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Review Article

Is neutrophil lymphocyte ratio a prognostic marker of acute ST elevation myocardial infarction?

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ABSTRACT

Several inflammatory biomarkers have been implicated in the pathogenesis of acute coronary syndromes. The present study aims to determine the prognostic value of neutrophil lymphocyte ratio (NLR) to predict the immediate outcomes in patients with acute ST elevation myocardial infarction and if any correlation exists between NLR and TIMI risk score. A review of articles published in Pubmed database on the prognostic importance of neutrophil lymphocyte ratio in determining major adverse cardiac events (MACE) such as arrhythmias, cardiogenic shock and in hospital mortality was done. NLR was found to be a reliable prognostic tool to assess the immediate outcome in ST elevation myocardial infarction (STEMI) patients.

Keywords: NLR, STEMI, MACE, TIMI

INTRODUCTION

The underlying mechanism of acute coronary syndrome (ACS) is decreased blood flow to part of heart musculature, which is usually secondary to plaque rupture and formation of thrombus. Atherosclerotic plaque rupture or erosion is the formation of thrombus, and distal embolism is the basic pathophysiological mechanism of myocardial ischemia.[1,2] Plaque composition, vulnerability (plaque type) and stenosis (plaque size) are the risk factors for plaque rupture.[3]

Several studies have reported that WBC counts provide independent and additional predictive value to short-term mortality risk stratification in patients with acute myocardial infarction.[4,5] The mechanisms that cause this association include leukocyte-mediated no-reflow, leukocyte-mediated hypercoagulability and indirect cardiotoxicity mediated by proinflammatory cytokines.[6,7]

Inflammation has been proven to be the basis of many cardiovascular diseases, especially those that involve atherosclerosis, a mechanism similar to coronary artery disease.[8-10] Inflammation is related to the occurrence, development and instability of atherosclerotic plaques. Lymphocytes and monocytes are discovered in the early stages of plaque formation.[11] Bone marrow responds to inflammation by releasing white blood cells (especially neutrophils). Studies have shown that various haematological indicators such as total white blood cell count, neutrophils and monocytes have a role in the prognosis of STEMI patients.[11]

DISCUSSION

Major adverse cardiac events (MACE)

There is no specific definition of MACE, but with the passage of time, various definitions have been used for MACE as a primary or secondary endpoint in cardiovascular research. Since the mid-1990s, various authors have defined it as including a series of overlapping adverse events.[12,13] As part of MACE, various adverse events included in different studies are heart failure,

cardiac rupture, arrhythmias, non-fatal reinfarction, recurrent angina, re-hospitalization for cardiovascular related diseases, repeated percutaneous coronary intervention (PCI), coronary artery bypass surgery and all-cause mortality.[14] MACE may also include unplanned coronary revascularization, stroke, re-infarction and all-cause death and mortality.[15]

Neutrophil lymphocyte ratio

The measurement of troponin is still considered as one of the most selective markers in detecting myocardial damages. The long-term elevation in serum levels and the need for examination in successive sequences caused ambiguity in the use of troponin in the rapid triage of ACS patients.[16,17] Several inflammatory biomarkers such as interleukin (IL)-6, C-reactive protein and matrix metalloproteinases have been identified as independent predictors of adverse outcomes in patients with ACS.[18-21] However, these biomarkers are not used routinely for patients with ACS. Therefore, efforts are continuing to find markers capable of accelerating diagnostic and decision-making processes for ACS patients.[22,23]

TIMI risk score is used as a predictor of 30-day mortality in acute STEMI patients. There is inadequate research regarding the correlation between NLR and TIMI risk score, one study had shown a positive correlation and we have found similar result in our study. The advantages of NLR is the high speed of testing and very low cost, which helps not only save a lot of time in the decision process, but also reduces the cost of treatment and prevent further diagnostic measures on admission at the emergency department.

First clinical uses of NLR

NLR was initially used in animals under stress to detect severe infections.[24-26] Later, in cancer cachexia patients, leucocyte-to-lymphocyte ratio was used as a predictor of survival.[27] In 1995, NLR was used as a marker of acute appendicitis in humans, NLR with more than 3.5 was a good predictor for detecting the disease.[28] It has been subsequently utilised in diagnosing pleural tuberculosis along with ADA.[29] NLR has a key role as a prognostic marker in gastric and colorectal disease.[30,31] In 2006, one study showed in patients before percutaneous coronary intervention, higher NLR levels was associated with a higher mortality rate.[32] Subsequently in 2008, one study showed that NLR more than 2.55 had the highest risk of predicting cardiac death in coronary heart disease patients.[33]

Use in cardiovascular disease

NLR integrates two WBC subtypes, which have opposite effects on vascular inflammation. Therefore, the ratio is more predictive than using any one parameter alone. Several studies have found that high NLR is associated with poor clinical prognosis in patients with coronary heart disease.[34-36] One study found that NLR at admission was an independent predictor of hospitalization and 6-month mortality in acute coronary syndrome.[34] NLR was associated with grave prognosis, higher frequency of MACE and a greater degree of coronary obstruction.[37] There was a higher rate of stent restenosis and mortality seen in patients with high NLR after a percutaneous intervention.[38,39]

In a study there was a comparison between the NLR and complexity of CAD, it was seen that NLR of 2.3 was associated with complex CAD compared to NLR of 1.6.[40] Another study proved that severity of coronary artery disease was directly proportional with increasing NLR.[41]

Overall, in-hospital and long-term mortality appeared to increase in patients with higher NLR.[42]

Use in other diseases

NLR has been found to be a good predictor of death in cerebrovascular diseases. It is observed that in peripheral vascular disease, higher NLR is associated with higher rates of critical stenosis, amputation and greater disease severity. In patients treated with revascularisation procedures like embolization and grafting, post-procedure complications and mortality were found to be higher in those with higher NLR.

In diabetic patients, NLR can be a more accurate marker than albuminuria in predicting worse prognosis.[43] NLR has been found to be significantly higher in patients with endothelial dysfunction. Few studies have shown a direct association between high NLR and insulin resistance by estimating the HOMA index (homeostasis model assessment) which can detect the severity of insulin resistance in diabetic patients.[44] Surprisingly, if patients were on statins, NLR was found to be lower in them, probably due to the anti-inflammatory effect.[45]

CONCLUSION

Neutrophil lymphocyte ratio has been found to be a good prognostic marker in acute STEMI to determine the MACE and in hospital mortality. NLR also positively correlates with TIMI risk score, hence can be used as a reliable admission biomarker to determine prognosis in acute STEMI patients.

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