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Turkish Title: Kolesleatumlu ya da Kolesteatomsuz Kronik Otitis Media'da Nötrofil-Lenfosit Oranı Ve Platelet Hacminin Prediktif Değeri

Turkish Running Head: Kronik Otitis Mediada NLO ve MPV

Title: Neutrophil-Lymphocyte Ratio And Mean Platelet Volume In Chronic Otitis Media With Or Without Cholesteatoma

Running Head: NLR and MPV Chronic Otitis

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Öz

Amaç: Kemikçik zincir/kemik destrüksiyonu veya kolesteatomu olan ve olmayan kronik otitis media hastalarında Nötrofil-Lenfosit oranlarının ve Platelet Hacminin değerlendirilerek prediktif ve prognostik değerlerinin incelenmesi

Yöntemler: Hastanemizde opere olan kronik otit hastaları retrospektif analiz ile incelenerek üç gruba ayrıldı: Grup 1: sadece timpanik membran perforasyonu olan hastalar, Grup 2: eşlik eden kemikçik zincir deformitesi olan ancak kolesteatomu olmayan hastalar, Grup 3: Kolesteatomu olan hastalar. Kontrol Grup (Grup 0) otolojik bir semptomu ve bulgusu olmayıp hastanemizde septoplasti olan hastalardan oluşmaktaydı. Tüm hastaların ve kontrol grubundaki vakaların ameliyat öncesi kan değerleri incelendi, Platelet Hacmi, Nötrofil ve Lenfosit değerleri kaydedildi, Nötrofil/Lenfosit oranı hesaplandı. Değerler, gruplar arasında karşılaştırıldı.

Bulgular: Çalışmaya 157 kronik otit hastası ve 50 kontrol vakası dahil edildi. Grup 1 ve 2 de 50 hasta, Grup 3 te 57 hasta, kontrol grubunda 50 hasta vardı. Nötrofil, Lenfosit, Nötrofil/Lenfosit oranı ve Platelet Hacmi gruplar arasında fark göstermemekteydi.

Sonuç: Nötrofil/Lenfosit oranı ve Platelet Hacmi birçok hastalığın seyri ve şiddetiyle ilişkili olmasına rağmen, çalışmamızda bu oranlar ile kronik otit arasında bir ilişki bulunamamıştır. Bu değerlerin aynı zamanda kronik otitte kemikçik zincir destrüksiyonu ve kolesteatom varlığını ve prognozu ön görmekte prediktif değeri yoktur.

Anahtar Kelimeler: NLR, MPV, kronik otit

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Abstract

Introduction: To show the Neurtophil-Lymphocyte Ratio (NLR) and Mean Platelet Volume (MPV) values in chronic otitis media with or without ossicular/bony destruction or colesteatoma and to investigate the predictive values of these parameters.

Methods: Patients with chronic otitis media were retrospectively analyzed and were divided into three groups: Group 1 had only tympanic membrane perforation without any ossicular/bony erosions or cholesteatoma; Group 2 had ossicular/bony erosion but no colesteatoma and Group 3 had colesteatoma. The control group (group 0) included subjects who were scheduled for septoplasty in our hospital who did not have any otologic complaints and had normal otologic examination. Blood samples including complete blood count were obtained from all patients in their preoperative visit. Neutrophil, Lymphocyte, Platelet counts, and MPV (Mean Platelet Volume) values were obtained. Neutrophil-lymphocyte ratio (NLR) was calculated by dividing the number of neutrophils by the number of lymphocytes.

Results: The study included 157 patients and 50 controls. There were 50 patients in group 1 and 2 and 57 patients in group 3. The Neutrophil, Lymphocyte, NLR, MPV and RDW values showed no statistical significant difference between groups.

Conclusion: Although NLR is related to the prognosis and severity of several diseases, we found no association between NLR, MPV and chronic ear disease. NLR and MPV also have no value in predicting prognosis and the accompanying ossicular or bony erosion accompanying COM

Keywords: NLR, MPV, chronic otitis

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Introduction

Chronic otitis media (COM) leads to a chronic inflammation of the middle ear mucosa which can be accompanied by ossicular erosions and/or bony destructions. When there is also an accumulation of keratinizing squamous epithelium in these spaces, it is called chronic otitis media with cholesteatoma. The role of oxidative stress and inflammation has been shown to play role in several middle ear infections (1-4).

Lymphopenia, and neutrophilia show the general inflammatory status of the body (5-7). The neutrophil-to-lymphocyte ratio (NLR) can be used as a systemic inflammatory marker, as it reflects both the increase in neutophils and the decrease in lymphocytes (5,8). Mean platelet volume (MPV) can also be used as a marker of inflammation (9,10). It is a measurment of the volume of the circulating trombocytes, and an increased MPV indicates that the inflammation is more intense (9,10).

The NLR and MPV have been previously studied in COM, but the difference in inflammatory values between patients with different presentations of COM has not been previously investigated. The aim of this study is to show the NLR and MPV values in patients who have COM with or without ossicular / bony destruction or cholesteatoma, compare the results in different groups and to investigate the predictive values of these parameters in COM.

Methods

This retrospective study was performed after Local Ethical Committee Approval in accordance with the Declaration of Helsinki . The patients with COM who had surgery in our hospital were included. The operative notes, detailed patient data including history and preoperative blood tests were recorded from retrospective file research. Revision cases and cases without detailed operative note or preoperative blood count were excluded. Patients who had complications secondary to COM were also excluded.

The patients with COM were divided into three groups: Group 1 had only tympanic membrane perforation without any ossicular/bony erosions or cholesteatoma; Group 2 had COM and ossicular/bony erosion but without cholesteatoma and Group 3 included COM patients with

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cholesteatoma. Patients with only tympanic membrane perforation (corresponds to Group 1) who had granulation tissue or tympanosclerosis in the middle ear were excluded.

The control group (group 0) included subjects who were scheduled for septoplasty in our hospital who did not have any otologic complaints and had normal otologic examination. All these preoperative patients scheduled for septoplasty had normal preoperative test values and normal otologic exam under pneumatic otoscopy. Patients who had active ear disease or any infectious, inflammatory or systemic disease that could have an impact on blood counts were excluded. Patients who were noted to have OSAS or had symptoms of OSAS, patients with severe septal deviation totally obstructing the airway, patients with bilateral septal deviation patients with adenoid and tonsillar hypertrophy obstructing the airway were also excluded.

Blood samples including complete blood count were obtained from all patients in their preoperative visit. Neutrophil, Lymphocyte, Platelet counts, MPV (Mean Platelet Volume) and RDW (red cell distribution width) values were obtained. Neutrophil-lymphocyte ratio (NLR) was calculated by dividing the number of neutrophils by the number of lymphocytes.

Statistical Analysis

Statistical analyses were performed using SPSS for Windows (ver. 22.0; SPSS Inc, Chicago, IL). Descriptive statistics including mean, standard deviation, median value and minimum-maximum values of the variables of the study population were analyzed. To test the normality of the dataset; Kolmogorov Smirnov test was used. Kruskal Wallis test was used to compare the non-normally distributed dataset (Neutrophil/Lymphocyte Ratio, MPV and RDW) between control group and four different subgroups of cases. The Mann-Whitney U test was also used for comparing the non-normally distributed dataset (Neutrophil/Lymphocyte Ratio, MPV and RDW) between control group and COM case group (sum of groups 1, 2 and 3). ANOVA test was used to compare the normally distributed dataset (Neutrophil and Lymphocyte) between control group and four different subgroups. Independent samples t-test was also used for comparing the normally distributed dataset (Neutrophil and Lymphocyte) between control group and COM case group (sum of groups 1, 2 and 3). A p value less than 0,05 was considered as significant.

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Results

The study included 157 patients of which 70 were female and 87 were male (44.6% and 55.4% respectively). Control group comprised of 50 subjects of which 20 were female and 30 were male (40% and 60% respectively). There were 50 patients in group 1 and 2 and 57 patients in group 3. The mean age of the overall patients' group (groups 1+2+3) was 35.3 ± 12.3 y. The mean age of the control group (group 0) was 31.9 ± 10.6 y. There was no statistically significant difference between the age and gender distribution of the four different groups ($p > 0.05$). The Neutrophil, Lymphocyte, NLR, MPV and RDW values showed no statistical significant difference between groups ($p > 0.05$). These values for each group were shown in Table 1.

Next, all patients with COM (groups 1,2 and 3) were combined and these 157 patients were compared to the control group (group 0). There was no statistically significant difference between the age and gender distribution of the patients with COM and the control group ($p > 0.05$). The Neutrophil, Lymphocyte, NLR, MPV and RDW values showed no statistical significant difference between these groups ($p > 0.05$).

Discussion

Chronic otitis media is the inflammation of the middle ear mucosa and the temporal bone for more than 3 months, accompanied by the perforation of the tympanic membrane. The chronic inflammation may act differently in different patients. In some patients, there is only a perforation of the tympanic membrane without any ossicular or bony destruction. In some patients however, in addition to the tympanic membrane perforation, there is also an erosion or even destruction of the ossicles. This may or may not be accompanied by growth of keratinized epithelium in the middle ear, cholesteatoma, which is a lytic process and is generally accompanied by bony and ossicular erosions. These different inflammatory processes of the middle ear act differently, and the surgery to be performed to each of these pathologies is different. It is not easy to foresee which patients with COM will develop ossicular/bony erosions or cholesteatoma. It is also hard to predict what to expect during surgery, as the surgical approaches to all these pathologies are different. Thus, predictors that would differentiate these different types of chronic ear disease prior to surgery are necessary. This would help a physician inform his patient about the progress and prognosis of his chronic ear disease, and about what to expect what to expect after surgery. It would also be beneficial for a

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physician to predict the status of the middle ear prior to surgery. We thus aimed to compare the inflammatory values in these different types of COM. Although one would expect that all these processes causing inflammation would effect the NLR and MPV, this study showed that COM with or without ossicular/bony erosion or cholesteatoma had no impact on these values. Even the bone erosion and the osteoclastic activity seen in cholesteatoma had no effect on these values. These findings show that the inflammation in these pathologies remains local and does not lead to a systemic inflammatory reaction. Inflammations of the middle ear cavity, with or without an accompanying ossicular/bony erosion or cholesteatoma do not increase the NLR or MPV values.

NLR and MPV have been recognized as a systemic inflammatory marker and is a predictor of poor clinical outcomes for many diseases (11-16). Many biomarkers are available to detect inflammation inflammatory cytokines; however determining NLR and MPV are simple and readily available ways to detect inflammation without an extra cost. A complete blood cell count is sufficient to determine both values.

NLR has been studied in various diseases including cardiovascular diseases, chronic renal disease and diabetic nephropathy and several types of cancer (11-15,17) and in various otorhinolaryngological disorders including malignities (18-25), obstructive sleep apnea, Bell's palsy, sudden hearing loss, tinnitus, adenoidectomy and tonsillectomy (7,26-30). NLR has also been studied in patients with otitis media to see the effects of the inflammation in the middle ear on the inflammatory blood parameters. The effect of oxidative stress in acute otitis media, otitis media with effusion, chronic otitis media and tympanosclerosis have been shown, suggesting the role of inflammation in various inflammatory otologic disorders [1-4, 30-33]. The studies showed that NLR was higher in patients with OME and could help in determining the viscosity of the fluid accumulated in the middle ear (30-33). Otitis media with effusion can act as a precursor for COM and the inflammation shown in these studies may act by triggering the inflammatory pathway leading to chronic otitis media with or without cholesteatoma. In a study by Tansuker et al, the authors investigated the predictive value of NLR to differentiate active from inactive COM and concluded that NLR did not help to differentiate active COM from inactive COM (16).

The NLR has also been studied in patients with cholesteatoma. Inflammation causes squamous epithelial transformation in the middle ear leading to cholesteatoma, which may cause lytic and

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destructive inflammatory reaction. Kıllickaya et al investigated the systemic inflammatory effect of COM with cholesteatoma and showed that NLR had no predictive value in respect of bone erosions and associated complications in patients with cholesteatoma (34). Other than that, Eryılmaz et al studied the NLR in pediatric patients compared the value in chronic otitis media with and without cholesteatoma (10). NLR in the two groups showed no statistically significant difference. However, MPV was lower in patients with cholesteatoma compared with the controls which they suggested could act as a predictor for cholesteatoma.

Mean platelet volume (MPV) has also been shown to be a marker of inflammation and has been studied in various otolaryngological diseases (35, 36) . MPV has been studied in chronic ear disease also. It was reported that MPV was lower in pediatric patients with cholesteatoma and that MPV has a role to predict cholesteatoma in children [10]. This decrease in MPV however, has not been shown in our study.

As complications of chronic otitis media may lead to leukocytosis and systemic toxicity, patients who had complications secondary to chronic otitis media were excluded in this study. This is important as these inflammatory results could effect our results. Other than that, as hypoxia can cause inflammatory and oxidative response (7, 36, 37), patients who were prone to hypoxic conditions, patients who had OSAS or had symptoms of OSAS, patients with severe septal deviation totally obstructing the airway, patients with bilateral septal deviations and patients with adenoid and tonsillar hypertrophy were excluded to eliminate the impact of hypoxia on blood test results. One drawback of this study is the retrospective design and the lack of follow-up data after surgery.

To the best of our knowledge, this is the first study to investigate NLR and MPV in patients with chronic otitis media with or without ossicular/bony destruction or cholesteatoma. Our study shows that a chronic inflammation in the middle ear cavity with or without ossicular/bony erosion or cholesteatoma remains local and does not trigger a systemic inflammatory reaction.

Conclusion

This study is the first to assess the MPV and NLR values in patients with chronic otitis media and to investigate whether these values have any value in predicting the ossicular and bony erosions and presence of cholesteatoma in advance; however, this effect has not been shown. Although NLR is

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related to the prognosis and severity of several diseases, we found no association between NLR, MPV and chronic ear disease. NLR and MPV also have no value in predicting prognosis and the ossicular or bony erosion accompanying COM.

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Table Legends

Table 1. NLR* values in Patients with Chronic Otitis Media (Groups 1, 2 and 3) and Control Group (Group 0)

		Group 0	Group I	Group II	Group III	p
Age	Mean. \pm s.d	31,9 \pm 10,6	32,6 \pm 12,3	37,8 \pm 14,4	35,8 \pm 12,0	0,067 ^K
	Median	28,0	31,0	37,0	34,0	
Gender	Female n-%	20 40,0%	26 52,0%	26 52,0%	18 31,6%	0,090 ^{X²}
	Male n-%	30 60,0%	24 48,0%	24 48,0%	39 68,4%	
Neutrophil	Mean. \pm s.d	4,0 \pm 1,1	4,2 \pm 1,5	4,2 \pm 1,1	4,3 \pm 1,2	0,639 ^A
	Median	3,8	4,2	4,1	4,3	
Lymphocyte	Mean. \pm s.d	2,3 \pm 0,5	2,3 \pm 0,6	2,4 \pm 0,5	2,4 \pm 0,6	0,803 ^A
	Median	2,4	2,2	2,3	2,3	
NLR ¹	Mean. \pm s.d	1,8 \pm 0,7	1,9 \pm 0,8	1,9 \pm 0,7	1,9 \pm 0,5	0,878 ^K
	Median	1,7	1,7	1,7	1,8	
MPV ²	Mean. \pm s.d	88,3 \pm 4,2	87,3 \pm 4,7	87,5 \pm 3,9	87,1 \pm 3,5	0,603 ^K
	Median	87,4	86,9	87,3	86,8	
RDW ³	Mean. \pm s.d	13,1 \pm 0,7	13,4 \pm 1,1	13,3 \pm 0,7	13,3 \pm 0,6	0,559 ^K
	Median	13,1	13,2	13,2	13,1	
^A ANOVA / ^K Kruskal-Wallis / ^{X²} Ki-kare test ¹ Neutrophil-LymphocyteRatio ² MeanPlasma Volume ³ Red-Cell Distribution Width						

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