Neutrophil-Lymphocyte Ratio (NLR) Reflects Myocardial Inhomogeneities in Hemodialyzed Patients

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Introduction. Cardiovascular diseases (CVDs) are a leading cause of death in chronically hemodialyzed (HD) patients. In this group, inflammation exerts significant impact on the prevalence of CVD morbidity and mortality. Spatial QRS-T angle is an independent and strong predictor of CV events, including sudden cardiac death (SCD), both in general population and HD patients. Pathogenesis of widened QRS-T angle is complicated and is not well established. Objectives. The study is aimed at evaluating whether inflammation process can contribute to the wide QRS-T angle. Patients and Methods. The retrospective study was performed on 183 HD patients. The control group consisted of 38 patients. Demographic, biochemical, vectorcardiographic, and echocardiographic data were evaluated in all patients. Inflammation process was expressed as neutrophil-lymphocyte ratio (NLR), as well as C-reactive protein (CRP). Results. Both NLR (3.40 vs. 1.95 (p < 0.0001)) and spatial QRS-T angle (50.76 vs. 93.56 (p < 0.001)) were higher in the examined group, compared to the control group. Similarly, CRP was higher in the examined group than in the control group (8.35 vs. 4.06 (p < 0.001), respectively). The QRS-T angle correlated with NLR, CRP, some structural echocardiographic parameters, parathormone (PTH), and calcium (Ca) concentrations. Multiple regression analysis showed that NLR is an independent QRS-T angle predictor (r = 0.498, p = 0.0027). The ROC curve analysis indicated the cut-off point of NLR equaled 4.59, where the sensitivity and specificity were the highest for predicting myocardial inhomogeneities expressed as widened QRS-T angle. Conclusion. The NLR, as an inflammation marker, may indicate myocardial inhomogeneities in HD patients.

1. Introduction

CVD is the most common cause of death in patients chronically receiving HD [1, 2]. Chronic inflammation is highly prevalent in this group and plays a prominent role in CVD morbidity and mortality [1–3]. Moreover, it seems that inflammation has a greater impact for CVD prevalence in HD patients, compared to general population [1, 2].

The spatial QRS-T angle is an independent predictor of CVD risk, including SCD, both in general population and in HD patients. Moreover, it is a death indicator for cardiovascular causes and is also an important factor for general risk of death [4–10]. The spatial QRS-T angle is measured between the vectors of ventricular depolarization and repolarization and it can be determined from standard 12-lead electrocardiogram [6, 9, 11]. Pathogenesis of widened QRS-T angle is complicated and not well established [6]. The studies show that HD patients have abnormally wide QRS-T angle [9, 10]. It is thought that inflammation can play a role in this process [12].

CRP is an acute-phase protein and the most common marker of inflammation. It is produced by macrophages and hepatocytes [13, 14]. However, in recent years, there was an increase of interest in other inflammatory indicators, including NLR [13, 15]. NLR reflects the presence of systemic inflammation [16, 17]. NLR is easy to determine and it can be
based on simple morphology. Its major benefit is a possibility for retrospective calculation [18, 19]. NLR is a quotient of an absolute neutrophil count to absolute count of leucocytes [16, 20]. The norm of NLR is still undetermined, but usually NLR ≥ 4.5 stands for increased risk of death [16, 19]. Previous studies demonstrated that higher NLR values are associated with coronary and periaortic calcification in HD patients, which is an important CVD morbidity and mortality risk factor [1].

The study is aimed at evaluating whether the inflammation process can contribute to wide QRS-T angle.

2. Patients and Methods

The retrospective study was performed on 183 ESRD patients treated by hemodialysis. The following exclusion criteria were applied: HD treatment for less than 3 months (to include only patients with ESRD), advanced neoplastic diseases reducing life expectancy to below a year, and patients displaying symptoms of acute infections at baseline (to reduce the possible influence of transient factors on the NLR value). Given that estimating the population size meeting the criteria used in our study was impossible, the sample size calculation was not performed. All available HD patients in Lublin were included. The control group included 38 patients with normal GFR values. The groups did not differ in sex and age structure.

Results of routinely performed transthoracic echocardiography and electrocardiography (ECG) (vectorcardiography (VCG)) were used. Patients underwent these examinations according to the recommendations of the American Society of Echocardiography and European Association of Cardiovascular Imaging [21] every 6 months, as described elsewhere [9]. Based on planar measurements, left ventricle stroke volume (SV), cardiac output (CO), stroke index (SI), left ventricle ejection fraction (EF), E/E' , cardiac index (CI), left ventricle mass index (LVMI), left atrial volume index (LAVI), left ventricle mass (LVM), left atrial volume (LAV), left ventricle end-diastolic and end-systolic volumes (LVEDV and LVESV, respectively) were estimated. To calculate the body surface, the Gehan and George formula was used, as described in detail elsewhere [22, 23].

The digital ECG examination records, obtained with use of Cardiav device (IMED Co. Ltd., Budapest, Hungary), were used. Based on the recorded surface 12-lead resting ECG, the vectorcardiographical parameters were estimated by transforming them into Frank’s orthogonal leads, according to inverse Dower matrix [24]. Using the Cardiav software, the spatial QRS-T angle was calculated from the maximum QRS and T vectors. Wider than normal QRS-T angle was established as over 116 degrees for males [25].

Using automated analyzers, the following biochemical parameters were examined: blood morphology, electrolytes, creatinine, Ca, PTH, CRP, and lipid profile. NLR was calculated as quotient of the absolute number of neutrophils to the absolute number of lymphocytes. These tests were carried out no more than a month prior to the echocardiographic and ECG examinations.

| Parameter                        | Mean (X) ± standard deviation (SD) or median (M) (minimum–maximum) |
|----------------------------------|---------------------------------------------------------------------|
| Age (years)                      | 64.96 ± 10.92                                                      |
| Hemoglobin (g/dl)                | 10.45 ± 1.58                                                       |
| Hematocrit (%)                   | 31.71 ± 5.04                                                       |
| Neutrophils (×10³/μl)            | 4.18 ± 1.72                                                        |
| Lymphocytes (×10³/μl)            | 1.49 ± 0.53                                                        |
| Neutrophil-lymphocyte ratio      | 3.40 ± 1.29                                                        |
| C-reactive protein (mg/l)        | 8.35 (0.11–86.9)                                                   |
| Parathormone (pg/ml)             | 392.04 (8–1235)                                                    |
| Calcium (md/dl)                  | 4.09 ± 0.36                                                        |
| Potassium (mEq/l)                | 5.12 ± 1.00                                                        |
| Ferritin (μg/l)                  | 867.79 ± 482.04                                                   |
| Cholesterol (mg/dl)              | 188.3 ± 37.35                                                      |
| LDL cholesterol (mg/dl)          | 114.8 ± 30.11                                                      |
| HDL cholesterol (mg/dl)          | 43.82 ± 17.08                                                      |
| Triglycerides (mg/dl)            | 176.3 ± 59.27                                                      |

Data are expressed as the mean ± SD, except for PTH and CRP, which are expressed as the median and ranges.

| Parameter                        | r       | p value  |
|----------------------------------|---------|----------|
| Left ventricle mass index        | 0.61    | <0.001   |
| Left atrial volume index         | 0.46    | <0.001   |
| E/E’                             | 0.61    | <0.001   |
| Left ventricle ejection fraction | -0.675  | <0.001   |
| QRS duration                     | 0.431   | <0.001   |
| QTc                              | 0.54    | <0.001   |
| Neutrophil-lymphocyte ratio      | 0.498   | <0.001   |
| Parathormone                     | -0.201  | 0.021    |
| Calcium                          | -0.349  | <0.001   |
| C-reactive protein               | 0.411   | <0.001   |

The Bioethical Commission at Medical University in Lublin, Poland, approved this study with decision number: KE-0254/74/2016.

The normality of distribution of the variables was checked with the Shapiro-Wilk test. The variables with normal distribution were presented as the mean ± SD, and these which did not fulfill the normality criterion were presented as the median and range. Pearson’s correlation test and multivariable logistic regression were used to the statistical analysis. The aim of the multiple regression analysis was to identify independent predictors of QRS-T angle. Due to the most accurate correlation with QRS-T angle in the Pearson
test, left ventricle mass index, left atrial volume index, ejection fraction, PTH, NLR, and Ca were chosen to the multiple regression analysis. Due to a correlation with abovementioned variables and weak correlation with QRS-T angle in the Pearson test, other echocardiographic measurements and CRP were excluded. Also, ROC curve analysis was performed in order to determine the sensitivity, specificity, and cut-off point of NLR as a predictor of QRS-T angle. The considered level of significance was established as p value < 0.05. The entire analysis was performed with the TIBCO Software Inc. (2017) Statistica (data analysis software system), version 13 (http://statistica.io).

3. Results

There were 99 (54.1%) men and 84 (45.9%) women with an average age of 69.4 years. Patients had the following causes of kidney failure: diabetes mellitus (n = 82), glomerulonephritis (n = 37), hypertensive nephropathy (n = 16), polycystic kidney disease (n = 6), obstructive nephropathy (n = 5), chronic pyelonephritis (n = 4), and unknown/unsure (n = 32).

The basic biochemical parameters are presented in Table 1. Both the QRS-T angle and NLR were higher in the examined group, compared to the control group (50.76 vs. 8.35 vs. 4.06 (<0.001)). Similarly, CRP was higher in the examined group than in the control group (8.35 vs. 4.06 (<0.001), respectively).

Out of the whole group of the examined patients, 82 suffered from diabetes, 124 from hypertension, and 37 used nicotine. The following pharmacological treatment was used: ACE-I/ARB (n = 131), β-blockers (n = 125), statins (n = 139), and diuretics (n = 43).

The spatial QRS-T angle correlated with LVMI, LAVI, E/E’, EF, QRS duration, QTc, NLR, PTH, Ca, and CRP. The correlations of the abovementioned parameters with QRS-T are presented in Table 2.

Multiple regression analysis (r = 0.81, p < 0.0001) showed that NLR, but not CRP, was an independent indicator of the QRS-T angle (p = 0.0027). The details of the abovementioned analysis are shown in Table 3.

The ROC curves of NLR as predictor of the QRS-T spatial angle were performed. The analysis showed the AUC equal 0.601 and the sensitivity/specificity equal 0.677/0.601. The cut-off point was 4.59, so the value of NLR equal 4.59 has the biggest sensitivity and specificity. The ROC curves are presented in Figure 1 and described in details in Table 4.

4. Discussion

To our knowledge, this is the first study that shows the relation between inflammation process, expressed as NLR, and QRS-T angle, which is considered the indicator of myocardial inhomogeneities. Moreover, our study revealed that NLR is a better marker than CRP in predicting the widening of the spatial QRS-T angle.

Cardiovascular diseases are very common in HD patients, and SCD, especially, is the main cause of death [26]. Additionally, in HD patients, compared to the healthy controls, abnormally wide spatial QRS-T angle was observed, which affected mortality as well. Pathomechanisms between CVD and chronic kidney disease (CKD) are complicated, multifactorial, and yet not completely understood. Various
processes, such as vascular calcification [1], endothelial dysfunction [27], and chronic inflammation, among others, significantly contribute to development of these diseases [28]. There is a variety of inflammatory markers, such as CRP [29]; however, they are expensive and imprecise. It is difficult to obtain other inflammatory markers, like interleukin 2 (IL-2) [30] and interleukin 6 (IL-6) [6], in clinical practice, even though they might be more accurate [31]. Moreover, measuring the most common biomarker, which is CRP, with basic technique may not detect low-grade inflammatory process in patients with CKD [29]. It may explain why CRP does not correlate with the QRS-T angle. Thus, there is a need to find a simple, inexpensive, and precise marker, which can estimate the risk of CVD and SCD, especially in CKD patients treated with hemodialysis. Our study confirms that NLR can be that.

Spatial QRS-T angle is perceived as a measure of a global myocardial inhomogeneities [32]. It is a significant and independent predictor of CVD and all-cause mortality [5–8, 11, 33–37]. The results reported by Yamazaki et al. revealed that the QRS-T angle, contrary to classical cardiovascular and ECG risk factors, is the strongest marker of the increased risk of fatal cardiac incidents, including SCD [11]. Its border values differ depending on the sex, but due to different marking methods, they are not strictly standardised [9]. It is thought that abnormal spatial QRS-T angle is defined as ≥116 degrees in females and ≥130 degrees in males [6, 10, 25]. In our study, we have demonstrated that HD patients, but not healthy subjects, had increased values of the QRS-T angle. Owing to the fact that widend QRS-T angle pathogenesis in this group of patients has not been extensively investigated, there is little knowledge about it. However, it is believed that inflammatory process plays an important role in the widening of the spatial QRS-T angle and, consequently, SCD occurrence in HD patients. Therefore, NLR, with the highest sensitivity and specificity among other inflammatory biomarkers, seems to be the most precise.

NLR, as a commonly available marker of inflammation, has a great prognostic value for many different conditions and diseases [1, 2, 16, 29, 38–44], including cardiovascular disorders [20, 40, 42, 45]. Previously published studies have revealed that increased NLR values are observed in patients with hypertension [45], aneurysms in ascending aorta [20], and stable coronary artery disease [42]. According to the study performed by Benites-Zapata et al., high NLR levels were associated with increased mortality in patients with acute heart failure and increased heart transplantation risk [46]. Chronic obstructive pulmonary disease (COPD) [43], psoriasis [38], vitamin D deficiency [41], which is observed in the early stages of CKD [47], and also Behcet disease [44] are also associated with elevated NLR values. Moreover, NLR correlates with coronary and thoracic periaortic calcification in ESRD [1] and is an independent factor for increased carotid-femoral pulse wave velocity (cfPWV), reflecting arterial stiffness, as well as cardiovascular mortality in patients undergoing peritoneal dialysis (PD) [19].

NLR level ≥3.5 among HD patients [16] and ≥4.5 in general population [19] is associated with all-cause and cardiovascular mortality, which is in agreement with our examination. Thus, the NLR may be the new, easily obtained, and promising indicator of inflammation and can identify the high risk of cardiovascular diseases [16] and mortality in chronic HD patients early on [3, 16, 18]. The most common inflammatory marker, which is CRP, is not as precise as NLR [39]. Additionally, Dawood et al. did not find the correlation between CRP and the QRS-T angle [48], similarly as in our paper. It seems that NLR and CRP may determine various pathways of inflammatory condition, which is in accordance with results of Kwon et al. [15]. ROC analysis in our study showed that NLR greater than 4.59 is the best cut-off point value for an increased QRS-T angle and it is in agreement with previous studies by Durmus et al. [49] and Vano et al. [50]. Despite the fact that its pathogenesis is not fully known and needs further examination, NLR is thought to be a better indicator of myocardial inhomogeneities reflected by the wide spatial QRS-T angle than CRP, which is also consistent with other studies [16, 29, 39].

Our study has revealed that NLR is an inexpensive, easily obtained, and precise biomarker of inflammation reflecting myocardial inhomogeneities assessed as a widened QRS-T angle.

5. Limitations

This study has some limitations. Firstly, the group of patients was relatively small; nevertheless, it was big enough to conduct the above analysis. Secondly, among inflammation markers that may affect the QRS-T angle, only NLR and CRP were measured. The third limitation of this study was that certain parameters were marked only once. The assessment of NLR over time could probably positively affect its usefulness in QRS-T angle prediction in HD patients.

6. Conclusion

Inflammation may play a role in pathogenesis of myocardial inhomogeneities in HD patients. Thus, NLR as marker of inflammation and the independent predictor of spatial QRS-T angle might indicate this clinical state in the analyzed group of patients.

Data Availability

All data used and/or analyzed in the present study are presented in the manuscript or available from the corresponding author on request.
Conflicts of Interest

The authors declare that they have no conflicts of interest.

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References

[1] K. Turkmen, F. Ozciek, A. Ozciek, E. M. Akbas, F. M. Erdur, and H. Z. Tonbul, “The relationship between neutrophil-to-lymphocyte ratio and vascular calcification in end-stage renal disease patients,” *Hemodialysis International*, vol. 18, no. 1, pp. 47–53, 2014.

[2] A. Ozciek, F. Ozciek, G. Yildiz et al., “Neutrophil-to-lymphocyte ratio as a possible indicator of epicardial adipose tissue in patients undergoing hemodialysis,” *Archives of Medical Science*, vol. 1, no. 1, pp. 118–123, 2017.

[3] C. Catabay, Y. Obi, E. Streja et al., “Lymphocyte cell ratios and mortality among incident hemodialysis patients,” *American Journal of Nephrology*, vol. 46, no. 5, pp. 408–416, 2017.

[4] C. J. W. Borleffs, R. W. C. Scherptong, S.-C. Man et al., “Predicting ventricular arrhythmias in patients with ischemic heart disease: clinical application of the ECG-derived QRS-T angle,” *Circulation Arrhythmia and Electrophysiology*, vol. 2, no. 5, pp. 548–554, 2009.

[5] J. A. Kors, I. Kardys, I. M. van der Meer et al., “Spatial QRS-T angle as a risk indicator of cardiac death in an elderly population,” *Journal of Electrocardiology*, vol. 36, pp. 113–114, 2003.

[6] M. K. de Bie, M. G. Koopman, A. Gaasbeek et al., “Incremental prognostic value of an abnormal baseline spatial QRS-T angle in chronic dialysis patients,” *European Heart Journal*, vol. 15, no. 2, pp. 290–296, 2013.

[7] P. M. Rautaharju, C. Kooperberg, J. C. Larson, and A. LaCroix, “Electrocardiographic predictors of incident congestive heart failure and all-cause mortality in postmenopausal women: the Women’s Health Initiative,” *Circulation*, vol. 113, no. 4, pp. 481–489, 2006.

[8] P. M. Rautaharju, C. Kooperberg, J. C. Larson, and A. LaCroix, “Electrocardiographic abnormalities that predict coronary heart disease events and mortality in postmenopausal women: the Women’s Health Initiative,” *Circulation*, vol. 113, no. 4, pp. 473–480, 2006.

[9] A. Jaroszyński, J. Furmaga, T. Zapolski, T. Zaborowski, S. Rudzki, and W. Dąbrowski, “The improvement of QRS-T angle as a manifestation of reverse electrical remodeling following renal transplantation in end-stage kidney disease patients on haemodialysis,” *BMC Nephrology*, vol. 20, no. 1, pp. 441–448, 2019.

[10] N. J. Schoenmaker, W. F. Tromp, J. H. van der Lee, M. Offringa, J. C. Craig, and J. W. Groothoff, “Quality and consistency of clinical practice guidelines for the management of children on chronic dialysis,” *Nephrology Dialysis Transplantation*, vol. 28, no. 12, pp. 3052–3061, 2013.

[11] T. Yamazaki, V. F. Froelicher, J. Myers, S. Chun, and P. Wang, “Spatial QRS-T angle predicts cardiac death in a clinical population,” *Heart Rhythm*, vol. 2, no. 1, pp. 73–78, 2005.

[12] C. Voulgaris, N. Tentiolouris, D. Papadogiannis et al., “Increased left ventricular arrhythmogenicity in metabolic syndrome and relationship with myocardial performance, risk factors for atherosclerosis, and low-grade inflammation,” *Metabolism: Clinical and Experimental*, vol. 59, no. 2, pp. 159–165, 2010.

[13] J. C. Yombi, P. E. Schwab, and E. Thienpont, “Neutrophil-to-lymphocyte ratio (NLR) distribution shows a better kinetic pattern than C-reactive protein distribution for the follow-up of early inflammation after total knee arthroplasty,” *Knee Surgery, Sports Traumatology, Arthroscopy*, vol. 24, no. 10, pp. 3287–3292, 2016.

[14] M. K. Wasko, M. Struminski, K. Bobecka-Wesołowska, and J. Kowalczewski, “Neutrophil-to-lymphocyte ratio shows faster changing kinetics than C-reactive protein after total hip and knee arthroplasty,” *Journal of Orthopaedic Translation*, vol. 10, pp. 36–41, 2017.

[15] J. H. Kwon, J. W. Jang, Y. W. Kim et al., “The usefulness of C-reactive protein and neutrophil-to-lymphocyte ratio for predicting the outcome in hospitalized patients with liver cirrhosis,” *BMC Gastroenterology*, vol. 15, no. 1, pp. 1–7, 2015.

[16] H. Li, X. Lu, R. Xiong, and S. Wang, “High neutrophil-to-lymphocyte ratio predicts cardiovascular mortality in chronic hemodialysis patients,” *Mediators of Inflammation*, vol. 2017, 8 pages, 2017.

[17] J. Kuźniar-Placek, M. Pacyna, and A. Jaroszyński, “Znaczzenie wskaźnika neutrofilowo-limfocytowego w chorobach układu sercowo-naczyniowego,” *Folia Cardiologica*, vol. 11, no. 6, pp. 525–528, 2017.

[18] M. Yaprap, M. N. Turan, R. Dayanan et al., “Platelet-to-lymphocyte ratio predicts mortality better than neutrophil-to-lymphocyte ratio in hemodialysis patients,” *International Urology and Nephrology*, vol. 48, no. 8, pp. 1343–1348, 2016.

[19] X. Lu, S. Wang, G. Zhang, R. Xiong, and H. Li, “High neutrophil-to-lymphocyte ratio is a significant predictor of cardiovascular and all-cause mortality in patients undergoing peritoneal dialysis,” *Kidney and Blood Pressure Research*, vol. 43, no. 2, pp. 490–499, 2018.

[20] Ö. Cem, S. Yılmaz, A. Korkmaz, T. Fahrettin, İ. Sahin, and V. Demir, “Evaluation of the neutrophil-lymphocyte ratio in newly diagnosed nondiabetic hypertensive patients with ascending aortic dilatation,” *Blood Pressure Monitoring*, vol. 21, no. 4, pp. 238–243, 2016.

[21] R. M. Lang, L. P. Badano, V. Mor-Avi et al., “Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging,” *Journal of the American Society of Echocardiography*, vol. 28, no. 1, pp. 1–39.e14, 2015.

[22] T. Zapolski, J. Furmaga, A. P. Wysokma, T. Fahrettin, İ. Sahin, J. Kowalczewski, A. Wysocka, S. Rudzki, and A. Jaroszyński, “The atrial uremic cardiomyopathy regression in patients after kidney transplantation – the prospective echocardiographic study,” *BMC Nephrology*, vol. 20, no. 1, p. 152, 2019.

[23] E. A. Gehan and S. L. George, “Estimation of human body surface area from height and weight,” *Cancer Chemotherapy Reports Part 1*, vol. 54, no. 4, pp. 225–235, 1970.

[24] G. E. Dower, “A lead synthesizer for the frank system to lead changing kinetics than C-reactive protein after total knee arthroplasty,” *Journal of Electrocardiology*, vol. 1, no. 1, pp. 101–116, 1968.

[25] R. W. C. Scherptong, I. R. Henkens, S. C. Man et al., “Normal limits of the spatial QRS-T angle and ventricular gradient in 12-lead electrocardiograms of young adults: dependence on
sex and heart rate,” *Journal of Electrocardiology*, vol. 41, no. 6, pp. 648–655, 2008.

[26] D. Jain, H. K. Aggarwal, S. Goyal, J. Sen, and S. Seth, “Evaluation of serum homocysteine level and its relation with carotid intima-media thickness in patients of chronic kidney disease,” *Medical Studies*, vol. 33, no. 4, pp. 247–253, 2017.

[27] J.-i. Oyama, D. Nagatomo, G. Yoshioka et al., “The relationship between neutrophil to lymphocyte ratio, endothelial function, and severity in patients with obstructive sleep apnea,” *Journal of Cardiology*, vol. 67, no. 3, pp. 295–302, 2016.

[28] A. Jaroszyński, A. Jaroszyńska, T. Zaborowski, A. Drelich-Zbroska, T. Zapolski, and W. Dąbrowski, “Serum heat shock protein 27 levels predict cardiac mortality in hemodialysis patients,” *BMC Nephrology*, vol. 19, no. 1, pp. 359–359, 2018.

[29] S. Kato, T. Abe, B. Lindholm, and S. Maruyama, “Neutrophil-/lymphocyte ratio: a promising prognostic marker in patients with chronic kidney disease,” *Inflammation and Cell Signaling*, vol. 3, article e683, 2015.

[30] A. Laurence, C. M. Tato, T. S. Davidson et al., “Interleukin-2 signaling via STAT5 constrains Th17 cell generation,” *Immunity*, vol. 26, no. 3, pp. 371–381, 2007.

[31] S. X. Leng, J. E. McElhaney, J. D. Walston, D. Xie, N. S. Fedarko, and G. A. Kuchel, “ELISA and multiplex technologies for cytokine measurement in inflammation and aging research,” *Journals of Gerontology-Series A Biological Sciences and Medical Sciences*, vol. 63, no. 8, pp. 879–884, 2008.

[32] C. Vougliar, S. Pagoni, S. Tesfaye, and N. Teniourir, “The spatial QRS-T angle: implications in clinical practice,” *Current Cardiology Reviews*, vol. 9, no. 3, pp. 197–210, 2013.

[33] W. Dąbrowski, A. Jaroszyński, A. Jaroszyńska, Z. Rzecki, T. T. Schlegel, and M. L. N. G. Malbrain, “Intra-abdominal hypertension increases spatial QRS-T angle and elevates ST-segment J-point in healthy women undergoing laparoscopic surgery,” *Journal of Electrocardiology*, vol. 50, no. 2, pp. 214–222, 2017.

[34] A. TorbalDe, J. A. Kors, G. Van Herpen et al., “The electrical T-axis and the spatial QRS-T angle are independent predictors of long-term mortality in patients admitted with acute ischemic chest pain,” *Cardiology*, vol. 101, no. 4, pp. 199–207, 2004.

[35] Z.-m. Zhang, R. J. Primeas, D. Case, E. Z. Soliman, P. M. Rautaharju, and ARIC Research Group, “Comparison of the prognostic significance of the electrocardiographic QRS/T angles in predicting incident coronary heart disease and total mortality (from the Atherosclerosis Risk in Communities Study),” *American Journal of Cardiology*, vol. 100, no. 5, pp. 844–849, 2007.

[36] W. Whang, D. Shimbo, E. B. Levitan et al., “Relations between QRS/T angle, cardiac risk factors, and mortality in the third National Health and Nutrition Examination Survey (NHANES III),” *American Journal of Cardiology*, vol. 109, no. 7, pp. 981–987, 2012.

[37] T. Zapolski, A. Jaroszyński, A. Drelich-Zbroska et al., “Left atrial volume index as a predictor of ventricle repolarization abnormalities in adult dialyzed patients,” *Hemodialysis International*, vol. 16, no. 2, pp. 220–232, 2012.

[38] M. Yurtdaş, Y. T. Yaylali, Y. Kaya, M. Özdemir, I. Özkan, and N. Aladağ, “Neutrophil-to-lymphocyte ratio may predict subclinical atherosclerosis in patients with psoriasis,” *Echocardiography*, vol. 31, no. 9, pp. 1095–1104, 2014.

[39] E. Zhang, M. Gao, J. Gao et al., “Inflammatory and hematological indices as simple, practical severity predictors of microdysfunction following coronary intervention: a systematic review and meta-analysis,” *Angiology*, vol. 71, no. 4, pp. 349–359, 2020.

[40] M. Doanj, A. Akyel, T. Çimen et al., “Relationship between neutrophil-to-lymphocyte ratio and saphenous vein graft disease in patients with coronary bypass,” *Clinical and Applied Thrombosis/Hemostasis*, vol. 21, no. 1, pp. 25–29, 2013.

[41] E. M. Akbas, A. Gungor, A. Ozcicek, N. Askab, S. Akin, and M. Polat, “Vitamin D and inflammation: evaluation with neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio,” *Archives of Medical Science*, vol. 4, no. 4, pp. 721–727, 2016.

[42] O. K. Uysal, C. Turkglu, D. Y. Sahin et al., “The relationship between neutrophil-to-lymphocyte ratio and coronary collateral circulation,” *Clinical and Applied Thrombosis/Hemostasis*, vol. 21, no. 4, pp. 329–333, 2015.

[43] M. López-Sánchez, J. Dorca, and S. Santos, “Defining the role of neutrophil-to-lymphocyte ratio in COPD: a systematic literature review,” *International Journal of Chronic Obstructive Pulmonary Disease*, vol. 13, pp. 3651–3662, 2018.

[44] Z. Zhang, Q. Su, L. Zhang, Z. Yang, Y. Qiu, and W. Mo, “Diagnostic value of hemoglobin and neutrophil-to-lymphocyte ratio in Behcet disease,” *Medicine*, vol. 98, no. 52, article e18443, 2019.

[45] M. Karaman, S. Balta, S. A. AY et al., “The comparative effects of valsartan and amlodipine on VWF levels and N/L ratio in patients with newly diagnosed hypertension,” *Clinical and Experimental Hypertension*, vol. 35, no. 7, pp. 516–522, 2013.

[46] V. A. Benites-Zapata, A. V. Hernandez, V. Nagarajan, C. A. Cauthen, R. C. Starling, and W. H. Wilson Tang, “Usefulness of neutrophil-to-lymphocyte ratio in risk stratification of patients with advanced heart failure,” *American Journal of Cardiology*, vol. 115, no. 1, pp. 57–61, 2015.

[47] H. K. Aggarwal, D. Jain, A. Mittal, S. Pawar, and R. Ver, “The prevalence of vitamin D deficiency in pre-dialysis patients with chronic kidney disease,” *Medical Studies*, vol. 2, pp. 75–81, 2015.

[48] F. Z. Dawood, F. Khan, M. P. Roediger et al., “Electrocardiographic spatial QRS-T angle and incident cardiovascular disease in HIV-infected patients (from the Strategies for the Management of Antiretroviral Therapy [SMART] study),” *The American Journal of Cardiology*, vol. 111, no. 1, pp. 118–124, 2013.

[49] E. Durmus, T. Kivrak, F. Gerin, M. Sunbul, I. Sari, and O. Erdogan, “Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio are predictors of heart failure,” *Archivos Brasileiros de Cardiologia*, vol. 105, no. 6, pp. 606–613, 2015.

[50] Y.-A. Vano, S. Oudard, M.-A. By et al., “Optimal cut-off for neutrophil-to-lymphocyte ratio: fact or fantasy? A prospective cohort study in metastatic cancer patients,” *PLoS One*, vol. 13, no. 4, article e0195042, 2018.