ORIGINAL ARTICLE

Correlation between Ranson score and red cell distribution width in acute pancreatitis

Murat Özgür Kılıç, M.D., Canbert Çelik, M.D., Cemil Yüksel, M.D., Barış Doğu Yıldız, M.D., Mesut Tez, M.D.

Department of General Surgery, Numune Training and Research Hospital, Ankara-*Turkey*

ABSTRACT

BACKGROUND: Ranson's criteria are widely used to evaluate severity of acute pancreatitis (AP). Red blood cell distribution width (RDW) has been demonstrated to be useful marker to predict mortality in these patients. The aim of the present study was to investigate correlation between Ranson score and RDW in patients with AP.

METHODS: Total of 202 patients with AP were included in the study. Patients were classified as mild or severe AP, based on presence of organ failure for more than 48 hours and/or local complications.

RESULTS: Forty patients (19.8%) were diagnosed as severe AP. High sensitivity and specificity values were obtained from receiver operating characteristic curve for initial RDW and Ranson score in predicting severe AP. Ranson ≥4 was selected cut-off value for Ranson score and 14% was limit for RDW. RDW at time of admission was correlated with 48-hour Ranson score (r=0.22; p<0.002). However, at day 0, there was no correlation between RDW and 0-hour Ranson score (r=0.07; p=0.600).

CONCLUSION: Although there is no single, ideal method to assess severity of AP, RDW level at admission can be helpful in earlier prediction of AP severity, especially in first-line centers, taking into consideration disadvantages of multifactorial scoring systems.

Keywords: Acute pancreatitis; Ranson score; red cell distribution width.

INTRODUCTION

Acute pancreatitis (AP) is an acute inflammatory disease, and is one of the most frequent gastrointestinal causes of hospital admission. Prognosis of AP depends on its severity, which can be classified as mild or severe, according to latest revised Atlanta Classification. Majority of patients have mild, self-limited disease; however, approximately 20% of patients have severe form. Early assessment of severity is fundamental.

Several single and multiparameter predictors to evaluate severity of the disease have been described. Ranson criteria are widely used in clinical practice worldwide, but this scoring system has limitation that evaluation cannot be completed until 48 hours following admission, which may lead to missing an early therapeutic window and increased mortality.

Complete blood count (CBC) is a laboratory test frequently used in clinical practice, and comprises white blood cell, red blood cell, and platelet counts, and their morphological indices, such as red blood cell distribution width (RDW). RDW measures size variability of erythrocytes. It is used to differentiate etiology of anemia, and in a previous study, RDW was demonstrated to be useful marker for predicting mortality in AP patients.[1,2]

The present study is investigation of correlation between RDW and Ranson score in group of AP patients.

Address for correspondence: Murat Özgür Kılıç, M.D.
Ankara Numune Eğitim ve Araştırma Hastanesi, Genel Cerrahi Kliniği, Talatpaşa Bulvarı, No: 44, 06230 Ankara, Turkey
Tel: +90 312 - 508 40 00 E-mail: murat05ozgur@hotmail.com

Qucik Response Code

Ulus Travma Acil Cerrahi Derg
2017;23(2):112–116
doi: 10.5505/tjtes.2016.27895

MATERIALS AND METHODS

Patients

A total of 202 patients with AP treated between January 2012 and December 2014 were included in the study. AP was diagnosed with typical physical examination findings associated with plasma amylase level ≥3 times upper limit of normal level and radiological verification of disease with ultrasonography and/or abdominal tomography. AP was classified as mild or severe based on presence of organ failure for more than

48 hours and/or local complications, according to Atlanta criteria.[3] Organ failure included shock (systolic blood pressure <90 mmHg), pulmonary insufficiency (arterial partial pressure of oxygen <60 mmHg at room air or need for mechanical ventilation), or renal failure (serum creatinine level >2 mg/dL after rehydration or hemodialysis).

Demographic, radiographic, and laboratory data were collected from patient records for retrospective study. Ranson score was calculated using data recorded in first 24 hours and 48 hours after admission.

Statistical Analysis

Statistical analyses were performed using SPSS software, version 17.0 (IBM Corp., Armonk, NY, USA). Normality of data distribution was assessed with Kolmogorov-Smirnov or Shapiro-Wilk test. All values are expressed as median (interquartile range), mean±standard deviation or count (percentage), unless otherwise specified. Comparisons were made using (1) chi-square test or Fisher's exact test for categorical data, (2) unpaired or paired Student's t-test for continuous normally distributed variables, and (3) Mann-Whitney U-test for continuous non-normally distributed variables. Correlations of RDW with Ranson score were assessed with Spearman's correlation coefficient.

RESULTS

Mean age at presentation was 59.2 years, and 91 patients (45%) were males. Most frequent AP etiology was biliary, seen in 146 patients (72.3%). Forty patients (19.8%) were diagnosed as having severe AP (organ failure with local complications). Median length of hospital stay was 6 days (range: 3–11 days). Clinical characteristics and outcomes of all patients are summarized in Table 1.

Median RDW was 14.25% in severe AP group, while patients with mild AP had median RDW of 13.6%. Difference between these 2 groups was statistically significant (p=0.004). Receiver operating characteristic (ROC) curve for initial RDW predicting severe AP yielded area under curve (AUC) of 0.648 (95% CI, 0.55–0.74).

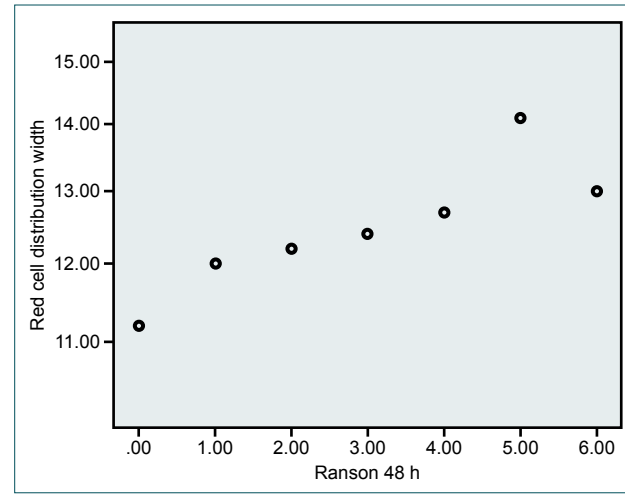

Figure 1. Correlation between RDW (at day 0) and 48-hour Ranson score (r=0.22; p<0.002). RDW: Red blood cell distribution width.

Median Ranson scores were 4 (range: 3–5) and 1 (range: 1–2) for severe AP patients and mild AP patients, respectively. ROC curve for Ranson score predicting severe AP yielded AUC of 0.625 (95% CI, 0.49–0.77).

On basis of highest sensitivity and specificity values generated from ROC curve, ≥4 was selected as cut-off value for Ranson score and 14% was used as RDW limit.

RDW at time of admission (day 0) was correlated with 48-hour Ranson score (r=0.22; p<0.002) (Figure 1). At day 0 there was no correlation between RDW and 0-hour Ranson score (r=0.07; p=0.6).

Table 1. Demographic and clinical characteristics of the patients with acute pancreatitis

Characteristics	Total (n=202)	Patients with mild acute pancreatitis (n=162)	Patients with severe acute pancreatitis (n=40)
Mean age (min–max)	59.2 (17–90)	56.9 (17–90)	69.1 (22–90)
Gender, n (%)			
Male	91 (45)	78 (85.7)	13 (75.7)
Female	111 (55)	84 (14.3)	27 (23.4)
Etiology, n (%)			
Biliary	156 (72.3)	126 (77.3)	30 (75)
Non-biliary	46 (27.7)	36 (22.3)	10 (25)
Median hospital stay	6 days (3–11)	6 days (4–9)	9 days (3–16)
Median red cell distribution width	13.8 (12.9–14.7)	13.6 (12.8–14.5)	14.25 (13.6–15.5)
Median Ranson score	1 (1–2)	1 (1–2)	4 (3–5)

Median RDW was found to be significantly higher in Ranson score ≥4 patients than Ranson <4 patients (14.2% [range: 13.6–15.2%] vs 13.8% [range: 12.9–14.6%]; p=0.046).

DISCUSSION

Initial assessment of severity is one of the most important issues in the management of AP. Approximately 15% to 20% of patients with AP develop severe disease, which complicates the clinical course and often causes organ failure.[1] Identifying severity of disease within 24 to 48 hours after admission is essential for planning initial treatment.

Our results indicated that RDW level at admission was significantly different between patients with mild or severe AP and was correlated with Ranson's score.

Ranson's criteria were the first widely used severity scoring system, described by John Ranson in 1970s, and included basic laboratory data and clinical variables obtained within 48 hours after hospital admission.[4] Since sensitivity of this score was found to be between 40% and 80%, especially among biliary etiology group,[5–8] Ranson group developed a modified index.[9] It is still the most common scoring system used to evaluate severity of AP, due to its simplicity. Papachristou et al.[10] compared predictive accuracy of multiparameter score determined by AUC, and found that Ranson score was the only score with AUC >0.9. However, primary disadvantage of this scoring system is need for 48 hours to elapse in order to complete evaluation.

Single prognostic serum markers are widely accepted in clinical use to determine AP severity. Hemoconcentration is acknowledged to be important factor in development of severe AP. Therefore, it could be assumed that hematocrit level on admission could be novel predictor of severity of the disease. Some studies have indicated that hematocrit level over 50% is sign of severity.[11] Other studies carried out in this field have demonstrated hematocrit level over 44% is associated with complications in AP.[12,13] However, whether changes in hematocrit level during follow-up could be used to assess severity is still unknown. Recent studies have reported that elevated hematocrit level on admission or within first 24 hours is satisfactory single prognostic variable when compared with Ranson criteria and Acute Physiology and Chronic Health Evaluation (APACHE) II system for predicting severity of AP.[11,12,14,15]

Creatinine and blood urea nitrogen (BUN) levels are easily measured, and they are routine, inexpensive tests that serve as indicator of acute renal failure. In one study, sensitivity and specificity of BUN elevation to predict severity of AP were determined to be 79% and 70%, respectively.[16]

C-reactive protein (CRP) is broadly recognized as indicator of severity 48 hours after disease onset with value greater than 150 mg/dL and other causes of inflammation, such as cholangitis and pneumonia, ruled out.[17–20] Sensitivity and positive predictive value of serum CRP level in patients with severe AP have been reported to be 83% to 90% and 75% to 86%, respectively, with remarkable increase from onset of AP through first 72 hours.[19] However, CRP level on admission is poor predictor of severity of the disease as result of increased hepatic synthesis due to inflammation-induced cytokine release, and has initial accuracy similar to that of APACHE II score.[7]

Interleukin 6 (IL-6) is major mediator of CRP and is released primarily by macrophages. Value measured at admission has sensitivity and specificity of between 69% to 100% and 70% to 86%, respectively, in distinguishing between severe and mild pancreatitis.[21] IL-6 rises with beginning of symptoms and peaks on third day. As it has short plasma half-life, degradation during course of disease can be used as indicator of progression.

IL-8 is a neutrophil-activating cytokine, and can be used as early predictor of severity and complications of AP.[21] Variety of results (sensitivity: 72–100%, specificity: 75–81%) have been reported for prediction of infected necrosis in AP.[22,23] Despite high prediction rates, however, it still has limited use in daily clinical practice.

IL-10 is a well-known anti-inflammatory cytokine. Though 1 study reported sensitivity of 67% and specificity of 100% with IL-10 for prediction of severity on first day of AP,[24] other studies have stated less reliable results compared with IL-6 and IL-8.[19]

Tumor necrosis factor alpha (TNF-α), which is produced primarily by macrophages, is a cytokine that stimulates acute phase reaction. Many clinicians have investigated its role in predicting severity of AP.[25,26] Unfortunately, outcomes of these studies are not very promising. As result of its rapid clearance, TNF-α is less useful than other cytokines in prediction of severity.

Serum procalcitonin level is known as reliable marker of infection and sepsis.[27] It has 94% sensitivity and 91% specificity rates for detection of infected necrosis in AP.[22] In a review, procalcitonin and relationship to infected necrosis was reported to have overall sensitivity of 80% and specificity of 91%.[28] In an article published in 2006, parallel results were obtained for procalcitonin level over 0.5 ng/mL.[29] Procalcitonin could be recognized as an indicator of infected necrosis, which is one of the major complications that can advance in the progress of AP. However, procalcitonin level is not preferred laboratory data in daily use, which is main handicap of this marker.

Urinary trypsinogen activation peptide (uTAP) is liberated during activation of trypsinogen to trypsin and has been used in recent years to predict severity of AP. According to 1992

Atlanta criteria, uTAP is rapid test that is reliable in prediction of severity of AP.[30] Several studies have demonstrated significant correlation between uTAP level and severity of disease. In a study published in 1997, level of uTAP greater than 10 ng/mL at admission was found to be predictor of severity with sensitivity and specificity rates of 100% and 85%, respectively.[31] Other subsequent studies revealed different sensitivity (58–100%) and specificity (65.8–77%) rates for different uTAP cut-off levels.[32–34] Meta-analysis determined sensitivity and specificity for uTAP >35 nmol/L of 71% and 75%, respectively (AUC=0.83).[34] Value of uTAP is that it provides useful information about severity at admission, but as it is not widely used in many hospitals, benefit is still limited.

RDW reflects systemic inflammation, and is a remarkable prognostic marker to determine risk of mortality in wide range of clinical manifestations.[35–38] Şenol et al.[39] demonstrated in their study that increased RDW value at admission was independent predictor of mortality in patients with AP. In this study, high RDW level, i.e., >14.8%, at onset of disease displayed more distinct correlation with non-survival than novel prognostic markers in the literature used to predict mortality.

In conclusion, analysis of CBC panel can provide valuable information, especially for patients with AP. RDW is routine part of CBC. RDW level at admission is helpful to make earlier prediction of severity of AP, especially at first-line centers, considering the disadvantages of multifactorial scoring systems. However, there is no single ideal method to assess severity of the disease. Institutional facilities influence method used for prognostic assessment of AP. Large, multicenter cohort studies are needed.

Financial Support

Authors declare that they received no financial support for this study.

Conflict of interest: None declared.

REFERENCES

1. Sarr MG, Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, et al. The new revised classification of acute pancreatitis 2012. Surg Clin North Am 2013;93:549–62. Crossref
2. Mofidi R, Duff MD, Wigmore SJ, Madhavan KK, Garden OJ, Parks RW. Association between early systemic inflammatory response, severity of multiorgan dysfunction and death in acute pancreatitis. Br J Surg 2006;93:738–44. Crossref
3. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102–11. Crossref
4. Ranson JH, Rifkind KM, Roses DF, Fink SD, Eng K, Localio SA. Objective early identification of severe acute pancreatitis. Am J Gastroenterol 1974;61:443–51.
5. Khanna AK, Meher S, Prakash S, Tiwary SK, Singh U, Srivastava A, et al. Comparison of Ranson, Glasgow, MOSS, SIRS, BISAP, APACHE-II, CTSI Scores, IL-6, CRP, and Procalcitonin in Predicting Severity, Organ Failure, Pancreatic Necrosis, and Mortality in Acute Pancreatitis. HPB Surg 2013;2013:367581. Crossref
6. Chatzicostas C, Roussomoustakaki M, Vlachonikolis IG, Notas G, Mouzas I, Samonakis D, et al. Comparison of Ranson, APACHE II and APACHE III scoring systems in acute pancreatitis. Pancreas 2002;25:331–5. Crossref
7. Taylor SL, Morgan DL, Denson KD, Lane MM, Pennington LR. A comparison of the Ranson, Glasgow, and APACHE II scoring systems to a multiple organ system score in predicting patient outcome in pancreatitis. Am J Surg 2005;189:219–22. Crossref
8. Wilson C, Heath DI, Imrie CW. Prediction of outcome in acute pancreatitis: a comparative study of APACHE II, clinical assessment and multiple factor scoring systems. Br J Surg 1990;77:1260–4. Crossref
9. Ranson JH. The timing of biliary surgery in acute pancreatitis. Ann Surg 1979;189:654–63. Crossref
10. Papachristou GI, Muddana V, Yadav D, O'Connell M, Sanders MK, Slivka A, et al. Comparison of BISAP, Ranson's, APACHE-II, and CTSI scores in predicting organ failure, complications, and mortality in acute pancreatitis. Am J Gastroenterol 2010;105:435–42. Crossref
11. Gan SI, Romagnuolo J. Admission hematocrit: a simple, useful and early predictor of severe pancreatitis. Dig Dis Sci 2004;49:1946–52. Crossref
12. Brown A, Orav J, Banks PA. Hemoconcentration is an early marker for organ failure and necrotizing pancreatitis. Pancreas 2000;20:367–72.
13. Sun B, Li HL, Gao Y, Xu J, Jiang HC. Factors predisposing to severe acute pancreatitis: evaluation and prevention. World J Gastroenterol 2003;9:1102–5. Crossref
14. Baillargeon JD, Orav J, Ramagopal V, Tenner SM, Banks PA. Hemoconcentration as an early risk factor for necrotizing pancreatitis. Am J Gastroenterol 1998;93:2130–4. Crossref
15. Corfield AP, Cooper MJ, Williamson RC, Mayer AD, McMahon MJ, Dickson AP, et al. Prediction of severity in acute pancreatitis: prospective comparison of three prognostic indices. Lancet 1985;2:403–7. Crossref
16. Fan ST, Lai EC, Mok FP, Lo CM, Zheng SS, Wong J. Prediction of the severity of acute pancreatitis. Am J Surg 1993;166:262–8. Crossref
17. Uhl W, Büchler M, Malfertheiner P, Martini M, Beger HG. PMN-elastase in comparison with CRP, antiproteases, and LDH as indicators of necrosis in human acute pancreatitis. Pancreas 1991;6:253–9. Crossref
18. Al-Bahrani AZ, Ammori BJ. Clinical laboratory assessment of acute pancreatitis. Clin Chim Acta 2005;362:26–48. Crossref
19. Imamura T, Tanaka S, Yoshida H, Kitamura K, Ikegami A, Takahashi A, et al. Significance of measurement of high-sensitivity C-reactive protein in acute pancreatitis. J Gastroenterol 2002;37:935–8. Crossref
20. Schütte K, Malfertheiner P. Markers for predicting severity and progression of acute pancreatitis. Best Pract Res Clin Gastroenterol 2008;22:75–90. Crossref
21. Pezzilli R, Billi P, Miniero R, Fiocchi M, Cappelletti O, Morselli-Labate AM, et al. Serum interleukin-6, interleukin-8, and beta 2-microglobulin in early assessment of severity of acute pancreatitis. Comparison with serum C-reactive protein. Dig Dis Sci 1995;40:2341–8. Crossref
22. Rau B, Steinbach G, Gansauge F, Mayer JM, Grünert A, Beger HG. The potential role of procalcitonin and interleukin 8 in the prediction of infected necrosis in acute pancreatitis. Gut 1997;41:832–40. Crossref
23. Stoelben E, Nagel M, Ockert D, Quintel M, Scheibenbogen C, Klein B, et al. Clinical significance of cytokines Il-6, Il-8 and C-reactive protein in serum of patients with acute pancreatitis. [Article in German] Chirurg 1996;67:1231–6. Crossref

24. Chen CC, Wang SS, Lu RH, Chang FY, Lee SD. Serum interleukin 10 and interleukin 11 in patients with acute pancreatitis. Gut 1999;45:895–9.
25. Papachristou GI. Prediction of severe acute pancreatitis: current knowledge and novel insights. World J Gastroenterol 2008;14:6273–5. Crossref
26. Novovic S, Andersen AM, Ersbøll AK, Nielsen OH, Jorgensen LN, Hansen MB. Proinflammatory cytokines in alcohol or gallstone induced acute pancreatitis. A prospective study. JOP 2009;10:256–62.
27. Assicot M, Gendrel D, Carsin H, Raymond J, Guilbaud J, Bohuon C. High serum procalcitonin concentrations in patients with sepsis and infection. Lancet 1993;341:515–8. Crossref
28. Mofidi R, Suttie SA, Patil PV, Ogston S, Parks RW. The value of procalcitonin at predicting the severity of acute pancreatitis and development of infected pancreatic necrosis: systematic review. Surgery 2009;146:72–81.
29. Bülbüller N, Doğru O, Ayten R, Akbulut H, Ilhan YS, Cetinkaya Z. Procalcitonin is a predictive marker for severe acute pancreatitis. Ulus Travma Acil Cerrahi Derg 2006;12:115–20. Crossref
30. Bradley EL. A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, Ga, September 11 through 13, 1992. Arch Surg 1993;128:586–90.
31. Tenner S, Fernandez-del Castillo C, Warshaw A, Steinberg W, Hermon-Taylor J, Valenzuela JE, et al. Urinary trypsinogen activation peptide (TAP) predicts severity in patients with acute pancreatitis. Int J Pancreatol 1997;21:105–10.
32. Neoptolemos JP, Kemppainen EA, Mayer JM, Fitzpatrick JM, Raraty MG, Slavin J, et al. Early prediction of severity in acute pancreatitis by urinary trypsinogen activation peptide: a multicentre study. Lancet 2000;355:1955–60. Crossref
33. Khan Z, Vlodov J, Horovitz J, Jose RM, Iswara K, Smotkin J, et al. Urinary trypsinogen activation peptide is more accurate than hematocrit in determining severity in patients with acute pancreatitis: a prospective study. Am J Gastroenterol 2002;97:1973–7. Crossref
34. Huang QL, Qian ZX, Li H. A comparative study of the urinary trypsinogen-2, trypsinogen activation peptide, and the computed tomography severity index as early predictors of the severity of acute pancreatitis. Hepatogastroenterology 2010;57:1295–9.
35. Ku NS, Kim HW, Oh HJ, Kim YC, Kim MH, Song JE, et al. Red blood cell distribution width is an independent predictor of mortality in patients with gram-negative bacteremia. Shock 2012;38:123–7. Crossref
36. Patel KV, Semba RD, Ferrucci L, Newman AB, Fried LP, Wallace RB, et al. Red cell distribution width and mortality in older adults: a meta-analysis. J Gerontol A Biol Sci Med Sci 2010;65:258–65. Crossref
37. Kim CH, Park JT, Kim EJ, Han JH, Han JS, Choi JY, et al. An increase in red blood cell distribution width from baseline predicts mortality in patients with severe sepsis or septic shock. Crit Care 2013;17:R282.
38. Hunziker S, Celi LA, Lee J, Howell MD. Red cell distribution width improves the simplified acute physiology score for risk prediction in unselected critically ill patients. Crit Care 2012;16:R89. Crossref
39. Şenol K, Saylam B, Kocaay F, Tez M. Red cell distribution width as a predictor of mortality in acute pancreatitis. Am J Emerg Med 2013;31:687–9. Crossref

ORİJİNAL ÇALIŞMA - *ÖZET*

Akut pankreatitte Ranson skoru ile eritrosit dağılım hacmi arasındaki korelasyon

Dr. Murat Özgür Kılıç, Dr. Canbert Çelik, Dr. Cemil Yüksel, Dr. Barış Doğu Yıldız, Dr. Mesut Tez

Numune Eğitim ve Araştırma Hastanesi, Genel Cerrahi Kliniği, Ankara

AMAÇ: Ranson kriterleri akut pankreatit (AP) şiddetini değerlendirmek için yaygın olarak kullanılır. Eritrosit dağılım genişliği (RDW) de bu gibi hastalarda mortaliteyi öngörmede yararlı bir belirteç olarak gösterilmiştir. Amaç, AP hastalarında Ranson skoru ile RDW arasındaki ilişkiyi araştırmaktır.
GEREÇ VE YÖNTEM: Toplam 202 AP hastası çalışmaya alındı. Hastalar, 48 saatten uzun süren organ yetersizliği ve/veya lokal komplikasyon varlığına bağlı olarak, hafif ve şiddetli AP olarak sınıflandırıldı.
BULGULAR: Kırk hastaya (%19.8) şiddetli AP tanısı kondu. Şiddetli AP'nin belirlenmesinde, başlangıç RDW ve Ranson skorları için hesaplanan ROC eğrisinde yüksek duyarlılık ve özgüllük değerleri elde edildi. Ranson skoru için 4'ten büyük değerler, RDW için %14 değeri cutoff değerler olarak belirlendi. Başvuru anındaki RDW değerinin 48. saat Ranson skoru ile korele olduğu saptandı ($r=0.22$, $p<0.002$). Ancak, 0. günde, RDW ile 0. saat Ranson skoru arasında korelasyon yoktu ($r=0.07$, $p=0.600$).
TARTIŞMA: Akut pankreatit şiddetini değerlendirmede tek bir ideal yöntem olmasa da, başvuru anındaki RDW seviyesi, birden çoklu skorlama sistemlerinin dezavantajları dikkate alındığında, özellikle birinci basamak sağlık merkezlerinde, AP şiddetinin erken tahmininde yararlı olabilir.
Anahtar sözcükler: Akut pankreatit; eritrosit dağılım hacmi; Ranson skoru.

Ulus Travma Acil Cerrahi Derg 2017;23(2):112–116 doi: 10.5505/tjtes.2016.27895