RESEARCH ARTICLE / Araştırma Makalesi

Assessment of the Relationship Between Leukocyte Count and Neutrophil-to-Lymphocyte Ratio and Clinical Course in Non-Variceal Upper Gastrointestinal System Bleeding

Nonvarisial Üst Gastrointestinal Sistem Kanamalarında Klinik Gidiş ve Nötrofil-Lenfosit oranı ve Lökosit Sayısı Arasındaki İlişkinin Değerlendirilmesi

Altay Kandemir[1], Mehmet Süle[2], İrfan Yavaşoğlu[3], Mevlüt Türe[4], Adil Coşkun[1], Abdülvahit Yükselen[1], M.Hadi Yasa[1]

[1] Adnan Menderes Üniversitesi Tıp Fakültesi İç Hastalıkları A:D, Gastroenteroloji B:D, AYDIN
[2] Borçka Devlet Hastanesi İç Hastalıkları Kliniği, Artvin
[3] Adnan Menderes Üniversitesi Tıp Fakültesi İç Hastalıkları A:D, Hematoloji B:D, AYDIN
[4] Adnan Menderes Üniversitesi Tıp Fakültesi Biyoistatistik B:D, AYDIN

Yazışma Adresi / Correspondence:
Altay Kandemir

Adnan Menderes Üniversitesi Tıp Fakültesi İç Hastalıkları Anabilim Dalı, Gastroenteroloji Bilim Dalı, Aydın
T: **+90 505 873 59 92** E-mail: **altaykandemir@yahoo.com**

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Abstract

Objective Nonvariceal upper gastrointestinal system bleeding (NVUGIB) is a life-threatening condition that can lead to mortality. It is important to identify the risk factors in terms of prognosis and mortality in patients with NVUGIB. In this study, we assessed the relationship between leukocytosis and neutrophil-to-lymphocyte ratio and the clinical course in patients with NVUGIB.
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Materials and Methods 156 patients were included who were diagnosed with NVUGIB between September 2013 and March 2017 in our clinic. The relationship between demographic data, endoscopic findings, need for erythrocyte suspension, length of hospital stay, need for intensive care, need for surgical intervention and mortality of the patients with the leukocyte count and neutrophil-to-lymphocyte ratio (NLR) was investigated.

Results 104 (66,7%) patients were male, 52 (33,3%) patients were female, and mean age was 63,8±17,6 years. According to endoscopic findings, the most common cause of the bleeding was peptic ulcer (77,6%).There was no statistically significant correlation between leukocyte count and NLR and need for intensive care, need for surgical intervention and treatment outcome. However, there was a statistically significant relationship between NLR and length of hospital stay (p=0,02)

Conclusion Evaluation of the patients with NVUGIB timely through their findings detected at admission and their laboratory results would make a positive contribution to treatment planning and follow up of the patient. Leukocyte count alone or in combination with other clinical and laboratory parameters can be a valuable marker in measuring mortality potential of acutely hospitalized patients. In our study, we found a significant relationship between NLR and the average length of hospital stay, which should be encouraged for further studies investigating its relation with the prognosis of the disease.

Keywords Nonvariceal upper gastrointestinal bleeding, leukocytosis, neutrophil-to-lymphocyte ratio

Öz

Amaç Nonvariseal üst gastrointestinal sistem kanamaları (NVUGIB) kanamaları yaşamı tehdit eden ve mortalite oluşturan kanamalardır. NVUGIB'li hastalarda prognoz ve mortalite için risk faktörlerini belirlemek önemlidir. Biz bu çalışmada, NVUGIB li hastalarda, lökositoz ve nötrofil-lenfosit oranının hastalığın klinik seyiri ile ilişkisini değerlendirdik. **(Sakarya Tıp Dergisi, 2018, 8(2):320-326).**

Gereç ve Yöntem Kliniğimizde, Eylül 2013 – Mart 2017 tarihleri arasında NVUGIB tanısı konulan 156 hasta çalışmaya alındı. Hastaların demografik verileri, endoskopik bulguları, eritrosit süspansiyonu ihtiyacı, hastanede yatış süresi, yoğun bakım ihtiyacı, cerrahi müdahaleye ihtiyaç, ölüm ile lökosit sayısı ve nötrofil-lenfosit oranı (NLR) ilişkisi araştırılmıştır.

Bulgular Hastaların 103'ü (%66,7) erkek, 52'si (%33,3) kadın, yaş ortalamaları 63,8 ± 17,6 saptandı. Endoskopi bulgularına göre kanamanın en sık nedeni peptik ülserdir (%77,6). Hem lökosit sayısı hem de NLR ile yoğun bakım ihtiyacı, cerrahi müdahaleye ihtiyaç ve tedavi sonucu arasında istatistiksel olarak anlamlı bir ilişki bulunmadı. Ancak Hastaların NLR'a göre hastanede yatış süre ortalaması arasında istatistiksel olarak anlamlı bir ilişki vardı (p:0,02)

Sonuç NVUGIB sahip hastaların hastaneye başvurusu sırasında saptanan bulguları ve laboratuvar verileri çerçevesinde önceden değerlendirebilmek hastanın takibine, tedavi planlamasına olumlu katkı yapmaktadır. Lökosit tek başına ya da diğer klinik ve laboratuar parametrelerle kombine edilerek, akut olarak hastaneye yatırılan hastalarda mortalite potansiyelinin ölçülmesinde önemli bir marker olabilir. Çalışmamızda NLR ile hastanede yatış süre ortalaması ile anlamlı ilişki saptanmış olup, hastalığın prognozu ile ilişkisini gösteren daha ileri çalışmalar yapmak için teşvik edici olmalıdır

Anahtar Kelimeler Nonvarisial üst gastrointestinal sistem kanaması, lökositoz, nötrofil-lenfosit oranı

Introduction

Nonvariceal upper gastrointestinal system bleeding (NVUGIB) is potentially life-threatening bleeding causing morbidity and occurs above the ligament of Treitz. It is observed in 48-160 per 100000 people every year[1] and more common among men and elderly.[2] Peptic ulcer bleeding is the most common cause of NVUGIB with a rate of 25-67%, although there are many other reasons (gastroduodenal erosions, Mallory-Weiss lesions, vascular malformations and severe esophagitis etc.).[3]

For the patients with UGIB (Upper GastroIntestinal Bleeding), age, comorbidity, shock, diagnosis, hemoglobin value at admission, presentation, ulcer size, stigmata of recent haemorrhage, and the need for transfusion were found to provide prognostic data for further haemorrhage and mortality. In addition, the presence of diabetes mellitus, endoscopic image of prominent visible vessel, treatment with proton pump inhibitors, and hypotension were found to be independent risk factors for poor prognosis.[4,5] Simple scoring systems were established to identify the risk factors for mortality in patients with UGIB. The most commonly used Rockall score (RS) consists of a pre-endoscopic evaluation part, which includes age, signs of shock and comorbidities, along with an endoscopic part, which evaluates high-risk endoscopic characteristics as well (known as the post-endoscopic RS).[5] The Glasgow-Blatchford score is a pre-endoscopic score and contains the following parameters: initial hemoglobin levels, urea, blood pressure, pulse, known syncope, melena, and liver or cardiac failure.[6] Neutrophils and lymphocytes are the cells playing primary roles in inflammatory processes and their numbers change temporarily in inflammation. Neutrophil-to-lymphocyte ratio (NLR) was introduced as a useful index for diagnosis or prognosis of different diseases (e.g.. hepatocellular carcinoma, metastatic gastric cancer, acute coronary syndrome, colorectal cancer,).[7-10] There is very limited data available regarding NLR in patients with NVUGIB. Again, very little information is available on the prevalence of leukocytosis as well as its significance, although development of leukocytosis is a well known fact among patients with UGIB.[11] In this study, we evaluated the relation between leukocytosis and NLR and the clinical course in patients with NVUGIB.

Materials and Methods

One hundred and fifty-six patients were included in the study who were diagnosed with NVUGIB in the Gastroenterology Clinic of Adnan Menderes University Medical Faculty between September 2013 and March 2017. The patients who aged ≥ 18 years and underwent upper gastrointestinal (GI) endoscopy due to symptoms of gastrointestinal bleeding (haematemesis, melena, and/or hematochezia) and determined to have bleeding in the esophagus, stomach and duodenum were included. In the presence of multiple foci of bleeding, the researcher decided which focus to be considered on the basis of endoscopic findings and clinical manifestations. All endoscopic procedures were performed by gastroenterologists.

Patients with a history of medical use known to cause leukocytosis (e.g. steroids), with a diagnosis of malignancy (hematologic or solid organ malignancy), and having gastrointestinal variceal hemorrhage, or a bleeding of unknown origin, those with no records available, and the patients having an active infection were excluded.

Gender, age, hemoglobin (Hb), hematocrit (Htc), white blood cell count (WBC), neutrophil,

lymphocyte, neutrophil-to-lymphocyte ratio (NLR), urea, creatinine, international normalized ratio (INR), Activated Partial Thromboplastin Time (APTT), comorbidities, additional drug use, esophagogastroduodenoscopy (EGD) findings, site of ulcer, Forrest classification, erythrocyte suspension (ES) replacement (unit), fresh frozen plasma (FFP) replacement (unit), length of hospital stay (days), need for intensive care, need for surgical intervention, and treatment outcomes were evaluated. The normal range for WBC device in our laboratory (BC-6800 Mindray) is 4-10x103/mm3; any value greater than 10x103/mm3 was considered abnormal.[12] The NLR cut-off value was accepted as 1.65.[13] In this study was descriptive and cross-sectional. Kolmogorov Smırnov Test was used for statistical distribution analysis. The data was processed by the Statistical Package for Social Sciences version 17.0 (SPSS Inc.; Chicago, IL, USA). Distribution of numbers and percent ages were analyzed by statistical analysis; Chi square test was used for categorical variables and Student's t test for continuous variables in the intergroup comparisons.P<0.05 was defined as significant for the analyzes. All the information about the patients was obtained retrospectively from electronic medical records. The study protocol wasapproved by the ethical committee of the Faculty of Medicine (August 11, 2017; approval number: 1208).

Results

Of 156 patients, 104 (66,7%) were male and 52 (33,3%) were female, with a mean age of 63,8±17,6 years. Mean values for female and male patients for ES replacement were 2,1±2,3 and 2,8±2,3 units (p>0.05), for FFP replacement as 0,9±2,3 and 0,5±1,5 units (p>0.05), and for total length of hospital stay as 4,8±2,9 and 5,4±3,1 days (p>0.05),respectively. Mean length of stay at hospital, Count of ES and FFP replacements showed no difference in males and females.

Table1: Patients' Characteristics and Laboratory Findings

Characteristics (n=156)	Mean±SD	Minimum-Maximum
Age (years)	63.8± 17.6	20-97
Hemoglobin (g/dL)	9.8 ± 2.4	4.2-15.6
Hematocrit (%)	30.4 ± 7.2	13.5-46.1
Leukocyte/mm3	10544.6 ± 3348.7	4020-20950
Neutrophil/lymphocyte	5.53 ± 5.22	0.77-49.0
Sodium (mg/dL)	137.7 ± 3.1	122-145
Urea (mg/dL)	76.0 ± 38.5	15-225
Creatinin (mg/dL)	0.91 ± 0.31	0.52-1.9
INR*	2.91 ± 1.71	0.88-6.3
APTT (seconds)	27.9 ± 11.8	15.6-123
ES replacement (units)	2.6 ± 2,2	0-10
FFP replacement (units)	0.6 ± 1,8	0-9

* Values are from 19 patients on warfarin treatment.
ES: Erythrocyte suspension FFP: Fresh Frozen Plasma

Sixty-eight (43.6%) of the 156 patients included in the study were followed in intensive care.Of the patients, 152 (97,4%) received medical treatment and 4 (2,6%) underwent surgical intervention.Four patients (2,6%) on medical treatment were lost. The mean length of hospital stay was 5,23±3,01 days.

Comorbidities were determined in 116 (74.4%) of the patients. Forty-eight (41,4%) patients had

hypertension (HT), 33 (28,4%) had cardiovascular diseases and 18 (15,5%) had diabetes mellitus. Eighty-six (55,1%) of the patients used various medicines; namely, 28 patients (32,6%) Acetylsalicylic acid, 22 (25,6%) NSAID, 19 (22,1%) warfarin, 7 (8,1% 0) dabigatran, 6 (7,0%) clopidogrel. EGD findings are given in table 2.

Table2 : Some characteristics of bleeding foci of patients with non-variceal upper gastrointestinal bleeding		
Characteristics	Number	Percent
EGD findings (n=156)		
Ulcer	121	77.6
Hyperemic pancreatitis	15	9.6
Erosive gastritis	14	9.0
Mallory-Weiss Syndrome	2	1.3
Angiodysplasia	2	1.3
Dieulafoy lesion	1	0.6
Gastric polyp	1	0.6
Localization of the ulcers (n=121)		
Duodenal	61	49.0
Gastric	54	44.6
Esophageal	6	6.4
Forrest classification (n=121)		
Forrest 1a	8	6.6
Forrest 1b	7	5.8
Forrest 2a	3	2.5
Forrest 2b	3	2.5
Forrest 2c	1	0.8
Forrest 3	99	81.8

The mean values for ES replacement, FFP replacement and length of hospital stay; and the relationship between leukocyte count and NLR are given in table 3. There was a statistically significant relation between NLR and length of hospital stay ($p<0.05$).

Table3: Distribution of the mean ESR replacement, TDP replacement and length of hospital stay by leucocyte count and neutrophil to lymphocyte rate, in patients with non-variceal upper gastrointestinal bleeding admitted in gastroenterology clinic						
	Leukocyte count /mm3			Neutrophil / Lymphocyte		
Characteristics	<10 000	≥10 000	p	<1,65	≥1,65	p
	n: 80	n: 76		n: 24	n: 132	
ES replacement Mean±SS (units)	2.6 ± 2.3	2.5 ± 2.1	0.78	1.8 ±1.4	2.6 ± 2.3	>0.05
TDP replacement Mean±SS (units)	0.8 ± 2.1	0.4 ± 1.4	0.15	-	0.7 ± 1.9	>0.05
Length of hospital stay Mean±SS (days)	4.9 ± 2.9	5.6 ± 3.1	0.12	3.3 ± 2.1	5.4 ± 3.0	<0.05
ES: Erythrocyte suspension	FFP: Fresh Frozen Plasma					

Thirty-three (41,3%) of 80 patients with a leukocyte count <10 000/mm3 were followed in the intensive care unit, 2 (2,5%) of these underwent surgical intervention, and 1 (1,3%) patient was lost. 76 patients with a leukocyte count ≥ 10 000/mm3, 35 (46,1%) were followed up in intensive care unit, 2 (2,6%) of these were administered surgical interventions and 3 (3,9%) patients were lost. There was no statistically significant correlation between leucocyte count and need for

follow-up in intensive care unit (p>0.05), need for surgical intervention (p>0.05), and treatment outcomes (p>0.05).

10 (41,7%) of 24 patients with NLR < 1,65 needed intensive care follow up, none of these cases ended with surgical intervention or mortality. Sixty-three (47,7%) of 132 patients with NLR ≥ 1,65 were followed up in intensive care unit, 4 (3%) of these needed surgical intervention and 4 (%3) patients were lost. There was no statistically significant relation between NLR and treatment in intensive care unit (p>0.05), surgical intervention (p>0.05) and treatment outcomes (p>0.05)

Discussion

Currently the patients with UGIB are frequently encountered in clinical practice, despite improved methods of diagnosis and treatment.[14] Among GIS diseases, UGIB remains to be the most common cause of hospitalization.[15] Numerous factors are known to affect the incidence and severity of UGIB. In this context, age, gender, diabetes mellitus, vital findings at admission, the use of proton pump inhibitors or NSAID, the cause of bleeding, and endoscopic findings can be mentioned. UGIB is more common among male and elderly patients.[16] In accordance with this, mean age of our patients was 63,8±17,6 and males constituted 66,7% of the sample. Various laboratory tests are used in order to determine the cause of bleeding and the level of blood loss. Hb and Hct are among those which are expected to decrease.[17] Mild leucocytosis and trombocytosis can be expected and urea may increase.[18] Predicting the prognosis of the disease will be helpful in diagnosis and treatment, eventually decrease morbidity and mortality.Mortality ranges between 3 to 14%. Surgical intervention is administered rarely in UGIB cases.[19] In our study group, surgical intervention was administered to very few patients (2,6%), almost half of the cases were followed in intensive care unit (43,6%) and four patients (2,6%) were lost. When compared with the literature, relatively lower rate of mortality in our group can be explained by our exclusion criteria concerning patients with poor-prognosis. In a retrospective multicenter study conducted in Turkey on 1339 NVUGIB patients, more than half of these patients were noted to have comorbidities, including cardiovascular diseases (36,5%) and DM (10,1%) at most.[20] Also in our study, three out four patients suffered comorbidities. In accordance with general population, HT (41,4%), coronary arter disease (28,4%) and DM (15,5%) were recorded. As for the causes of GISB, most frequently reported diseases were duodenal and gastric ulcers and generally in Forrest class 3.[21] Also in our study, peptic ulcer was the primary cause detected in EGD (77,6%). As for the localization of the ulcers, duodenal and gastric ulcers were detected at similar frequency whereas esophageal ulcers were rare. Similar to other studies, Forrest class 3 ulcers were detected at the highest frequency. Leukocytosis, which is widely accepted as an indicator of infection or inflammation, can also occur by trauma, exercise, drugs such as steroids or lithium, and other clinical conditions such as malignancy, poisoning, psychosis and diabetic ketoacidosis.[22] Studies investigating the correlation of leukocytosis with prognostic factors of the disease, such as increased risk of mortality and morbidity are limited. Such a correlation was well-defined for coronary heart disease[23] and cerebrovascular disease[24], but also suggested for hypertension[25], glucose intolerance[26] and overall risk of mortality.[27] Leukocytosis may occur in patients with NVUGIB, but studies on its significance and its incidence is rare.[11,12] In a study by Chalasani et al.[11], patients with UGIB were evaluated and leukocytosis >20,000/mm3 was determined in more than 5% of patients. Furthermore, leukocytosis was associated with poor prognosis since it reflects the severity of bleeding and the amount of blood loss. On the other hand, patients with leukocytosis were stated to have a high risk of tachycar-

dia and hypotension, that can indirectly reflect the severity of leukocytosis and bleeding. However, no significant difference was determined between UGIB patients with and without leukocytosis in terms of mortality. Srygley et al.[28] evaluated the severity of GI bleeding and they found increased severity associated with Hb<8 g/dL (4,5-6,2-fold), serum urea nitrogen>90 mg/dL (3,6-fold) or leukocyte levels>12 000/mm3 (3,4-fold). In our study, leukocytosis was detected in 76 (48,7%) of the patients. Statistically significant correlation was not determined between leucocyte count and the need for ES replacement (p=0,78), FFP replacement (p=0,15), need for intensive care (p=0,54), need for surgical intervention (p=1,00), treatment outcomes (p=0,36), length of hospital stay (p=0,12) and mortality (p=0,32). Such a correlation with mortality could not be shown in the analyzes, maybe because of the very small number of excitus cases (n=4; 2,6%).

Blood NLR is a potentially useful marker for predicting clinical course in some diseases. 7,9,10 In a retrospective analysis of patients with cirrhosis found NLR to associate with death within 1 year after non-elective hospitalization.[29] Preoperative NLR was an important prognostic factor for TNM stage I HCC after liver resection with curative intent.[30] There are studies showing correlation with NLR in children with gastrointestinal bleeding and Henoch-Schönlein purpura (HSP). Park CH et al.[31] found that NLR cut-off value of 3.90 could predict development of UGIB in adults with HSP with a sensitivity of 87,5% and specificity of 88,6%. Makay B. et al. found that higher NLR predicted GI bleeding in HSP.[32] Forget et al.[13] assessed the NLR values of 413 healthy adults and found that they ranged between 0,78 and 3,53 (mean 1,65). To the best of our knowledge, there are no studies in the literature regarding NLR in patients with NVUGIB. In this study, no statistically significant relation was found between NLR values as to whether it is over or under 1,65, and the need for ES replacement (p=0,19), TDP replacement (p=0,23), surgical intervention (p=1,00), but the mean length of hospital stay showed a positive correlation with NLR >1,65 (p=0.02).

In conclusion, timely evaluation of the patients with NVUGIB through their findings determined at admission as well as latest laboratory data would positively contribute to their follow up and treatment planning. Alone or in combination with other clinical and laboratory parameters, Leukocyte count may be an important marker in predicting probability of mortality in acutely hospitalized patients.[12] Further studies are needed to evaluate significance and mechanism of leukocytosis and the LNR in order to predict the prognosis and mortality in upper GI bleeding.

1. Rotondano G. Epidemiology and diagnosis of acute nonvariceal upper gastrointestinal bleeding. Gastroenterology clinics of North America 2014; 43: 643-63.
2. Longstreth GF. Epidemiology and outcome of patients hospitalized with acute lower gastrointestinal hemorrhage: a population-based study. The American journal of gastroenterology 1997; 92: 419-24.
3. Tielleman T, Bujanda D, Cryer B. Epidemiology and Risk Factors for Upper Gastrointestinal Bleeding. Gastrointestinal endoscopy clinics of North America 2015; 25: 415-28.
4. Coskun F, Topeli A, Sivri B. Patients admitted to the emergency room with upper gastrointestinal bleeding: factors influencing recurrence or death. Advances in therapy 2005; 22: 453-61.
5. Rockall TA, Logan RF, Devlin HB, Northfield TC. Risk assessment after acute upper gastrointestinal haemorrhage. Gut 1996; 38: 316-21.
6. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. Lancet. 2000;356:1318-1321.
7. Kim H, Ro SM, Yang JH, Jeong JW, Lee JE, Roh SY,et al.The neutrophil-to-lymphocyte ratio prechemotherapy and postchemotherapy as a prognostic marker in metastatic gastric cancer Korean J Intern Med. 2018 May 4.
8. Motomura T, Shirabe K, Mano Y, Muto J, Toshima T, Umemoto Y, et al. Neutrophil-lymphocyte ratio reflects hepatocellular carcinoma recurrence after liver transplantation via inflammatory microenvironment. Journal of hepatology 2013; 58: 58-64.
9. Tamhane UU, Aneja S, Montgomery D, Rogers EK, Eagle KA, Gurm HS. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. The American journal of cardiology 2008; 102: 653-7.
10. Walsh SR, Cook EJ, Goulder F, Justin TA, Keeling NJ. Neutrophil-lymphocyte ratio as a prognostic factor in colorectal cancer. Journal of surgical oncology 2005; 91: 181-4.
11. Chalasani N, Patel K, Clark WS, Wilcox CM. The prevalence and significance of leukocytosis in upper gastrointestinal bleeding. The American journal of the medical sciences 1998; 315: 233-6.
12. Asadollahi K, Hastings IM, Beeching NJ, Gill GV. Laboratory risk factors for hospital mortality in acutely admitted patients. QJM : monthly journal of the Association of Physicians 2007; 100: 501-7.
13. Forget P, Khalifa C, Defour JP, Latinne D, Van Pel MC, De Kock M. What is the normal value of the neutrophil-to-lymphocyte ratio? BMC research notes 2017; 10: 12.
14. Ghassemi KA, Jensen DM. What Does Lesion Blood Flow Tell Us About Risk Stratification and Successful Management of Non-variceal UGI Bleeding? Current gastroenterology reports 2017; 19: 17.
15. Laine L. CLINICAL PRACTICE. Upper Gastrointestinal Bleeding Due to a Peptic Ulcer. The New England journal of medicine 2016; 374: 2367-76.
16. Kim JJ, Sheibani S, Park S, Buxbaum J, Laine L. Causes of bleeding and outcomes in patients hospitalized with upper gastrointestinal bleeding. Journal of clinical gastroenterology 2014; 48: 113-8.
17. Tomizawa M, Shinozaki F, Hasegawa R, Shirai Y, Motoyoshi Y, Sugiyama T, et al. Laboratory test variables useful for distinguishing upper from lower gastrointestinal bleeding. World journal of gastroenterology 2015; 21: 6246-51.
18. Longo DL FA, Kasper DL, Hauser SL, Jameson J, Loscalzo J, et al. eds. . Gastrointestinal Bleeding. . In: Harrison's Manual of Medicine, 18th ed. New York: McGraw-Hill, 2014; 1281-1286. ed.
19. van Leerdam ME. Epidemiology of acute upper gastrointestinal bleeding. Best practice & research Clinical gastroenterology 2008; 22: 209-24.
20. Bor S, Dagli U, Sarer B, Gurel S, Tozun N, Sivri B, et al. A retrospective study demonstrating properties of nonvariceal upper gastrointestinal bleeding in Turkey. The Turkish journal of gastroenterology : the official journal of Turkish Society of Gastroenterology 2011; 22: 249-54.
21. Hay JA, Lyubashevsky E, Elashoff J, Maldonado L, Weingarten SR, Ellrodt AG. Upper gastrointestinal hemorrhage clinical--guideline determining the optimal hospital length of stay. The American journal of medicine 1996; 100: 313-22.
22. .Abramson N, Melton B. Leukocytosis: basics of clinical assessment. American family physician 2000; 62: 2053-60.
23. Barron HV, Harr SD, Radford MJ, Wang Y, Krumholz HM. The association between white blood cell count and acute myocardial infarction mortality in patients > or =65 years of age: findings from the cooperative cardiovascular project. Journal of the American College of Cardiology 2001; 38: 1654-61.
24. Kazmierski R, Guzik P, Ambrosius W, Kozubski W. [Leukocytosis in the first day of acute ischemic stroke as a prognostic factor of disease progression]. Wiadomosci lekarskie (Warsaw, Poland : 1960) 2001; 54: 143-51.
25. Tatsukawa Y, Hsu WL, Yamada M, Cologne JB, Suzuki G, Yamamoto H, et al. White blood cell count, especially neutrophil count, as a predictor of hypertension in a Japanese population. Hypertension research : official journal of the Japanese Society of Hypertension 2008; 31: 1391-7.
26. Fritsche A, Haring H, Stumvoll M. [White blood cell count as a predictor of glucose tolerance and insulin sensitivity. The role of inflammation in the pathogenesis of type 2 diabetes mellitus]. Deutsche medizinische Wochenschrift (1946) 2004; 129: 244-8.
27. de Labry LO, Campion EW, Glynn RJ, Vokonas PS. White blood cell count as a predictor of mortality: results over 18 years from the Normative Aging Study. Journal of clinical epidemiology 1990; 43: 153-7.
28. Srygley FD, Gerardo CJ, Tran T, Fisher DA. Does this patient have a severe upper gastrointestinal bleed? Jama 2012; 307: 1072-9.
29. Rice J, Dodge JL, Bambha KM, Bajaj JS, Reddy KR,Gralla J, et al. Neutrophil to Lymphocyte Ratio Associates Independently With Mortality in Hospitalized Patients with Cirrhosis.Clin Gastroenterol Hepatol. 2018. pii: S1542-3565(18)30407-5.
30. Okamura Y, Sugiura T, Ito T, Yamamoto Y, Ashida R, Mori K. Neutrophil to lymphocyte ratio as an indicator of the malignant behaviour of hepatocellular carcinoma.Br J Surg. 2016;103(7):891-8.
31. Park CH, Han DS, Jeong JY, Eun CS, Yoo KS, Jeon YC, et al. The Optimal Cut-Off Value of Neutrophil-to-Lymphocyte Ratio for Predicting Prognosis in Adult Patients with Henoch-Schonlein Purpura. PloS one 2016; 11: e0153238.
32. Makay B, Gucenmez OA, Duman M, Unsal E. The relationship of neutrophil-to-lymphocyte ratio with gastrointestinal bleeding in Henoch-Schonlein purpura. Rheumatology international 2014; 34: 1323-7.