



Original Article

The role of platelet parameters in thrombosed hemorrhoids



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ABSTRACT

Objectives: The most common disease of anus is hemorrhoids. The definition of external hemorrhoids suggests the acute phase, often characterized by thrombosis or edema. External thrombosed hemorrhoid is a specific complication. In this study, we aimed to investigate the effects of different platelet parameters in the presence of internal or external thrombosed hemorrhoids.

Methods: Patients examined were divided into two groups: Group 1: Thrombosed hemorrhoids group (THG), Group 2: Hemorrhoidectomy group (HG). Demographic and clinical data were identified. In terms of laboratory findings, preoperative hemoglobin, hematocrit and all platelet parameters were recorded.

Main results: Fifty-two patients in THG, and 75 patients in HG were included in the study. In female sex and young age group, the risk of developing thrombosed hemorrhoids was statistically significant ($p = 0.029$, $p = 0.039$, respectively). When the platelet parameters were evaluated; while PDW was higher in THG ($p = 0.008$), any significant difference could not be found in all other values ($p > 0.05$). Thrombosed hemorrhoids were mostly (59.25%) found to be located in the left laterodorsal part of anus.

Conclusion: Internal hemorrhoids are frequently seen in the ages of 45–65 with similar rates in both sexes, while external thrombosed hemorrhoids occur at a younger age (<45) and more often in women. Comparing in terms of platelet indexes, PDW value was found to be significantly higher in THG. In young people, thrombosed hemorrhoids may develop more frequently, as the connective tissue that forms the anal pads is not loose enough to form an internal hemorrhoid, as more seen in older patients.

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O papel dos parâmetros plaquetários nas hemorróidas trombosadas

R E S U M O

Palavras-chave:

Hemorróidas
Cirurgia
Plaquetas
Canal anal

Objetivos: A doença anal mais comum são as hemorróidas. A definição de hemorróidas externas sugere a fase aguda, muitas vezes caracterizada por trombose ou edema. A hemorróida externa trombosada é uma complicação específica. Neste estudo, objetivamos investigar os efeitos de diferentes parâmetros plaquetários na presença de hemorróidas trombosadas internas ou externas.

Métodos: Os pacientes examinados foram divididos em dois grupos: Grupo 1, Grupo de Hemorróidas Trombosadas (GHT); Grupo 2, Grupo de hemorroidectomia (GH). Os dados demográficos e clínicos foram identificados. Em termos de achados laboratoriais, a hemoglobina pré-operatória, o hematócrito e todos os parâmetros plaquetários foram registrados.

Resultados principais: Cinquenta e dois pacientes em GHT e 75 pacientes em GH foram incluídos no estudo. No sexo feminino e na faixa etária jovem, o risco de desenvolver hemorróidas trombosadas foi estatisticamente significativo ($p=0,029$, $p=0,039$, respectivamente). Os parâmetros plaquetários avaliados mostraram que, enquanto a Amplitude de Distribuição de Plaquetas (PDW, do inglês *platelet distribution width*) foi maior no GHT ($p=0,008$), nenhuma diferença significativa foi encontrada para todos os outros valores ($p>0,05$). A maioria das hemorróidas trombosadas (59,25%) localizava-se na região lateral-dorsal esquerda do ânus. **Conclusão:** As hemorróidas internas são frequentemente vistas nas idades de 45 a 65 anos com taxas semelhantes em ambos os sexos, enquanto as hemorróidas externas trombosadas ocorrem em uma idade mais jovem (<45) e mais frequentemente em mulheres. Comparando em termos de índices de plaquetas, foi observado que o valor de PDW foi significativamente maior no GHT. Em pessoas jovens, as hemorróidas trombosadas podem se desenvolver com mais frequência, pois o tecido conjuntivo que forma as almofadas anais não é flácido o suficiente para formar uma hemorróida interna, como ocorre com mais frequência em pacientes mais velhos.

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Introduction

The most common disease among benign anorectal diseases is hemorrhoids. There are quite different numbers of different sources about the prevalence and incidence of hemorrhoids. It was emphasized that the prevalence of hemorrhoids varies between 4–55% according to different screening studies. It has been reported that the prevalence of hemorrhoids varies between 4–55% according to different screening studies.¹ It has been reported that the prevalence of hemorrhoids varies between 4–55% according to different screening studies.¹ The difference between these rates is that most individuals with this disease do not take it seriously, considering that the symptoms of this disease do not affect their normal vital activities much.

Many studies indicate that internal hemorrhoids are frequently seen at 45–65 years of age and in similar rates in women and men.^{1–4} The vast majority of hemorrhoids regress only by changing diet and bowel habits. Again, in a large group of patients, adequate regression occurs with medical treatment. Surgical intervention is required in approximately 10% of hemorrhoid patients.⁵

Hemorrhoids can be classified as internal and external hemorrhoids according to their relationship with the dentate

line.⁶ The worldwide accepted classification of hemorrhoids is a classification developed by Goligher.⁷ This scale is divided into grades from I to IV, depending on the degree of prolapse of internal hemorrhoids. This classification guides the patient's treatment planning.

The definition of external hemorrhoids suggests the acute phase, often characterized by thrombosis or acute edema. Thrombosed external hemorrhoid is a specific complication of hemorrhoids. Clinically manifestation is as acute, severe anal pain and a blue-purple perianal swelling. In general, complaints may regress if thrombectomy is performed under local anesthesia in the first three days after the formation of thrombosis. However, thrombectomy may be difficult if the thrombosis has occurred for more than 3 days, and therefore conservative treatment is recommended.

Platelets, the most important cells of the coagulation process, play a key role in thrombosis and clot formation. In addition, platelets exhibit complex interactions with circulating cells and vascular wall during a wide variety of inflammatory processes that occur in many types of diseases.⁸ They are considered to have an important role in coagulation, inflammation and immune response.

While most patients with hemorrhoids experience symptoms such as swelling and bleeding, in some cases of hemorrhoids, thrombosis occurs. In the literature, we could

not find a study that examined the relationship between hemorrhoids and platelets, or investigated their role in the formation of thrombosed hemorrhoids. In this study, we aimed to investigate the effects of different platelet parameters in the presence of internal or external hemorrhoids and thrombosis.

Methods

A retrospective, cross-sectional study was planned. Ethics committee approval was obtained for the study. Computer data records and patient files between January 1, 2018 and December 31, 2019 were examined. Two groups were created for the study: Group 1, Thrombosed Hemorrhoids Group (THG); Group 2, Hemorrhoidectomy Group (HG).

In the first group (THG), patients diagnosed with thrombosed hemorrhoids during rectoscopy in our endoscopy-colonoscopy unit were listed. In the second group (HG), patients who underwent hemorrhoidectomy operation in the general surgery clinic within this date range were listed. As a result of these lists, it was determined that there were 147 patients in the first group (TGH) and 96 patients in the second group (HG). Data of these patients regarding age, gender, complaints, duration of complaints; and data of the anatomic localizations operated in the anal region during surgery or thrombectomy were collected. In terms of laboratory findings, preoperative hemoglobin (Hb), hematocrit (HCT), platelet count (PLT), mean platelet volume (MPV), plateletcrit (PCT), platelet distribution width (PDW) and platelet mass index (PMI) values were recorded. These data were evaluated and 116 patients without sufficient data were excluded from the study. There was a lack of data in terms of blood tests, especially since the patients in the THG group were intervened in the outpatient clinic conditions and emergency procedures were performed. A total of 127 patients, including 52 in THG and 75 in HG, were included in the study.

Analysis of blood

Complete blood count parameters were analyzed using a Roche brand automated blood cell counter. Platelet mass index was calculated with the formula of “platelet counts \times MPV/ 10^3 ” (fL/nL), (fL = femtoliters, nL = nanoliters).

Statistical analysis

Analysis of all data obtained during the study and recorded on the study form was done using the IBM SPSS 20.0 (Chicago, IL, USA) statistical program. Whether the distribution of discrete and continuous numerical variables is suitable for normal distribution was investigated with the Kolmogorov Smirnov test. Descriptive statistics were shown as median (inter quartile range 25–75) for discrete and continuous numerical variables, and categorical variables as number of cases and (%). Categorical variables were evaluated by Chi-square and continuous variables were evaluated by Mann Whitney U test Results for $p < 0.05$ were considered statistically significant.

Table 1 – Demographic and laboratory findings of patients.

Gender, n (%)	
Female	40 (31.5%)
Male	87 (59.1%)
Age, years, (median IQR 25–75)	40 (32–49)
Presenting symptoms, n (%)	
Pain	51 (40.2%)
Lump	26 (20.5%)
Bleeding	17 (13.4%)
Pain and bleeding	17 (13.4%)
Lump and pain	11 (8.7%)
Pain and pruritis	5 (3.9%)
Previous surgery, n (%)	4 (3.1%)
Procedure or operation type, n (%)	
No procedure	22 (17.3%)
Thrombectomy	32 (23.6%)
Hemorrhoidectomy	41 (32.3%)
Hemorrhoidectomy and LIS	34 (26.8%)
Laboratory findings, median (IQR 25–75)	
Hemoglobin (mg/dL)	14.4 (13.1–16)
Hematocrit (%)	43.7 (39–47.4)
Platelet ($10^3/\mu\text{L}$)	251 (208–290)
MPV (fL)	9.4 (8.5–10)
PCT (%)	2.35 (2–2.7)
PDW (fL)	16.1 (15.8–16.6)
PMI (fL/nL)	2332.8 (1955.2–2714.4)

Results

127 patients were included in the study. 52 patients were in THG and 75 patients in HG. 31.5% of the patients were female and the median age was 40 (IQR 25–75, 32–49). The most common complaint in patients was pain in the anal verge. The average duration of complaints was 2¹⁻⁷ days in the majority of THG patients. Although there is no clear information about the average duration of complaints of HG patients in general, most patients stated that they have different complaints from time to time for many months and years.

Thrombectomy was performed in 32 of 52 patients in THG. Medical treatment was planned for 20 patients due to late admission or refusal of thrombectomy. The majority of (41 cases) HG patients underwent hemorrhoidectomy. In addition, lateral internal sphincterotomy (LIS) was applied to 34 patients in HG, due to accompanying chronic anal fissure or 3 hemorrhoid packs remove during the operation. The demographic data and laboratory values of the patients are shown in [Table 1](#).

In female sex and young age group, the risk of developing thrombosed hemorrhoids was higher and these differences were statistically significant ($p = 0.029$, $p = 0.039$, respectively). When the platelet indexes of the groups are evaluated; while platelet distribution width (PDW) was higher in THG ($p = 0.008$), we could not find any statistically significant difference in all other values ($p > 0.05$ for all values) ([Table 2](#)).

The anatomical location of the hemorrhoid packs in HG, which was resected due to internal hemorrhoids, is shown in [Fig. 1](#). According to the anatomical localization in the knee elbow position, surgical intervention was performed on hemorrhoids at most 1, 5 and 9, according to the clock dials. Among these, the most resection was at 9 o'clock (40.6%). The anatom-

Table 2 – Comparison of data between THG and HG patients.

	THG	HG	p
Gender, n (%)			
Female	22 (42.4%)	18 (24%)	
Male	30 (57.7%)	57 (76%)	0.029
Age, years, median (IQR 25–75)	37 (28–47.7)	42 (35–52)	0.039
Laboratory findings, median (IQR 25–75)	14.5 (13.–15.8)	14.7 (13.1–16.1)	0.789
Hemoglobin	43.4 (38.4–47.6)	43.7 (39–47.4)	0.730
Hematocrit (%)			
Platelet (10 ³ /μL)	250.5 (208.7–289)	251 (206–290)	0.879
MPV (fL)	9.2 (8.2–9.6)	9.4 (8.8–10.3)	0.177
PCT (%)	2.28 (1.9–2.7)	2.43 (2–2.8)	0.178
PDW (fL)	16.3 (15.9–16.8)	16.1 (15.6–16.4)	0.008
PMI (fL/nL)	2293 (1947–2716.4)	2363 (1968–2714)	0.689

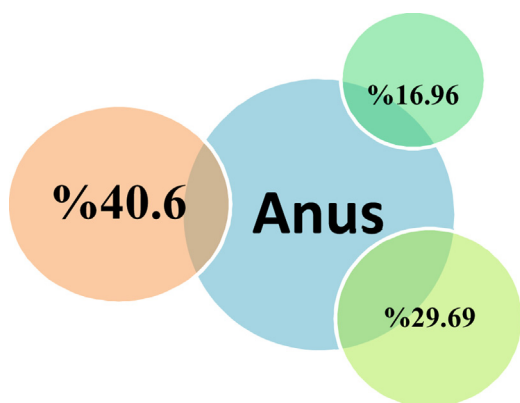


Fig. 1 – Anatomical location of hemorrhoid packs in HG, which was resected due to internal hemorrhoids (according to knee elbow position 1, 5 and 9).

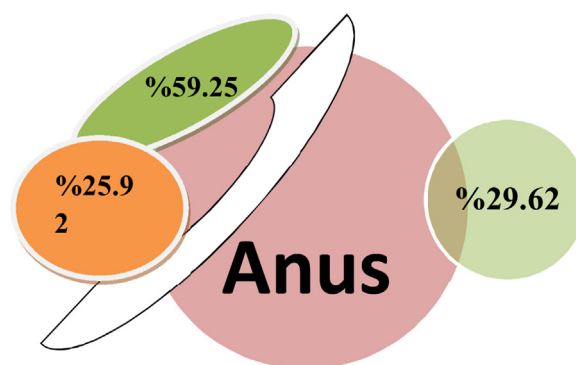


Fig. 2 – Anatomical location of thrombosed packages in THG (according to knee elbow position).

ical locations of the thrombosed packages in THG are shown in Fig. 2. It was observed that 29.62% of the thrombosed hemorrhoids intervened was at 3 o'clock and 25.92% at 9 o'clock. 77.77% of them were found to be located in the lateral and dorsal parts.

Discussion

According to two studies conducted before 2000 in the US, the prevalence of hemorrhoids was reported to be between 4–8%.^{3,9} Epidemiological data from the UK claim that the prevalence of hemorrhoids is between 13–36% in the general population.¹⁰ In a study based on screening of colonoscopy data, about 38% of the population had hemorrhoids, but only 44% of patients with this hemorrhoid reported symptoms.⁴ Tournu et al.¹¹ conducted a prospective study in France between 2014 and 2015, conducted by general practitioners and involving 1061 patients. According to this study, 15.6% of patients stated that they had anorectal symptoms. Although the most common detected disease is hemorrhoids in 42 (3.96%) patients, it should be taken into consideration that less than 10% of the patients in this study underwent physical examination. In Germany, in a study of 807 patients referred to proctologists with anal symptoms or findings, 401 (49.69%) patients had hemorrhoids.¹² The reason why

patients do not come to the examination or apply late, although they have anal complaints, are sometimes social and cultural reasons.¹³ The conclusion from all these studies shows that different figures are pronounced all over the world about the prevalence of hemorrhoids. The reason we overestimate the prevalence issue is to emphasize that there is a lot to be clarified about hemorrhoid disease, although it is such a common disease and affects a large part of the society. We think that all missing information should be minimized in order to be able to control the disease more. Therefore, it is important to conduct different studies on hemorrhoids that have never been tried before, like our study.

The most accepted risk factors for hemorrhoid are chronic constipation and slow bowel movements.¹⁴ However, in general, it is thought that factors that cause increased intra-abdominal pressure (obesity, heavy lifting jobs, occupations requiring prolonged sitting, cirrhosis etc.) and straining during defecation trigger hemorrhoids. In internal hemorrhoids etiology, long-term and chronic exposure to these factors is important. However, in external thrombosed hemorrhoids etiology, we often encounter acute constipation and forced defecation. In our study, we observed that THG patients had mostly acute and HG patients had chronic complaints.

According to the anatomical classification, hemorrhoids are divided into internal or external hemorrhoids. Internal hemorrhoids are often located in three primary hemorrhoidal

columns. These can be in the left lateral, right anterolateral and right posterolateral positions of the anal canal (at 1, 5 and 9 at prone position), and can be in or out of the anal canal depending on its relationship with the dentate line. These are known as localizations, which are mostly valid for internal hemorrhoids. In our study, the most frequently performed hemorrhoidectomy lesions in HG patients who underwent operations were the packages at 1, 5 and 9 levels when the patients were in the knee elbow position. Jongen et al. reported that they encountered thrombosis mostly in the left lateral and dorsal quadrants (66%) in the series of 340 cases in which they performed thrombectomy.¹⁵ In this study, we also found that thrombosed hemorrhoids were located left lateral and dorsally (59.25%). In fact, in this study, it is seen that hemorrhoids occur more in the left laterodorsal part of the body in both groups.

Hemorrhoid symptoms vary depending on whether the hemorrhoid is internal or external, and its stage. Sometimes a single symptom may appear, but more than one symptom is generally seen in patients applying for examination. The most encountered symptoms of hemorrhoid are bleeding, pain, prolapse, swelling, itching, and mucous soiling.¹ Similar findings were found in our study, in terms of symptoms. However, since the prominent symptom in all patients with thrombosed hemorrhoids is pain, the most common symptom was observed as pain.

Although hemorrhoid is a disease that can be seen at almost any age, the period during which the complaints increase most and the age of diagnosis is generally 45–65 years.^{16,17} Although there is no significant difference in terms of gender, it is known that it is more common in women, especially during pregnancy and postpartum period.⁷ It has been reported that thrombosed hemorrhoids are seen at a younger age compared to internal hemorrhoids, especially between the ages of 20–50.¹⁵ In this study, it was observed that THG patients were younger than HG patients. Beyond that, we found that thrombosed hemorrhoids are more common in women, with a statistically significant level.

We examined the platelet parameters, which draw attention with their coreless cellular structure and have been frequently researched in recent years, for the first time in a research related to hemorrhoids. Irrespective of cancer type, activation of platelets and coagulation correlates with the extent of tumor progression and negative clinical outcomes.¹⁸ It is demonstrated that platelet activation causes colon cancer cell proliferation and this response can be reversed with aspirin.¹⁹ There are studies which argue that the preoperative PDW value may be a potential marker to predict the prognosis of patients such as non-small cell lung cancer and hilar cholangiocarcinoma.^{20,21} Platelets, which make up the majority of the source of microparticles in the bloodstream, mediate many functions related to hemostasis and immunity.²² Patients with chronic disease and higher PDW values during hospitalization to the internal medicine ward had higher 90-day mortality risk.²³

While major symptoms occur in some hemorrhoids patients as bleeding, thrombosis in some patients is thought-provoking. We started this study with the aim of answering some questions on this subject. We wanted to see if there is a difference between an internal hemorrhoid and an exter-

nal thrombosed hemorrhoid, in terms of blood elements. In this study, when the platelet indexes were examined, we found that there was a significant difference only in terms of PDW value. PDW was at higher levels in THG. In terms of other laboratory values, the values between the two groups were very close to each other. The probable reason for this is the density of young platelets that have recently entered the bloodstream, instead of the platelets used due to the formation of thrombosis. This is not a reason to explain thrombosis formation, as we thought when planning this study, but a result of thrombosis formation. The reason for the fact that thrombosis is mostly seen in young patients may be due to the fact that these patients do not lose their elasticity of connective tissue yet, that their hemorrhoidal columns do not prolapse out of the anus, and therefore, cracks in the external superficial veins due to excessive strain and pressure. However, in the anal region where skin elasticity is high, bleeding from these cracks cannot come out of the skin and turn into a painful swelling, namely thrombosed hemorrhoid. Bleeding is a more common symptom in internal hemorrhoids, which are frequently seen in older ages, since it is covered with thin mucosal epithelium and prolapsed from the anus.

A new prospective study has been published, examining the role of mutations in four different genes related to thrombosis and vascular diseases, in the etiopathogenesis of thrombosed hemorrhoidal disease.²⁴ Abuoglu et al. concluded that genetic mutations have no role in etiology, however, they can contribute to other environmental, mechanical and hemodynamic factors. In our study, we planned to approach thrombosis formation in hemorrhoids in terms of platelet parameters and obtain novel results related to pathogenesis. However, as in this study, the results in our study were not as expected.

The first and most important weakness of our study is its retrospective character. Another weakness is that only 127 patients can be included in the study because of the insufficient data, although there were 243 patients who normally meet the study criteria during the planned period of this study. However, being a study to compare internal hemorrhoids and thrombosed hemorrhoids in many respects may be a strong aspect.

Conclusions

Hemorrhoid is such a common disease that affects almost everyone in their lifetime. Internal hemorrhoids are frequently seen in the age range of 45–65 years, with similar rates in men and women, while thrombosed external hemorrhoids occur at a younger age (<45) and more often in women. When these two disease groups are compared in terms of platelet indexes, PDW value was found to be significantly higher in THG. However, we believe that this is not a reason to explain thrombosis formation, but a result caused by thrombosis formation. In young people, thrombosed hemorrhoids may develop more frequently, as the connective tissue that forms the anal pads is not loose enough to form an internal hemorrhoid, as more seen in older patients.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

1. Yamana T. Japanese practice guidelines for anal disorders I. Hemorrhoids. *J Anus Rectum Colon*. 2018;1:89–99.
2. Morgagni J.B. *Sears and causes of diseases*, Vol. 2, Letter 32, Article 10. 1749. (Translated by Benjamin Alexander, 1769. London, A. Miller, p. 105–106).
3. Johanson JF, Sonnenberg A. The prevalence of hemorrhoids and chronic constipation. An epidemiologic study. *Gastroenterology*. 1990;98:380–6.
4. Riss S, Weiser FA, Schwameis K, Riss T, Mittlböck M, Steiner G, et al. The prevalence of hemorrhoids in adults. *Int J Colorectal Dis*. 2012;27:215–20.
5. Guttadauro A, Maternini M, Chiarelli M, Lo Bianco G, Pecora N, Gabrielli F. Evolution in the surgical management of hemorrhoidal disease. *Ann Ital Chir*. 2018;89:101–6.
6. Schubert MC, Sridhar S, Schade RR, Wexner SD. What every gastroenterologist needs to know about common anorectal disorders. *World J Gastroenterol*. 2009;15:3201–9.
7. Goligher JC. *Surgery of the anus, rectum and colon*. 4th edition London: Ballière Tindal; 1980.
8. Koupenova M, Clancy L, Corkrey HA, Freedman JE. Circulating platelets as mediators of immunity, inflammation, and thrombosis. *Circ Res*. 2018;122:337–51.
9. Nelson RL, Abcarian H, Davis FG, Persky V. Prevalence of benign anorectal disease in a randomly selected population. *Dis Colon Rectum*. 1995;38:341–4.
10. Loder PB, Kamm MA, Nicholls RJ, Phillips RK. Haemorrhoids: pathology, pathophysiology and aetiology. *Br J Surg*. 1994;81:946–54.
11. Tournu G, Abramowitz L, Couffignal C, Juguët F, Sénéjoux A, Berger S, et al. Prevalence of anal symptoms in general practice: a prospective study. *BMC Fam Pract*. 2017;18:78, <http://dx.doi.org/10.1186/s12875-017-0649-6>.
12. Kuehn HG, Gebbensleben O, Hilger Y, Rohde H. Relationship between anal symptoms and anal findings. *Int J Med Sci*. 2009;6:77–84, <http://dx.doi.org/10.7150/ijms.6.77>.
13. Abramowitz L, Benabderrahmane M, Pospait D, Philip J, Laouénan C. The prevalence of proctological symptoms amongst patients who see general practitioners in France. *Eur J Gen Pract*. 2014;20:301–6.
14. Acheson RM. Haemorrhoids in the adult male: a small epidemiological study. *Guys Hosp Rep*. 1960;109:184–95.
15. Jongen J, Bach S, Stübinger SH, Bock J-U. Excision of thrombosed external hemorrhoid under local anesthesia: a retrospective evaluation of 340 patients. *Dis Colon Rectum*. 2003;46:1226–31.
16. Mott T, Latimer K, Edwards C. Hemorrhoids: diagnosis and treatment options. *Am Fam Physician*. 2018;97:172–9.
17. Lorenzo-Rivero S. Hemorrhoids: diagnosis and current management. *Am Surg*. 2009;75:635–42.
18. Mitrugno A, Tormoen GW, Kuhn P, McCarty OJ. The prothrombotic activity of cancer cells in the circulation. *Blood Rev*. 2016;30:11–9.
19. Mitrugno A, Sylman JL, Rigg RA, Tassi Yunga S, Shatzel JJ, Williams CD, et al. Carpe low-dose aspirin: the new anti-cancer face of an old anti-platelet drug. *Platelets*. 2018;29:773–8.
20. Liu C, Zhang H, Qi Q, Zhang B, Yue D, Wang C. The preoperative platelet distribution width: a predictive factor of the prognosis in patients with non-small cell lung cancer. *Thorac Cancer*. 2020;11:918–27.
21. Li B, Lu J, Peng DZ, Zhang XY, You Z. Elevated platelet distribution width predicts poor prognosis in hilar cholangiocarcinoma. *Medicine (Baltimore)*. 2020;99:e19400.
22. Morrell CN, Aggrey AA, Chapman LM, Modjeski KL. Emerging roles for platelets as immune and inflammatory cells. *Blood*. 2014;123:2759–67.
23. Tzur I, Barchel D, Izhakian S, Swarka M, Garach-Jehoshua O, Krutkina E, et al. Platelet distribution width: a novel prognostic marker in an internal medicine ward. *J Community Hosp Intern Med Perspect*. 2019;9:464–70. Published 2019 Dec 14.
24. Abuoğlu HH, Gunay E, Uzunoğlu H. Effect of genetic factors on the etiopathogenesis of thrombosed hemorrhoidal disease. *Chirurgia (Bucur)*. 2019;114:89–94.