduce morbidity and mortality due to CVDs. According to [57-59] for high-risk groups, individual-based primary prevention can be directed to prevent the onset of CVD by reducing the exposure to risk factors and for people with established CVD, secondary prevention and treatments can be directed for the early detection and prevention of cardiac events [60]. The use of digital platforms such as online CVD risk estimating tools plays a key role in both the early detection and treatment of cardiac diseases. According to ACC/AHA 2013 guidelines, using the ASCVD risk estimator, individuals having estimated 10-year ASCVD risk of 5-7.5% (borderline risk) are mentioned for drug therapy with statins (under certain circumstances), those having 7.5% to <20% (intermediate risk) are mentioned for the initiation of moderate to high intensity statin therapy, and for those are having ≥20% are mentioned for the high intensity statin therapy [14].

8. CONCLUSION AND FUTURE DIRECTIONS

In current practices, for diagnosis of CVDs, clinicians do clinical examination, and biochemical investigations such as lipid profile; to study the different types and levels of lipids. Apart from the blood tests, some radiological examinations are used for the diagnosis of CVD. Some of these investigations are expensive, need preparation of the patients and are also time consuming.

The current trend is to predict CVDs using cardiac risk estimators. They express the CVD risk of an individual using his/her anthropometric parameters, some of the biochemical parameters like cholesterol levels, some of the current treatments and lifestyle aspects as mentioned in the review. Most of the risk estimating tools were developed in western countries and they are not practical to be used in other ethnic groups like Asians without any modifications, as there are different CVD profiles in-between Western and Asian populations. To our knowledge, the presence of first line relatives who are having CVDs has been considered only in very much smaller number of currently used estimators. As stated by Lloyd-Jones in 2006, it may be more beneficial if there is a system to predict the long-term lifetime CVD risk of an individual based on a particular ethnic group especially confined to young adults.

Introducing NLR and PLR as hematological parameters, and AST/ALT ratio as biochemical parameters to develop risk calculators are new trends of predictors of CVD risk as proved by many research groups. In this review, we discussed the impact and the possibilities of employing some of the biochemical parameters; AST/ALT ratios, parameters of lipid Profile as well as hematological parameters; NLR, PLR to predict the risk of CVD. So, if one can develop a CVD risk estimator using both biochemical and hematological parameters the output results would be more accurate. To our knowledge, the above-mentioned ratios have not collectively been used directly in the development of currently using risk estimators. Therefore, we propose to include more biochemical and hematological parameters to develop risk indicators for CVDs to further improve the accuracy of risk estimation.

ACKNOWLEDGEMENTS

We acknowledge General Sir John Kotelawala Defence University for providing facilities for research.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Cardiovascular diseases Who.int; 2021. (Accessed: February 15, 2024). Available:https://www.who.int/health-topics/cardiovascular-diseases
2. Cardiovascular disease nhs.uk; 2023. (Accessed: February 15, 2024). Available:https://www.nhs.uk/conditions/cardiovascular-disease/
3. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, et al. Global, Regional, and national burden of cardiovascular diseases for 10 Causes, 1990 to 2015. Journal of the American College of Cardiology. 2017;70(1):1–25. Available:https://doi.org/10.1016/j.jacc.2017.04.052
4. Rehman H, Samad Z, Mishra SR, Merchant AT, Narula JP, Mishra S, et al. Epidemiologic studies targeting primary cardiovascular disease prevention in South Asia. Indian Heart Journal, 2018; 70(5): 721–730. Available:https://doi.org/10.1016/j.ihj.2018.01.029

5. Ranawaka UK, Wijekoon CN, Pathmeswaran A, Kasturiratne A, Gunasekera D & Chackrewarthy S, et al. Risk estimates of cardiovascular diseases in a Sri Lankan community. The Ceylon Medical Journal. 2016;61(1): 11–17.
Available:https://doi.org/10.4038/cmj.v61i1.8253
6. Kokubo Y, Matsumoto C. Hypertension is a risk factor for several types of heart disease: Review of prospective studies. Advances in Experimental Medicine and Biology. 2017;956:419–426.
Available:https://doi.org/10.1007/5584_2016_99
7. Kilkenny MF, Dunstan L, Busingye D, Purvis T, Reyneke M, Orgill M, et al. Knowledge of risk factors for diabetes or cardiovascular disease (CVD) is poor among individuals with risk factors for CVD. Plos One. 2017;12(2):e0172941.
Available:https://doi.org/10.1371/journal.pone.0172941
8. Feather A, Randall D, Waterhouse M. Kumar and clark's clinical medicine e-book: Kumar and clark's clinical medicine e-book. Elsevier Health Sciences; 2016.
9. Zhao B, Jose PO, Pu J, Chung S, Ancheta IB, Fortmann SP, et al. Racial/ethnic differences in hypertension prevalence, treatment, and control for outpatients in northern California 2010-2012. American Journal of Hypertension. 2015;28(5): 631–639.
Available:https://doi.org/10.1093/ajh/hpu189
10. Garg, N., Muduli, S. K., Kapoor, A., Tewari, S., Kumar, S., Khanna, R., & Goel, P. K. (2017). Comparison of different cardiovascular risk score calculators for cardiovascular risk prediction and guideline recommended statin uses. Indian Heart Journal, 69(4), 458–463.
Available:https://doi.org/10.1016/j.ihj.2017.01.015
11. Bosomworth NJ. Practical use of the Framingham risk score in primary prevention: Canadian perspective. Canadian Family Physician Medecin De Famille Canadien. 2011;57(4):417–423.
12. Collins GS Altman, DG. An independent and external validation of QRISK2 cardiovascular disease risk score: A prospective open cohort study. BMJ (Clinical Research Ed.). 2010;340:c2442.
Available:https://doi.org/10.1136/bmj.c2442
13. Hippisley-Cox J., Coupland C, Brindle P. Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: Prospective cohort study. BMJ, j2099; 2017.
Available:https://doi.org/10.1136/bmj.j2099
14. Lloyd-Jones DM, Leip EP, Larson MG, D'Agostino RB, Beiser A, Wilson PWF, et al. Prediction of Lifetime Risk for Cardiovascular Disease by Risk Factor Burden at 50 Years of Age. Circulation. 2006;113(6):791–798.
Available:https://doi.org/10.1161/CIRCULATIONAHA.105.548206
15. Selvarajah S, Kaur G, Haniff J, Cheong KC, Hiong TG, van der Graaf Y, et al. Comparison of the framingham risk score, score and who/ish cardiovascular risk prediction models in an asian population. International Journal of Cardiology. 2014;176(1):211–218.
Available:https://doi.org/10.1016/j.ijcard.2014.07.066
16. Walters MC, Abelson HT. Interpretation of the complete blood count. Pediatric Clinics of North America. 1996;43(3):599–622.
Available:https://doi.org/10.1016/s0031-3955(05)70424-7
17. Haybar H, Pezeshki SMS, Saki N. Evaluation of complete blood count parameters in cardiovascular diseases: An early indicator of prognosis? Experimental and Molecular Pathology. 2019;110: 104267.
Available:https://doi.org/10.1016/j.yexmp.2019.104267
18. Lassale C, Curtis A, Abete I, van der Schouw YT, Verschuren WMM, Lu Y, et al. Elements of the complete blood count associated with cardiovascular disease incidence: Findings from the EPIC-NL cohort study. Scientific Reports. 2018;8(1): 3290.
Available:https://doi.org/10.1038/s41598-018-21661-x
19. Tahir N, Zahra F. Neutrophilia. In StatPearls. StatPearls Publishing; 2023.
Available:http://www.ncbi.nlm.nih.gov/books/NBK570571/
20. Thein TL, Lye DC, Leo YS, Wong JGX, Hao Y, Wilder-Smith A. Severe neutropenia in dengue patients: Prevalence and significance. The American Journal of Tropical Medicine and Hygiene. 2014;90(6):984–987.

Available:https://doi.org/10.4269/ajtmh.14-0004

21. Arruda-Olson AM, Reeder GS, Bell MR, Weston SA, Roger VL. Neutrophilia predicts death and heart failure after myocardial infarction: A community-based study. Circulation. Cardiovascular Quality and Outcomes. 2009;2(6):656–662. Available:https://doi.org/10.1161/CIRCOUTCOMES.108.831024
22. Berezné A, Bono W, Guillevin L, Mouthon L. Orientation diagnostique devant une lymphopénie. Presse Medicale (Paris, France 1983). 2006;35(5):895–902. Available:https://doi.org/10.1016/S0755-4982(06)74709-1
23. Majmundar M.et al. Absolute lymphocyte count as a predictor of mortality and readmission in heart failure hospitalization. International Journal of Cardiology. Heart & vasculature. 2022;39(100981):100981. DOI: 10.1016/j.ijcha.2022.100981
24. Acanfora D, Gheorghiade M, Trojano L, Furgi G, Pasini E, Picone C, et al. Relative lymphocyte count: A prognostic indicator of mortality in elderly patients with congestive heart failure. American Heart Journal. 2001;142(1):167–173. Available:https://doi.org/10.1067/mhj.2001.115792
25. Vinholt PJ, Hvas AM, Frederiksen H, Bathum L, Jørgensen MK, Nybo M. Platelet count is associated with cardiovascular disease, cancer and mortality: A population-based cohort study. Thrombosis Research. 2016;148:136–142. Available:https://doi.org/10.1016/j.thromres.2016.08.012
26. Du J, Wang Q, He B, Liu P, Chen JY, Quan H. Association of mean platelet volume and platelet count with the development and prognosis of ischemic and hemorrhagic stroke. International Journal of Laboratory Hematology. 2016;38(3):233–239. Available:https://doi.org/10.1111/ijlh.12474
27. Danese E, Lippi G, Montagnana M. Red blood cell distribution width and cardiovascular diseases. Journal of Thoracic Disease. 2015;7(10):E402-411. Available:https://doi.org/10.3978/j.issn.2072-1439.2015.10.04
28. Horta-Baas G, Romero-Figueroa MDS. Clinical utility of red blood cell distribution width in inflammatory and non-inflammatory joint diseases. International Journal of Rheumatic Diseases. 2019;22(1):47–54. Available:https://doi.org/10.1111/1756-185X.13332
29. Arkew M, et al. Red blood cell distribution width as novel biomarker in cardiovascular diseases: A literature review, Journal of blood medicine. 2022;13:413–424. DOI: 10.2147/JBM.S367660
30. Larmann J, Handke J, Scholz AS, Dehne S, Arens C, Gillmann HJ et al. Preoperative neutrophil to lymphocyte ratio and platelet to lymphocyte ratio are associated with major adverse cardiovascular and cerebrovascular events in coronary heart disease patients undergoing non-cardiac surgery. BMC Cardiovascular Disorders. 2020;20(1):230. Available:https://doi.org/10.1186/s12872-020-01500-6
31. Forget P, Khalifa C, Defour JP, Latinne D, Van Pel MC, De Kock M. What is the normal value of the neutrophil-to-lymphocyte ratio? BMC Research Notes. 2017;10(1):12. Available:https://doi.org/10.1186/s13104-016-2335-5
32. Zahorec R. Neutrophil-to-lymphocyte ratio, past, present and future perspectives. Bratislava Medical Journal. 2021;122(07):474–488. Available:https://doi.org/10.4149/BLL_2021_078
33. Özpelit E, et al. Prognostic value of neutrophil-to-lymphocyte ratio in pulmonary arterial hypertension. The Journal of international medical research. 2015;43(5):661–671. DOI: 10.1177/0300060515589394
34. Kurtul A, Ornek E. Platelet to lymphocyte ratio in cardiovascular diseases: A systematic review. Angiology. 2019;70(9):802–818. Available:https://doi.org/10.1177/0003319719845186
35. Ye GL, Chen Q, Chen X, Liu YY, Yin TT, Meng QH, et al. The prognostic role of platelet-to-lymphocyte ratio in patients with acute heart failure: A cohort study. Scientific Reports. 2019;9(1):10639. Available:https://doi.org/10.1038/s41598-019-47143-2
36. Angkananard T, Anothaisintawee T, McEvoy M, Attia J, Thakkinstian A. Neutrophil lymphocyte ratio and cardiovascular disease risk: A systematic

review and meta-analysis. Bio Med Research International. 2018;2703518. Available:https://doi.org/10.1155/2018/2703518

37. Durmus E, Kivrak T, Gerin F, Sunbul M, Sari I, Erdogan O. Neutrophil- to-lymphocyte ratio and platelet- to-lymphocyte ratio are predictors of heart failure. Arquivos Brasileiros de Cardiologia; 2015. Available:https://doi.org/10.5935/abc.20150126
38. Benites-Zapata VA, Hernandez AV, Nagarajan V, Cauthen CA., Starling RC, Tang WHW. Usefulness of neutrophil-to-lymphocyte ratio in risk stratification of patients with advanced heart failure. The American Journal of Cardiology. 2015;115(1):57–61. Available:https://doi.org/10.1016/j.amjcard.2014.10.008
39. Cho KI, Ann SH, Singh GB, Her AY, Shin ES. Combined usefulness of the platelet-to-lymphocyte ratio and the neutrophil-to-lymphocyte ratio in predicting the long-term adverse events in patients who have undergone percutaneous coronary intervention with a drug-eluting stent. Plos One. 2015;10(7):e0133934. Available:https://doi.org/10.1371/journal.pone.0133934
40. Sari I, Sunbul M, Mammadov C, Durmus E, Bozbay M, Kivrak T, et al. Relation of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio with coronary artery disease severity in patients undergoing coronary angiography. Kardiologia Polska. 2015;73(12):1310–1316. Available:https://doi.org/10.5603/KP.a2015.0098
41. Coelho VG, Caetano LF, Liberatore Júnior RDR, Cordeiro JA, Souza DRS. Perfil lipídico e fatores de risco para doenças cardiovasculares em estudantes de medicina. Arquivos Brasileiros de Cardiologia. 2005;85(1):57–62. Available:https://doi.org/10.1590/S0066-782X2005001400011
42. Gaggini M, Gorini F, Vassalle C. Lipids in atherosclerosis: Pathophysiology and the role of calculated lipid indices in assessing cardiovascular risk in patients with hyperlipidemia. International journal of molecular sciences. 2022;24(1):75. DOI: 10.3390/ijms24010075
43. Arsenault BJ, Boekholdt SM, Kastelein JJP. Lipid parameters for measuring risk of cardiovascular disease. Nature reviews. Cardiology. 2011;8(4):197–206. DOI: 10.1038/nrcardio.2010.223
44. Edens MA, Kuipers F, Stolk RP. Non-alcoholic fatty liver disease is associated with cardiovascular disease risk markers. Obesity Reviews. 2009;10(4):412–419. Available:https://doi.org/10.1111/j.1467-789X.2009.00594.x
45. Rahmani J, Miri A, Namjoo I, Zamaninour N, Maljaei MB, Zhou K, et al. Elevated liver enzymes and cardiovascular mortality: A systematic review and dose-response meta-analysis of more than one million participants. Eur J Gastroenterol Hepatol. 2019 May;31(5):555–62. DOI: 10.1097/MEG.0000000000001353.
46. Ndrepepa G. Aspartate aminotransferase and cardiovascular disease—A narrative review. Journal of Laboratory and Precision Medicine. 2021;6:6–6. Available:https://doi.org/10.21037/jlpm-20-93
47. Ewid M, Sherif H, Allihimy AS, Alharbi SA, Aldrewesh DA, Alkuraydis SA, Abazid R. AST/ALT ratio predicts the functional severity of chronic heart failure with reduced left ventricular ejection fraction. BMC Research Notes. 2020;13(1):178. Available:https://doi.org/10.1186/s13104-020-05031-3
48. Fernando S, Wijewickrama A, Gomes L, Punchihewa CT, Madusanka SDP, Dissanayake H, et al. Patterns and causes of liver involvement in acute dengue infection. BMC Infectious Diseases. 2016;16(1):319. Available:https://doi.org/10.1186/s12879-016-1656-2
49. Nyblom H, Bjornsson E, Simren M, Aldenborg F, Almer S, Olsson R. The AST/ALT ratio as an indicator of cirrhosis in patients with PBC. Liver International. 2006;26(7):840–845. Available:https://doi.org/10.1111/j.1478-3231.2006.01304.x
50. Liu H, Ding C, Hu L, Li M, Zhou W, Wang T, et al. The association between AST/ALT ratio and all-cause and cardiovascular mortality in patients with hypertension. Medicine. 2021;100(31):e26693. Available:https://doi.org/10.1097/MD.0000000000026693
51. Karatas M, Keles N, Parsova KE, Ciftci HO, Ozkok S, Kahraman E, et al. High AST/ALT Ratio Is Associated with Cardiac

Involvement in Acute COVID-19 Patients. Medicina. 2023 Jun;59(6):1163.
DOI: 10.3390/medicina59061163

52. Weng SF, Kai J, Guha IN, Qureshi N. The value of aspartate aminotransferase and alanine aminotransferase in cardiovascular disease risk assessment. Open Heart. 2015;2(1):e000272.
Available:https://doi.org/10.1136/openhrt-2015-000272

53. Yokoyama M, Watanabe T, Otaki Y, Takahashi H, Arimoto T, Shishido T, et al. Association of the aspartate aminotransferase to alanine aminotransferase ratio with BNP level and cardiovascular mortality in the general population: The yamagata study 10-year follow-up. Disease Markers. 2016; 4857917.
Available:https://doi.org/10.1155/2016/4857917

54. Lazo M, Hernaez R, Bonekamp S, Kamel IR, Brancati FL, Guallar E, et al. Non-alcoholic fatty liver disease and mortality among US adults: Prospective cohort study. BMJ (Clinical Research Ed.). 2011;343:d6891.
Available:https://doi.org/10.1136/bmj.d6891

55. Flora GD, Nayak MK. A brief review of cardiovascular diseases, associated risk factors and current treatment regimes. Current Pharmaceutical Design. 2019; 25(38):4063–4084.
Available:https://doi.org/10.2174/1381612825666190925163827

56. Kumar A, Siddharth V, Singh SI, Narang R. Cost analysis of treating cardiovascular diseases in a super-specialty hospital. Plos One. 2022;17 (1):e0262190.
Available:https://doi.org/10.1371/journal.pone.0262190

57. Badawy MAEMD, Naing L, Johar S, Ong S, Rahman HA, Tengah D, et al. Evaluation of cardiovascular diseases risk calculators for CVDs prevention and management: Scoping review. BMC Public Health. 2022;22(1):1742.
Available:https://doi.org/10.1186/s12889-022-13944-w

58. Chapman BL. Effect of coronary care on myocardial infarct mortality. Heart. 1979; 42(4):386–395.
Available:https://doi.org/10.1136/hrt.42.4.386

59. Zhang Y, Miao H, Chia YC, Buranakitjaroen P, Siddique S, Shin J, et al. Cardiovascular risk assessment tools in Asia. Journal of Clinical Hypertension (Greenwich, Conn.). 2022; 24(4): 369–377.
Available:https://doi.org/10.1111/jch.14336

60. Durmuş G, Belen E, Can MM. Increased neutrophil to lymphocyte ratio predicts myocardial injury in patients undergoing non-cardiac surgery. Heart & Lung: The Journal of Critical Care. 2018;47(3): 243–247.
Available:https://doi.org/10.1016/j.hrtlng.2018.01.005

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/113882