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The Impact of Smoking on Platelet Indices Among Acute Myocardial Infarction Patients

Akut Miyokard Enfarktüsü Hastaları Arasında Sigara İçmenin Trombosit İndeksleri Üzerine Etkisi

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ÖZ

Amaç: Bu çalışmanın amacı, akut miyokard infarktüsü (AMI) hastaları arasında sigara içmenin trombosit indeksleri üzerindeki etkisini incelemek ve sigara içenler ile içmeyenler arasındaki karşılaştırmalı boyutları vurgulamaktır.
Araçlar ve Yöntem: Kasım 2023- Mart 2024 tarihleri arasında koroner anjiyografi planlanan AMI hastası bu çalışmaya dahil edilmiştir. Katılımcılar sigara içme durumlarına göre iki gruba ayrılmıştır. Trombosit indeksi, trombosit sayısı, ortalama trombosit hacmi (MPV), trombosit dağılım genişliği (PDW) ve trombokrit (PCT) değerleri karşılaştırılmıştır. Daha sonra sigara içen hastalar sigara içme sürelerine göre beş gruba ayrılmıştır.
Bulgular: 224 hastanın dahil edildiği çalışmada sigara içmeyenler arasında, NSTEMI grubunda MPV değerleri, STEMI grubuna göre anlamlı derecede yüksek bulunmuştur (p=0.013). Sigara içme süresi ile trombosit indeksleri arasındaki ilişki incelendiğinde, artan sigara içme süresi ile trombosit indeksi anlamlı olarak azalmıştır (p<0.001), trombosit sayısı artmıştır (p<0.001), PDW azalmıştır (p=0.02), PCT artmıştır (p=0.001) ve MPV azalmıştır (p=0.002).
Sonuç: Sigara içmenin AMI hastalarında trombosit indeksleri üzerinde önemli etkilere sahip olduğunu göstermektedir. Özellikle, sigara içme süresinin artması ile trombosit fonksiyonlarındaki değişiklikler, kardiyovasküler hastalıkların ilerlemesi ve trombojenik riskin artışı açısından önem taşımaktadır. Bu sonuçlar, sigara içmenin trombosit üzerindeki etkilerinin daha derinlemesine anlaşılması ve kardiyovasküler risk yönetiminde dikkate alınması gerektiğini vurgulamaktadır.

Anahtar Kelimeler: akut koroner sendrom; kardiyovasküler risk; trombosit fonksiyonu; tütün

ABSTRACT

Purpose: The purpose of this study is to investigate the impact of smoking on platelet indices among patients with acute myocardial infarction (AMI), and to highlight comparative dimensions between smokers and non-smokers.
Materials and Methods: A patient diagnosed with AMI and scheduled for coronary angiography between November 2023 and March 2024 was included in this study. Participants were divided into two groups based on their smoking status. Platelet indices, including platelet count, mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT), were compared. Subsequently, the smoking patients were categorized into five groups based on their smoking duration.
Results: In the study, which included 224 patients, MPV values in the NSTEMI group among non-smokers were found to be significantly higher compared to the STEMI group (p=0.013). When the relationship between smoking duration and platelet indices was analyzed, it was observed that with increasing smoking duration, platelet indices significantly decreased (p<0.001), platelet count increased (p<0.001), PDW decreased (p=0.02), PCT increased (p=0.001), and MPV decreased (p=0.002).
Conclusion: The findings indicate that smoking has significant effects on platelet indices in AMI patients. Particularly, changes in platelet functions associated with increased duration of smoking are of importance for the progression of cardiovascular diseases and the increase in thrombogenic risk. These results highlights the need for a deeper understanding of the effects of smoking on platelet function and the consideration of these effects in the management of cardiovascular risk.

Keywords: acute coronary syndrome; cardiovascular risk; platelet function; tobacco

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INTRODUCTION

Cardiovascular diseases, notably myocardial infarction (MI), persist as a prominent contributor to global health challenges, reflected in significant rates of hospitalizations and mortalities each year.[1] The development of MI is a multifaceted process, influenced by an interplay of genetic, environmental, and lifestyle elements. Among these, smoking is recognized as a modifiable risk factor with a notable association with cardiovascular pathology.[2]

The involvement of platelets in cardiovascular pathologies, particularly in the thrombotic events characteristic of myocardial infarction, has been attracting increasing attention. Beyond their primary role in hemostasis, platelets are implicated in inflammatory processes and the formation of atherosclerotic plaques.[3] Various platelet indices, including platelet count, mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT), may provide insights into platelet behavior and functionality. These indices are considered to potentially reflect changes in platelet production, activation, and aggregation, which are integral to the thrombotic dynamics in MI.[4]

The influence of smoking on platelet function and coagulation pathways has been documented, with nicotine and other components in cigarette smoke potentially affecting platelet activation and aggregation, thereby possibly increasing thrombotic risk.[5] However, the specific impact of smoking on platelet indices in the context of myocardial infarction warrants further investigation.[6] Such an inquiry could be instrumental in elucidating the mechanisms through which smoking exacerbates cardiovascular risk and in aiding the classification of patients according to their thrombotic risk profiles.

Accordingly, this study aims to perform a comprehensive analysis of platelet indices in myocardial infarction patients, with a particular emphasis on the comparative aspects between smokers and non-smokers.

MATERIALS and METHODS

This study included patients admitted to the intensive care unit with an initial diagnosis of AMI, scheduled for coronary angiography from November 2023 to March 2024. Using G*Power (version 3.1.9.7) with an effect size of 0.350 for MPV levels, a power of 0.80, and an alpha of 0.05, a t-test for two independent groups was conducted. The required sample size was 102 per group, totaling 204 patients. Participants were divided into two groups based on their smoking status. Approval for this study was obtained from Necmettin Erbakan University Drug and Non-Medical Device Research Ethics Committee (dated 03.11.2023 and numbered 2023/4612).

Exclusion criteria included individuals with malignancies, autoimmune diseases, hyperthyroidism, chronic renal disease, rheumatologic conditions, a history of thrombocytopathy, those who received revascularization through fibrinolytic therapy, a history of pulmonary embolism, or drug use affecting platelet functions. Blood samples were analyzed for a complete blood count (including hemoglobin, platelet count, MPV, PDW, and PCT) using the COULTER DXH 800 hematology analyzer. The Platelet Index was calculated using the following formula: Platelet Index= (MPV x PDW) / (Platelet Count x PCT).

The diagnosis of ST-segment elevation myocardial infarction (STEMI) was made electrocardiographically, typically requiring ST-segment elevation at the J point in two contiguous leads, with elevations of ≥2.5 mm in men under 40, ≥2 mm in men over 40, and ≥1.5 mm in women in leads V2-V3, and/or ≥1 mm in other leads. Similarly, the presence of ST-segment depression in leads V1-V3, particularly with terminal T-wave positivity (suggestive of myocardial ischemia equivalent to ST-elevation), was diagnosed with accompanying ST elevation of ≥0.5 mm in leads V7-V9.

The diagnosis of non-ST-segment elevation myocardial infarction (NSTEMI) was based on the absence of ST-segment elevation in the ECG, with at least one troponin value above the 99th percentile upper reference limit.

Prospective participants were informed about the study details and volunteered to participate upon providing informed consent.

Statistical Analysis

The statistical analyses of the study were conducted using the Statistical Package for Social Sciences for Windows (IBM SPSS version 29.0, Armonk, NY, USA). The assumption of normality for continuous quantitative variables was tested with the Kolmogorov-Smirnov test. Descriptive statistics for the variables were presented as Median (25th-75th percentiles) and frequencies n (%). In the study, the comparisons between two groups for continuous quantitative variables, where the assumption of normality was not met, were conducted using the Mann-Whitney U test. The comparison of numerical variables among the five study groups was performed using either one-way ANOVA or the Kruskal–Wallis test, depending on the suitability for parametric analysis.

RESULTS

A total of 224 patients participated in the study. Of these, 158 (70.5%) were male and 66 (29.5%) were female. Descriptive statistics and group comparisons for the NSTEMI and STEMI groups under the categories of 'Smokers' and 'Non-Smokers', as well as the results of the group comparisons between the 'Smokers' and 'Non-Smokers' groups, are presented in Supplementary Table 1. Examination of these results revealed that the creatinine levels in patients in the NSTEMI group who do not smoke were found to be higher than those in STEMI patients, and this difference was statistically significant ($p=0.022$). In the non-smoking group, the difference in MPV values between patients in the NSTEMI and STEMI groups was statistically significant ($p=0.013$). The average MPV values in patients in the NSTEMI group were significantly higher than those in the STEMI group. The differences in other variables between the NSTEMI and STEMI groups in the non-smoking patient group were not statistically significant ($p>0.05$).

When examining the comparisons between NSTEMI and STEMI groups among smokers, a statistically significant difference was only found in glucose values between the NSTEMI and STEMI groups ($p=0.037$). The glucose values in patients in the NSTEMI group were significantly higher than those in the STEMI group.

Upon examining the group comparisons between smokers and non-smokers, a significant effect of smoking status was only detected for urea values. The average urea values in smokers were significantly higher than those in non-smokers.

The descriptive statistics and group comparisons for the 'Smoking' and 'Non-Smoking' groups under the NSTEMI and STEMI categories, as well as the comparison results between NSTEMI and STEMI groups, are presented in Supplementary Table 2. Upon examining Supplementary Table 2, it was found that in the NSTEMI group, the creatinine values of patients who do not smoke were higher than those of patients who smoke. This difference in creatinine values based on smoking status is statistically significant ($p=0.031$). For other variables, the difference between non-smoking and smoking patients is not statistically significant ($p>0.05$). When examining the values of patients in the STEMI group, it was determined that the effect of smoking status is not significant across all variables ($p>0.05$).

Comparing the results between the NSTEMI and STEMI groups, it was identified that the glucose values of patients in the STEMI group were significantly higher than those in the NSTEMI group ($p=0.002$). The MPV values of patients in the NSTEMI group were found to be significantly higher than those in the STEMI group ($p=0.048$). For other variables presented in Supplementary Table 2, the difference between patients in the NSTEMI and STEMI groups is not statistically significant ($p>0.05$).

In the analysis of platelet indices relative to cigarette smoking duration, a significant gradient effect was observed across the defined groups, ranging from 0-50 packs/year. The study stratified participants into five groups based on their smoking history, revealing notable differences in platelet indices, platelet count, PDW, PCT, and MPV. These findings are presented in Supplementary Table 3 for reference.

The platelet index demonstrated a marked decrease with increased smoking duration, moving from 5.47 in Group 1 (0-10 packs/year) to 2.11 in Group 5 (40-50 packs/year), indicating a significant correlation ($p<0.001$). Similarly, the platelet count increased from

171.5×10³/µl in Group 1 to 275×10³/µl in Group 5, suggesting a positive association between smoking duration and platelet count, with statistical significance ($p<0.001$). The PDW showed a slight but statistically significant decrease across the groups, from 16.9 in Group 1 to 16.3 in Group 5 ($p=0.02$), indicating subtle changes in platelet size variability with increased exposure to cigarette smoke.

Furthermore, PCT values, indicative of the volume of platelets in the blood, exhibited a progressive increase from 0.15 in Group 1 to 0.21 in Group 5 ($p=0.001$), while MPV, a measure of the average size of platelets, decreased from 8.7 in Group 1 to 7.6 in Group 5 ($p=0.002$).

DISCUSSION

The findings from our study reveal a confounding relationship between thrombocyte dynamics and smoking habits. Notably, our investigation on the specific influence of smoking on platelet indices within the context of myocardial infarction, both as a whole and within subgroup comparisons, demonstrates a notable absence of significant alterations. This outcome at first glance stands against previous researches that have variably posited smoking as a potent modifier of platelet function and thrombogenicity.

Costa et al. investigated platelet indices in patients with acute coronary syndrome (ACS) and found significantly higher MPV and PDW values in the ACS group compared to controls. They observed a positive correlation between MPV and CK-MB levels, suggesting that increased MPV could be indicative of higher thrombotic potential and increased platelet reactivity in ACS patients .[7] Similarly, Al-Obeidi et al. demonstrated that patients with myocardial infarction and unstable angina had significantly elevated MPV, PDW, platelet count, and PCT compared to healthy controls.[8] Their study concluded that larger platelets are hemostatically more active and pose a greater risk for coronary thrombosis and acute coronary events.

Our study aligns with these findings by showing that smoking duration significantly affects platelet indices. Specifically, we found that prolonged smoking was associated with a decrease in platelet index and MPV, alongside an increase in platelet count and PCT. These changes reflect enhanced thrombopoiesis and altered platelet functionality, which may contribute to greater cardiovascular risk observed in chronic smokers.

Studies conducted by Turk et al., Pujani et al., and Hlapčić et al. have provided foundational insights into the complex interplay between platelet behavior and cardiovascular disease processes, highlighting the potential modulatory role of smoking.[9-11] These studies collectively underscore the heterogeneity in platelet reactivity and function in response to tobacco exposure, hinting at an intricate balance between prothrombotic and antithrombotic forces within the vascular milieu of smokers.

Moreover, the differential impact of smoking on platelet indices observed in various cohorts, including those with stable chronic obstructive pulmonary disease (COPD) as explored by Hlapčić et al., suggests that the cardiovascular implications of smoking are multifactorial and may be contingent upon a constellation of factors beyond mere tobacco exposure.[10] These factors are likely to encompass genetic predispositions, environmental influences, and other lifestyle variables, which altogether modulate the risk profile for thrombosis and atherogenesis among smokers.

Our study's findings, particularly the lack of significant changes in platelet indices with smoking status, might also reflect the complexity of platelet physiology and its regulation. Platelets exhibit a remarkable plasticity in response to physiological and pathological stimuli. This adaptability might explain the observed insensitivity to smoking status in our MI patient cohort, suggesting that the impact of smoking on platelet dynamics could be either counterbalanced by other factors or manifest in pathways not directly captured by conventional platelet indices such as MPV, PDW, and PCT.

Additionally, the nuanced relationship between smoking and platelet function underscores the necessity for further exploration of the mechanisms through which tobacco use influences thrombocyte behavior, particularly in the context of acute coronary syndromes.[12] The role of novel biomarkers, including platelet activation markers and

inflammatory cytokines, deserves further investigation as potential mediators of the smoking-platelet interaction.[13] Such an inquiry could unveil previously unrecognized pathways through which smoking exacerbates cardiovascular risk.[14]

The analysis of platelet indices in relation to smoking duration provides compelling evidence on the influence of chronic smoking on platelet physiology. The observed trend of decreasing platelet index with increasing smoking duration from 0-10 packs/year to 40-50 packs/year is indicative of significant alterations in platelet functionality associated with prolonged tobacco exposure. This decrease in platelet index could reflect an elevated thrombotic potential, which is further supported by the corresponding increase in platelet count across the same smoking- duration groups. The escalation in platelet count with prolonged smoking suggests an enhanced thrombopoiesis and potentially exacerbated risk of thrombotic events among chronic smokers. Such findings underscore the critical role of smoking duration in modulating the platelet behaviors.

Moreover, the alterations in PDW and PCT with increased smoking duration highlight the impact of smoking on platelet size variability and volume, respectively. The slight but statistically significant decrease in PDW suggests a reduction in the heterogeneity of platelet size, which could imply a more uniform population of platelets with enhanced prothrombotic properties. Conversely, the progressive increase in PCT across smoking durations reflects an elevated total platelet mass in the bloodstream, which, in conjunction with a decrease in MPV, suggests a shift towards smaller, yet more numerous platelets. These changes in platelet morphology and distribution may further contribute to the thrombotic risk associated with smoking.[14-16] Collectively, these findings emphasize the importance of assessing smoking history in the clinical evaluation of patients, as chronic smoking appears to induce significant changes in platelet indices.

One notable limitation of this study is its cross-sectional design which inhibit the ability to infer causality between smoking duration and alterations in platelet indices. Furthermore, the study may not account for confounding factors such as diet, physical activity, or the use of medications that can influence platelet function and cardiovascular health. Another limitation includes the potential variability in the accuracy of self-reported smoking history, which could introduce bias in categorizing smoking duration. Additionally, the study's findings are based on a specific patient population with acute myocardial infarction, which may limit the generalizability of the results to other populations or to individuals with different stages of cardiovascular disease.

In the light of these considerations, our study may contribute to the evolving pile of information on the impact of smoking on platelet function and cardiovascular disease risk. While we did not observe significant modulation of platelet indices by smoking status in our MI patient population, this finding may prompt the researchers reevaluate the current understanding of smoking-related thrombogenic mechanisms. It also highlights the need for continued research to delineate the complex biological underpinnings that govern the relationship between smoking, platelet function, and cardiovascular disease outcomes. Such efforts are essential for advancing risk stratification and personalized therapeutic strategies in the management of myocardial infarction, ultimately enhancing patient care and prognostication in this high-risk population.

Conclusion

Our study may make a significant contribution to the ongoing discussion about the effects of smoking on platelet function and its implications for cardiovascular disease, particularly in patients with acute myocardial infarction. Although we did not identify a significant modulation of platelet indices by smoking status, our findings underscore the complex interaction between smoking duration and platelet physiology, as evidenced by a decrease in platelet index and an increase in platelet count correlating with prolonged smoking duration. These observations highlight the potential for chronic smoking to alter thrombocyte behavior, suggesting a cumulative impact on thrombogenic risk.

Conflict of Interest

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

Ethics Committee Permission

Approval for this study was obtained from Necmettin Erbakan University Drug and Non-Medical Device Research Ethics Committee (dated 03.11.2023 and numbered 2023/4612).

Authors' Contributions

Concept/Design: MSA, AY, FK, ZK. Data Collection and/or Processing: MSA, MFK, FK, Bİ. Data analysis and interpretation: MSA, MÇ, Bİ, ZK. Literature Search: MÇ, ZK, MFK, AY. Drafting manuscript: MSA, AY, FK, MFK. Critical revision of manuscript: MSA, Bİ, MÇ.

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