Assessment of the neutrophil/lymphocyte ratio in patients with supraventricular tachycardia

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ABSTRACT

Objective: The neutrophil/lymphocyte ratio (NLR) has been evaluated as a new predictor of cardiovascular risk. Inflammation has been shown to be associated with various arrhythmias including supraventricular tachycardias (SVTs). In this study, we aimed to investigate the relation between NLR and SVT in patients with a documented atrial tachyarrhythmia.

Methods: The study used a retrospective cross-sectional design. Patients who had SVT but were otherwise healthy were included. The exclusion criteria included drug use (except antiarrhythmic agents), morbid obesity, acute or chronic infection, inflammatory diseases, systemic diseases, and cancer. Total and differential leukocyte counts and routine biochemical tests were performed before the ablation procedure.

Results: The study included 150 patients with SVT and 98 healthy controls. The biochemical and hematological parameters were comparable between the groups, except neutrophil and lymphocyte counts. The neutrophil count was significantly higher (4.7±1.5x10^3/µL versus 4.1±1.0x10^3/µL; p<0.001) and lymphocyte count was significantly lower (2.2±0.6x10^3/µL versus 2.5±0.6x10^3/µL; p=0.001) in the SVT group than in the control group. As a result, the SVT group had significantly higher NLR values than the control group (2.2±0.9 versus 1.7±0.5; p<0.001). In addition, NLR values were higher in patients in whom tachycardia was induced during an electrophysiological study (EPS) (2.3±0.9 versus 2.0±0.8; p=0.02). The association between NLR and SVT remained significant after multivariate analysis (odds ratio: 1.5, 95% confidence interval: 1.001-2.263, p=0.049).

Conclusion: Our study indicated that NLR values were significantly higher in patients with documented SVT than in control subjects. Inducibility of SVT during EPS was associated with higher NLR values. (Anatol J Cardiol 2016; 16: 29-33)

Keywords: supraventricular tachycardia, inflammation, neutrophil/lymphocyte ratio

Introduction

The term supraventricular tachycardia (SVT) includes many tachycardias in which the atrial or atrioventricular (AV) nodal tissue is essential for sustaining arrhythmia. SVTs usually manifest themselves as recurrent palpitations, can seriously impair the quality of life, and often prompt visits to primary care doctors and acute medical units (1). An increase in the count of white blood cells (WBCs) and its subtypes is an important cardiovascular risk factor (2, 3). The neutrophil/lymphocyte ratio (NLR) has been evaluated as a new predictor of cardiovascular risk (2). Previous studies have shown that inflammation acts as a facilitator in the induction of SVT and a recent study has shown that increased inflammatory markers may have a role in predicting atrial tachycardia (AT) in selected patients (4). Data about the relationship between NLR and SVT is lacking. Therefore, in this study, we aimed to investigate the relation between NLR and SVT in patients with a documented atrial tachyarrhythmia.

Methods

The study used a retrospective cross-sectional design. All patients who underwent catheter ablation of SVT between June 2012 and July 2014 at our center were included in the study. Age- and sex-matched healthy volunteers (n=98) were recruited for the control group. The investigation complied with the principles outlined in the Declaration of Helsinki. The study was approved by the local ethics committee, and all participants provided written informed consent before participating. Patient information regarding indication, procedural details, and possible complica-
tions of the ablation procedure was provided during an outpatient visit at our institution or at the referring institution prior to the planned procedure. SVT included AV nodal reentry tachycardia (AVNRT), AV reentry tachycardia (AVRT), and AT. An initial diagnostic electrophysiological study (EPS) with standard diagnostic catheters was performed in patients with a prediagnosis of SVT. In patients with detected arrhythmia focus, radiofrequency (RF) ablation therapy was performed. All patients in whom the ablation procedure was performed were given intravenous 5000 IU heparin. We described procedural success as being unable to provoke a tachycardia after ablation, even after an atropine challenge. Patients who had SVT but were otherwise healthy were included. The exclusion criteria included drug use (except antiarrhythmic agents), morbid obesity (body mass index of ≥35 kg/m2), diabetes mellitus, metabolic syndrome, dyslipidemia, renal dysfunction (serum creatinine levels of >1.5 mg/dL, blood urea nitrogen levels of >30 mg/dL), heart failure, valvular diseases, asthma, chronic obstructive pulmonary disease, peripheral and cerebral vascular disease, hematological disorders, acute or chronic infection, cancer, inflammatory diseases, and hepatic dysfunction.

The study population consisted of 248 subjects (64% female; mean age: 40±14 years). The baseline demographic, biochemical, and hematological characteristics of the study population are shown in Table 1. There were no statistically significant differences between the groups with respect to age, sex, body mass index, smoking status, or hemoglobin levels. More than 93% of the patients with SVT had symptoms persisting for more than a year and more than 85% of those had at least 2 episodes per month. Overall, 81% of the patients with SVT were on at least 1 antiarrhythmic agent (beta blockers and calcium channel blockers commonly) and 5 patients were on propafenone. Angiography was performed in 16 SVT patients (mean age: 55±13 years) who had chest pain or were at a higher risk (age or family history) to exclude ischemia. These patients had normal coronary arteries (NCAs). With respect to SVTs, 90 (60%) patients had AVNRT, 18 (12%) patients had concealed AVRT, 37 (24.7%) patients had Wolff-Parkinson-White (WPW) syndrome, and 5 (3.3%) patients had AT. RF ablation treatment was given to 150 patients.

The biochemical and hematological parameters were comparable between the groups, except neutrophil and lymphocyte counts. The neutrophil count was significantly higher (4.7±1.5x10^3/µL versus 4.1±1.0x10^3/µL; p<0.001) and the lymphocyte count was significantly lower (2.2±0.6x10^3/µL versus 2.5±0.6x10^3/µL; p<0.001) in the SVT group than in the control group. As a result, the SVT group had significantly higher NLR compared with the control group (2.2±0.9 versus 1.7±0.5; p<0.001) (Fig. 1). The association between NLR and SVT remained significant after multivariate analysis (odds ratio: 1.5, 95% confidence interval: 1.001-2.263, p=0.049) (Table 2).

Results

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SVT patients were further categorized into 2 groups depending on whether or not tachycardia was induced during EPS (Table 3). Patients in whom tachycardia was induced during EPS showed higher NLR values than those in whom tachycardia was not induced (2.3±0.9 versus 2.0±0.8; p=0.02). However, C-reactive protein (CRP) levels were comparable between the groups.

The receiver-operating characteristic (ROC) curve explored the relationship between NLR and inducibility of SVT during EPS. Using a cut-off point of 1.74, NLR predicted the inducibility of SVT with a sensitivity of 68% and specificity of 61% (area under the ROC curve: 0.651, 95% CI: 0.542-0.760, p=0.005; Fig. 2).

**Discussion**

In the present study, higher values of NLR, a reliable marker of inflammation, were found to be statistically associated with the presence of SVT. In addition, we detected higher NLR values in patients in whom tachycardia was induced during EPS. To the best of our knowledge, this is one of the first studies in the literature to evaluate the relationship between NLR and SVT.

The term SVT is generally used to refer to AVNRT, AVRT, and AT. People of all ages, sex, and ethnicity can develop SVT. The prevalence of the different SVT mechanisms varies. Based on a study of 1754 patients undergoing catheter ablation of 1856 SVTs [excluding atrial fibrillation (AF), atrial flutter, and inappropriate sinus tachycardia] between 1991 and 2003, Porter et al. (5) found AVNRT as the predominant SVT mechanism (56%), followed by AVRT (27%), and AT (17%).

SVTs are the most common disturbance seen in the cardiology department. In general, improvement in the quality of life is a major therapeutic goal in case of SVTs, and treatment strategies are selected according to symptoms and patient preference. Patients troubled by recurrent symptomatic episodes are offered treatment, with options including drug therapy or catheter ablation. Patients can learn Valsalva maneuvers and some find this helpful in controlling their symptoms. There are no large-scale randomized studies comparing these treatments. However, data from prospective non-randomized studies suggest that catheter ablation results in a greater reduction in symptoms and higher quality of life scores compared with medical treatment (6-8).

Leukocyte subtype counts and NLR are also indicators of systemic inflammation (9, 10). Recent studies have demonstrated the predictive and prognostic significance of NLR in a wide range of cardiovascular diseases (11-15).

Inflammation has been shown to have an important role in SVTs in previous studies (16, 17). They reported that increased inflammatory markers, such as CRP, may have a predictive value for the presence of AT in some patients. According to their results, patients with lone atrial arrhythmias had higher CRP values than control subjects. In addition, they proposed that increased CRP levels may be associated with AF burden (18). In another study, histological evaluation of the atria of patients with lone AF revealed infiltration of inflammatory cells (19). Furthermore, some studies have reported diminished inflammation after the treatment of atrial arrhythmias (16, 20). Although a causal relationship could not be identified in these studies, we can deduce that atrial tachyarrhythmias have are associated with the inflammatory status of the body. On the other hand, premature ventricular and atrial contractions usually cause the initiation of SVTs. There has been a close relationship between...
presence of premature ventricular contraction, NLR, and other myocardial inflammatory conditions (14, 21, 22). As premature contractions are the most common triggering factor for SVTs, the inflammatory status causing premature contractions may have a role in the initiation of SVTs. Consistent with these data, we speculated that an increased inflammatory status of the body, as measured by NLR in this study, may have a role in the inducibility of SVT during EPS.

In addition, in a previous study, the levels of circulating pro-inflammatory cytokines (interleukin-6 and tumor necrosis factor-\(\alpha\)) were found to be higher in the serum of young patients with ventricular arrhythmias and without structural heart disease than in healthy participants (23). AVNRT and AVRT constitute the vast majority of SVTs. It has been reported that dual AV nodal physiology can be demonstrated in up to 10% of patients without a history of AVNRT (24-26). Although some patients have dual nodal physiology or an accessory pathway, they do not develop tachycardia. Inflammation may have a role in the initiation of SVT in patients having dual AV nodal physiology or an accessory pathway.

In some patients, AVNRT coexists with AF (27). Recent reports have suggested that it may serve as a trigger for AF and its elimination may help to treat AF (reduce AF burden) (27, 28). In particular, this condition may be related to the inflammatory status.

**Study limitations**

The major limitation of our study was its retrospective design. In addition, the study was single centered and included a relatively small number of patients. Our study provided no data regarding causality between NLR and SVT. Lack of CRP measurements in all patients and postprocedural assessment of inflammatory markers is another limitation. Furthermore, we did not perform coronary angiography in all patients. Despite these limitations, to our knowledge, this is one of the first studies to evaluate the relationship between NLR and SVT.

**Conclusion**

We found significantly higher NLR values in patients with documented SVT compared with control subjects. In addition, we detected higher NLR values in patients in whom tachycardia was induced during EPS. Further large-scale, prospective, and multicenter studies are needed to elucidate and confirm the association between NLR and SVT.

**Conflict of interest:** None declared.

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions:** Concept - M.A., A.Y., M.Y., N.P., A.A., Y.I.; Design - M.A., A.Y., M.Y., N.P., A.A., Y.I.; Supervision - M.A., A.Y., M.Y., N.P., A.A., Y.I.; Resource - M.A., A.Y.; Materials - Y.I., M.A.; Data collection &/or processing - M.A., A.A.; Analysis &/or interpretation - M.Y., N.P.; Literature search - M.A., N.P.; Writing - M.A., A.Y.; Critical review - M.Y., Y.I.

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