The Utility of Red Cell Distribution Width to Predict Mortality of Septic Patients in Tertiary Hospital of Nepal

Rajan Ghimire (biplawi.shashi@gmail.com)
Nick Simmons Institute https://orcid.org/0000-0001-5095-8477

Yogendra Man Shakya
Maharajgunj MedicalCampus, Institute of Medicine, Tribhuvan University

Tirtha Man Shrestha
Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan

Ram Prasad Neupane
Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University

Research article

Keywords: red cell distribution width, sepsis, emergency care, mortality

Posted Date: June 5th, 2019

DOI: https://doi.org/10.21203/rs.2.10110/v1

Version of Record: A version of this preprint was published at BMC Emergency Medicine on May 26th, 2020. See the published version at https://doi.org/10.1186/s12873-020-00337-8.

Abstract

Background Sepsis is common problem encountered in emergency room which needs to be intervened early. Predicting prognosis is always a difficult task in busy emergency room using present scores which has numbers of variables to calculate. Red cell distribution width (RDW) is easy, cheap and efficacious score to predict severity and mortality of patients with sepsis. Method This prospective analytical study was conducted in emergency room of Tribhuvan University Teaching Hospital among patients of age ≥16 years with clinical diagnosis of sepsis using qSOFA score. 148 patients were analyzed in study by using nonprobability purposive sampling method. Result RDW is more efficacious test to predict mortality in sepsis (Area under the Curve of 0.734; 95% C. I= 0.649-0.818) than APACHE II (AUC of 0.728; 95% C. I= 0.637 to 0.819) or SOFA (AUC of 0.680, 95% C.I =0.591-0.770). Cutoff of RDW 15.05 has sensitivity of 73% (positive likelihood ratio 1.82) and specificity of 60% (negative likelihood ratio 0.45) while cutoff of RDW 16.1 has Sensitivity of 56% (PLR 2.07) and specificity of 73% (NLR 0.6). Out of 44 patients with septic shock 16 died (36.4%) and among 104 patients without septic shock,24 died (22.9%) with odds ratio of 0.713 (p=0.555, 95% C. I= 0.231-2.194). Overall mortality was 27.02% (n=40). RDW subgroup analysis showed no mortality in low RDW (<13.1) subgroup, 3.6% mortality in moderate (13.1 to 14) RDW group, 22.0% mortality in high (14 to >15.6) RDW group and 45.9% mortality in very high (>15.6) RDW group. Significant mortality difference seen in high and very high RDW subgroup with p value 0.003 and 0.008 respectively. Conclusion RDW is more efficacious test to predict mortality in sepsis than APACHE II or SOFA. Cutoff of RDW 15.05 has sensitivity of 73% and specificity of 60%. So RDW can be used as a good prognostic score to predict severity and mortality of patients with sepsis in emergency room.

Introduction

Sepsis is defined as life threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction can be represented by an increase in the Sequential (Sepsis-related) Organ Failure Assessment (SOFA) score of 2 points or more.[1] Septic shock can be clinically identified by a vasopressor requirement to maintain a mean arterial pressure of 65 mmHg or greater and serum lactate greater than 2 mmol/L in the absence of hypovolemia.[1] Patients with infection can be identified to have sepsis if they have at least two of following clinical criteria that together constitute a new bedside clinical score termed quickSOFA (qSOFA): respiratory rate of 22/min or greater, altered mentation or systolic blood pressure of 100mmHg or less.[1,2]

Incidence of sepsis varies among different studies with a wide range from 300 to 1000 cases/100,000 persons per year.[3] Over 500,000 patients each year present to emergency department with suspected severe sepsis. [4]Sepsis incidence increases > 100 fold with the age (0.2 per 1000 in children age 10 to 14 years to 26.2 per 1000 in those > 85 years of age).[5] In one of study conducted in Tribhuvan University Teaching Hospital, 10.49% of patients showed bacterial growth in blood or bone marrow samples. [6]

Even a modest degree of organ dysfunction, when the infection is first suspected, is associated with an in-hospital mortality in excess of 10%.[1] Study of S. Lakhey et.al in one of private hospital of Nepal showed overall mortality from sepsis as 39.3% and higher mortality rate among elderly patients (46.7%).[7]A comparative meta-analysis showed 28-day mortality of 33.2% among severe sepsis patient. [8]Ongoing mortality in patients with sepsis remains elevated up to 2 years and beyond. [9]

In the emergency condition like sepsis, a tool that can predict the severity and thus the prognosis of a patient is crucial in deciding the modality of treatment including the vasopressor, possible need of ventilator, empiric antibiotics or higher group of antibiotics. In today's clinical practice a number of indicators are being used to predict prognosis of sepsis. Commonly used prognostic indicators include Acute Physiological and chronic health evaluation II (APACHE II), sequential organ failure Assessment (SOFA), Mortality in Emergency Department Score (MEDS), New York Sepsis severity score. In recent years Red cell distribution Width (RDW) is being investigated for its prognostic value in septic patients.

Red cell distribution width (RDW) is an index of variation of erythrocyte volume (i.e. ansiocytosis). It is conventionally included in a standard complete blood count (CBC) and is automatically calculated by dividing the standard deviation (SD) of erythrocyte volume from the mean corpuscular volume (MCV). The result of this equation is then multiplied by 100 to express results in percentage. RDW has been used to help classify anemia as it reflects the degree of variation in erythrocyte size. The value of this parameter increases parallel with ansiocytosis. It is conventionally increased in patients with anemia attributable to iron deficiency, deficit of folic acid/vitamin B12, patients with autoimmune disorders, myelodysplastic syndrome, hemolytic anemia, liver impairment, sickle cell disease and blood transfusions.[10]The normal range of RDW is 11.5% to 14.5% with no clinical scenarios that produce RDW <11.5%. Any process that results in the release of reticulocytes into the circulation will result in an increase in RDW.

When patients are infected, microbes release various toxins/lipopolysaccharides which activate inflammatory cascade via various interleukins, cytokines.[11]Cytokines are responsible for the clinically observable effects of the bacteremia in the host.[12] These cytokines induce direct red cell blood cell damage by erythrophagocytosis or apoptosis, interfere with iron homeostasis, inhibit erythropoiesis by myelosuppression and down regulate erythropoietin-receptor expression.[11] These mechanism is thought to lead to ansiocytosis and increased RDW. [13]

RDW is being investigated as a useful tool for predicting prognosis in various critical conditions. RDW has been utilized in diverse diseases other than traditionally for interpretation of anemia. In chronic diseases, elevated RDW was associated with increased mortality among healthy middle-aged and older adults from the general population and patients with cardiovascular disease, stroke, heart failure, and chronic dialysis. [13–21] In acute conditions, RDW can also be used as a mortality predictor among patients with acute pancreatitis, acute dyspnea during an emergency department visit, out-of-hospital cardiac arrest, and critical illnesses in ICU setting. [14,15,19,22,23] For septic patients, RDW was also found to be an independent indicator of mortality in patients with gram-negative bacteremia, community-acquired pneumonia, severe sepsis, and septic shock. [24,25]

For every 1% increment in RDW, total mortality risk increased by 14% (adjusted hazard Ratio 1.14; 95% C.I 1.11-1.17) among older adults. [20]

In the resource limited setting of developing countries like Nepal, and also in busy places like emergency room, calculating other prognostic indicators like APACHE II, MEDS, SOFA will be costly as well as time consuming. RDW is cost effective and easy tool to predict prognosis of critically ill patients including sepsis. Only few studies of this type are conducted in developed nations and as developing nations has different health set up this prospective analytical observational study is designed to find whether RDW can predict prognosis of septic patients in one of tertiary center of Nepal or not. Better efficacy of RDW as predictive score can help to guide the aggressiveness of treatment as per severity of disease.

Methodology

Aim of this study was to determine the utility of red cell distribution width (RDW) as prognostic factor in septic patients and compare with efficacy of APACHE II and SOFA scores

Study Design

This prospective observational quantitative study was conducted in Tribhuvan University Teaching Hospital (TUTH), Emergency Room, Maharajgunj, Kathmandu, Nepal from June 2017 to August 2018. Patients ≥16years with clinical diagnosis of sepsis in emergency room of TUTH were included in the study. Sepsis was diagnosed using qSOFA score. Following patients were excluded from the study:

Patient who received blood transfusion within 90 days before emergency admission.

Patient known to have long-term conditions causing anemia like sickle cell anemia, thalassemia, iron deficiency anemia.

Patient with incomplete information and data.

Patient who deny consent.

Data collection:

Patients with suspected infection and hence sepsis suggested by qSOFA score were enrolled into the study after getting formal written/oral consent from patient or legal guardian available at the Emergency room. Sampling was nonprobability and purposive. Patient’s basic demographic information, vital signs on ER arrival, symptoms and underlying diseases, provisional diagnosis and laboratory values required for analysis of RDW, APACHE II and SOFA score were collected. Outcome of patients were followed by phone calls made at 28-day from the day of ER admission. Collected data were then analyzed. Data collection was done by researcher.

Statistical analysis:

Primary outcome was the performance of RDW in predicting mortality among septic patients. The finding was compared between RDW and clinical prediction scores viz. APACHE II and SOFA. Descriptive statistics of demographic and laboratory variable are calculated as medians, numbers and percentages. Patients were further stratified a priori based on RDW results as: RDW <13.1%- low; RDW ≥13.1% -14% - moderate; RDW >14% - 15.6% - high; RDW ≥15.6% - very high. Chi square test and odd ratio was used to compare differences in mortality between groups. Binary logistic regression was used to evaluate potential confounding between risk factors, RDW and mortality. Receiver operating characteristics (ROC) curve analysis was done to evaluate the performance of RDW in predicting mortality within 28 day of ER admission. Area under the ROC curve was compared between different clinical prognosis score viz. RDW, APACHE II and SOFA. All p values <0.05 were considered statistically significant. Statistical analysis was performed using IBM SPSS (Statistical Package for Social Sciences) version 25.

Results

Total of 148 patients were analyzed. Mean age was 51.29years (S. D= 20.22) with mean age in survival group 48.4years (S. D =19.94) and in mortality group 59.10years (S. D=19.1). Maximum number of people lied in age-group 60-70 years (n=28, 18.9%) followed by 20-30 and >70 years both of which has same numbers. Data is negatively skewed (-0.217). In the study there were more female (88, 59.5%) than male (60, 40.5%).

Figure 1 histogram of RDW classification; 1=low RDW <13.1, 2= moderate RDW ≥13.1-14, 3= high RDW >14-15.6, 4= very high RDW ≥15.6

Most of patients lie in very high RDW group (n=60, 40.5%). (Figure *1*). Mean RDW was 15.933 (S.D =2.69), median was 15 (S. D= 2.69). Data for RDW groups was negatively skewed (-0.678).

As data did not follow normal distribution (negatively skewed) nonparametric test (Mann-Whitney U test) was done to test difference of distribution of Age, RDW, APACHE II and SOFA across the categories of outcome (improved and mortality). Test showed significant difference between the improved and mortality group with p value of 0.005, 0.000, 0.000, 0.002 for age, RDW, APACHE II, SOFA respectively (*Table 1*).

Bivariate logistic regression analysis was done to analyze effect of confounding factors like age, sex, presence of septic shock on mortality. Results showed no significant effect of these confounding factors on mortality except for sex (p=0.029, Odds ratio= 2.950, 95% C.I =1.120-7.773) (*Table 2*). Among the predictive scores viz. RDW, APACHE II and SOFA scores; only RDW had significant difference in predicting mortality with odds ratio of 1.551 (p=0.000003, 95% C.I =1.292-1.863). So RDW is better prognostic test to predict mortality in septic patients.

Patients were further divided into two groups sepsis and septic shock. Out of 44 patients with septic shock 16 died (36.4 %) and among 104 patients without septic shock, 24 died (23.1%) with odds ratio of 0.713 (p=0.555, 95% C.I= 0.231-2.194)(*Table 2*). Overall mortality was 27.02% (n=40).

RDW subgroup analysis showed no mortality in low RDW (<13.1) subgroup , 3.6% mortality in moderate RDW (>13.1-14) group, 22.0% mortality in high RDW (>14-15.6) group and 46.7% mortality in very high (>15.6) RDW group (Table 3). Significant mortality difference seen in high and very high RDW subgroup with p value 0.003 and 0.008 respectively. This shows increased trend of mortality with increase in RDW value and vice-versa.

Receiver Operating Characteristic (ROC) curve was used to test the efficacy of different clinical scores viz. RDW, SOFA, APACHE II to predict mortality in septic patients (Figure2). Area under the ROC curve was analyzed which shows RDW is more efficacious test to predict mortality in sepsis with AUC of 0.734 (95% C.I 0.649-0.818) than APACHE II (AUC of 0.7.28, 95% C. I= 0.637 to 0.819) or SOFA (AUC of 0.680, 95% C.I 0.591-0.770) (*Table 4*). AUC of RDW is >0.7 which is considered fair test.

Figure2 Receiver operating characteristics curve analysis for RDW, SOFA and APACHE II to predict mortality in sepsis

Cutoff of RDW 15.05 has sensitivity of 73% (positive likelihood ratio= 1.82) and specificity of 60% (negative likelihood ratio =0.45) while cutoff of RDW 16.1 has Sensitivity of 56% (positive likelihood ratio=2.07) and specificity of 73% (negative likelihood ratio = 0.6). Increasing the value of RDW decreases the sensitivity of test and increases the specificity of test.

Discussion

This prospective analytical study illustrated the significance differences in RDW levels between mortality and survivor groups of septic patients. The aim of this study was to find the performance of RDW to predict mortality of septic patients. The performance of RDW to predict mortality in septic patients was found better than other clinical scores like SOFA, APACHE II.

The overall mortality in septic patients was 27.02% (n=40) and the mortality in septic shock patients was 36.4% which is near to mortality rate shown by meta-analysis of multicenter randomized- trials by Stevenson EK and et al.[8] This meta-analysis had 33.2% mortality from severe sepsis.

Mortality was high in septic shock group than patients without septic shock (36.4% vs 23.07%). In another study, among the severely septic patients (n=2110), 13.8% died (n=290), which is significantly higher compared with the non-severe septic group (3.8%, n=187, P< 0.001). [26]

Mortality was more in very high RDW group (RDW ≥15.6) with 46.7% mortality among patients with RDW≥15.6. Mortality subsequently increased from low RDW group to very high RDW group. Kim J et al showed that RDW was a particularly strong predictor of all-cause mortality, 30 days following critical care initiation with a significant risk gradient across RDW quintiles following multivariable adjustment: RDW 13.3–14.0% OR 1.19 (95% CI, 1.08–1.30; P<0.001); RDW 14.0–14.7% OR 1.28 (95% CI, 1.16–1.42; P<0.001); RDW 14.7–15.8% OR 1.69 (95% CI, 1.52–1.86; P<0.001); RDW > 15.8% OR 2.61 (95% CI, 2.37–2.86; P<0.001); all relative to patients with RDW ≤13.3%. (1,2,3) RDW quartile was independently associated with all-cause mortality (HR = 1.95; 95% CI 1.05–3.60; p = 0.034) during 30-day post-resuscitation period. [17]

Mann-Whitney U test showed significant ability of RDW to predict mortality in septic patients (p=0.000). Further analysis was done using ROC curve and Area under the ROC curve which showed fair capacity of RDW to predict mortality in septic patients (AUC= 0.734) which is better than SOFA and APACHE II (AUC = 0.680 and 0.728). in other study the area under the receiver operating characteristic curve of RDW to predict mortality was 0.75 (95% confidence interval, 0.72–0.77), which is significantly higher than the areas under the curve of clinical prediction rules (SIRS, MEDS, and CURB65).[26]AUC of RDW is >0.7 which is considered fair test. [27]

Sensitivity of RDW with cutoff of 15.05 was 73% (Positive likelihood ratio=1.82) and Specificity of 60% (Negative likelihood ratio=0.45). Decreasing the cutoff value increases sensitivity while decreasing the specificity and vice versa. In a study of Chen et al; using 12% as a cutoff of RDW, the sensitivity in predicting mortality would be 99.4% (negative likelihood ratio: 0.30). On the other hand, the specificity in predicting mortality would be 89.9% if 17% used as the cutoff of RDW (positive likelihood ratio: 3.16). [26]

There are certain limitations in our study. All the data and patients were collected in a single center so the findings may not apply in general population. As purposive non-probability sampling method was used there is chance of selection bias. The severity of disease, patient characteristics, value of RDW and treatment protocol may vary with different institutes and hence the outcome of patients. Though the findings in patients with hematocrit <36% is also applicable, patients with undiagnosed chronic anemia may have created biasness and baseline hemoglobin of patient visiting emergency room was lacking. Sepsis was diagnosed clinically using qSOFA which has low sensitivity due to which less case might have been enrolled in study.

RDW is cheap and widely available test that has efficiency equivalent if not more than SOFA or APACHE II score. So it can be used in emergency room or bedside or in set-up where ABG is not available to predict severity /mortality of septic patients. This study provides level III evidence for its use in day to day life. However, multicenter study involving different geographical condition and randomized sampling method will help reduce biasness involved in the study. Separate studies need to be done before using findings to patients with anemia of different causes.

Conclusion

RDW is more efficacious test to predict mortality in sepsis in comparison to APACHE II or SOFA. Cutoff of RDW 15.05 has sensitivity of 73% and specificity of 60%. So RDW can be used as a good prognostic score to predict severity and mortality of patients with sepsis in

emergency room.

Abbreviations

APACHE II: Acute Physiological and Chronic Health Evaluation II; AUC: Area under the curve; ER: Emergency Room; qSOFA: quick Sequential Organ Failure Assessment; RDW: red cell distribution width; SOFA: Sequential Organ Failure Assessment

Declarations

Acknowledgements

Not applicable

Funding

This study was funded by authors.

Availability of data

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors Contributions

As this study was conducted for partial fulfillment of requirement of Doctor of Medicine in General Practice and Emergency Medicine, RG conducted the whole of the process of study. YMS, TMS and RPN guided through the process as guide and co-guides respectively.

Ethical consideration:

Ethical clearance was done from Institutional Review Board of Institute of Medicine, Tribhuvan University. Written/oral consent was taken from patient or legal guardian.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests

Authors details

[1] MD General Practice and Emergency Medicine, Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University. [2] Professor and Head of Department, Department of General Practice and Emergency Medicine, Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University. [3,4] Department of General Practice and Emergency Medicine, Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University

References

1. Singer M, Deutschman Clifford S. SCW, Manu S-H, Djillali A, Michael B, Bellomo R, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315:801–10. DOI:10.1001/jama.2016.0287.

2. Jones AE, Stephen T, Kline JA. The Sequential Organ Failure Assessment score for predicting outcome in patients with severe sepsis and evidence of hypoperfusion at the time of emergency department presentation. Crit Care Med. 2009;37:1649–54. DOI:10.1097/CCM.0b013e31819def97

3. Gaieski DF, Edwards JM, Kallan MJ, Carr BG. Benchmarking the Incidence and Mortality of Severe Sepsis in the United States*. Crit Care Med. 2013;41:1167–74. DOI:10.1097/CCM.0b013e31827c09f8

4. Puskarich, Michael A; Jones AE. Sepsis. In: Tintinalli, Judith E; Stapczynski, J. Sthephan; Ma, O John; yealy, Donald M; Meckler, Garth D; Cline DM, editor. Tintinalli's Emerg Med A Compr study Guid. 8th ed. McGraw-Hill; 2016. p. 1021–9.

5. Angus D, Linde-Zwirble W, Lidicker J, Clermont G, Carcillo J, Pinsky M. Epidemiology of severe sepsis in the United States_ analysis of incidence, outcome, and associated costs of care. Crit Care Med. 2001;29:1303–10.

6. Chaudhary R, Karmacharya S, Shrestha S, Dahal RK, Mishra SK, Banjade NR, et al. Incidence of Bacteremia and Septicemia in patients attending in tertiary care center , Nepal [Internet]. J. Inst. Med. 2012. p. 32–8. Available from: www.jiom.com.np

7. Lakhey S, Karki B, Shrestha B, Shakya S, Pandey SB. Sepsis_ a private hospital experience in Nepal _ Lakhey _ Journal of Institute of Medicine. J Inst Med. 2006;28.

8. Stevenson EK, Rubenstein AR, Radin GT, Wiener RS, Walkey AJ. Two Decades of Mortality Trends among Patients with Severe Sepsis: A Comparative Meta-analysis Elizabeth. Crit Care Med. 2014;42:625–31. DOI:10.1097/CCM.0000000000000026.

9. Winters BD, Eberlein M, Leung J, Needham DM, Pronovost PJ SJ. Long-term mortality and quality of life in sepsis_ a systematic review. Crit Care Med. 2010;38:1276–86. DOI:10.1097/CCM.0b013e3181d8cc1d

10. Lippi G, Plebani M. Red blood cell distribution width (RDW) and human pathology . One size fits all. Clin Chem Lab Med. 2014;1–3. DOI:10.1515/cclm-2014-0585

11. Gogos CA, Drosou E, Bassaris HP, Skoutelis A. Pro- versus Anti-inflammatory Cytokine Profile in Patients with Severe Sepsis : A Marker for Prognosis and Future Therapeutic Options [Internet]. J. Infect. Dis. 2000. p. 176–80. Available from: https://academic.oup.com/jid/article-abstract/181/1/176/892417

12. Kobayashi M, Tsuda Y, Yoshida T, Takeuchi D, Utsunomiya T, Takahashi H, et al. Bacterial Sepsis and Chemokines. Curr Drug Targets. 2006;7:119–34. DOI:10.2174/138945006775270169

13. Bazick HS, Chang D, Mahadevappa K, Gibbons FK, Christopher KB. Red cell distribution width and all-cause mortality in critically ill patients*. Crit Care Med. 2011;39:1913–21. DOI:10.1097/CCM.0b013e31821b85c6

14. Musikasinthorn C, Harvey S, McKnight CL, Inouye D, Kuroda J, Nakamur C, et al. Red cell distribution width (RDW) as predictor of hospital mortality in critically ill patients. Crit Care Med. 2014;42:466.

15. Bazick HS, Chang D, Mahadevappa K, Gibbons FK, Christopher KB. Red Cell Distribution Width and all cause mortality in critically ill patients. Crit Care Med. 2011;39:1913–21. DOI:10.1097/CCM.0b013e31821b85c6.Red

16. Uyarel H, Isik T, Ayhan E, Ergelen M. Red Cell Distrubition Width (RDW): A novel risk factor for cardiovascular disease. Int J Cardiol [Internet]. Elsevier Ireland Ltd; 2011;351–2. Available from: http://dx.doi.org/10.1016/j.ijcard.2011.10.126 DOI:10.1016/j.ijcard.2011.10.126

17. Kim J, Kim K, Hyuk J, Hwan Y, Eui J, Yun T, et al. Red blood cell distribution width as an independent predictor of all-cause mortality in out of hospital cardiac arrest . Resuscitation [Internet]. European Resuscitation Council, American Heart Association, Inc., and International Liaison Committee on Resuscitation.~Published by Elsevier Ireland Ltd; 2012;83:1248–52. Available from: http://dx.doi.org/10.1016/j.resuscitation.2012.01.038 DOI:10.1016/j.resuscitation.2012.01.038

18. Sicaja M, Pehar M, Star B, Vuleti V, Bo V. Red blood cell distribution width as a prognostic marker of mortality in patients on chronic dialysis : a single center , prospective longitudinal study. Croat Med J. 2013;54:25–32. DOI:10.3325/cmj.2013.54.25

19. Hong N, Oh J, Kang S, Kim S, Won H, Chan J, et al. Red blood cell distribution width predicts early mortality in patients with acute dyspnea. Clin Chim Acta [Internet]. Elsevier B.V.; 2012;413:992–7. Available from: http://dx.doi.org/10.1016/j.cca.2012.02.024 DOI:10.1016/j.cca.2012.02.024

20. Patel K V, 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;65A:258–65. DOI:10.1093/gerona/glp163

21. Ani C, Ovbiagele B. Elevated red blood cell distribution width predicts mortality in persons with known stroke. J Neurol Sci [Internet]. Elsevier B.V.; 2009;277:103–8. Available from: http://dx.doi.org/10.1016/j.jns.2008.10.024 DOI:10.1016/j.jns.2008.10.024

22. Perlstein TS, Weuve J, Pfeffer MA, Beckman JA. Red blood cell distribution width and mortality risk in a community-based prospective cohort: NHANES III: RDW and mortality risk. Arch Intern Med. 2009;169:588–94. DOI:10.1001/archinternmed.2009.55

23. 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. DOI:10.1016/j.ajem.2012.12.015

24. Jo YH, Kim K, Lee JH, Kang C, Kim T, Rn HP, et al. Red cell distribution width is a prognostic factor in severe sepsis and septic shock. Am J Emerg Med [Internet]. Elsevier Inc.; 2013;31:545–8. Available from: http://dx.doi.org/10.1016/j.ajem.2012.10.017 DOI:10.1016/j.ajem.2012.10.017

25. 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 [Internet]. 2013;17. Available from: http://ccforum.com/content/17/6/R282 DOI:

26. Chen C-K, Lin S-C, Wu C-C, Chen L-M, Tzeng I-S, Chen K-F. The utility of red cell distribution width to predict mortality for septic patients visiting the emergency department. Medicine (Baltimore) [Internet]. 2016;95:e3692. Available from: http://dx.doi.org/10.1097/MD.0000000000003692 DOI:10.1097/MD.0000000000003692

27. Tape TG. The Area Under an ROC Curve [Internet]. Interpret. Diagnostic Test. [cited 2018 Oct 22]. Available from: http://gim.unmc.edu/dxtests/ROC3.htm

Tables

Table 1 Mann-Whitney U test for outcome

Variable	Mann-Whitney U-Test	p-value
Age	2808.5	0.005
RDW	3422.0	0.000
APACHE II	3119.5	0.000
SOFA	2866.5	0.002

Table 2 Binary logistic regression analysis of confounding factors and prognosis predictive scores

	Outcome										
	Improved/Cured (N=108)			Mortality (N=40)			p-value	Odds Ratio	95% C.I		
	Mean	Row %	n	Mean	Row %	n			Lower	Upper	
Age (years)	48.4	73.0%	108	59.10	27.0%	40	0.101	1.250	0.958	1.632	
Hematocrit %	35.3	73.0%	108	33.6	73.0%	40	0.315	0.979	0.941	1.020	
SOFA	6	73.0%	108	8	27.0%	40	0.062	1.221	0.990	1.506	
APACHE II	16	73.0%	108	21	27.0%	40	0.157	1.053	0.983	1.131	
RDW	15.2	73.0%	108	17.9	27.0%	40	0.000003	1.551	1.292	1.863	
Sex	Male	-	65.0%	39	-	35.0%	21	0.029	2.950	1.120	7.773
	Female	-	78.4%	69	-	21.6%	19				
Septic shock	Yes	-	63.6%	28	-	36.4%	16	0.555	0.713	0.231	2.194
	No	-	76.9%	80	-	23.1%	24				

Table 3 Binary logistic regression of RDW subgroup and outcome

RDW Classification	Improved/Cured (N=108)			Mortality (N=40)			Odds Ratio	p value	95% C.I	
	N	Row %	Column %	N	Row %	Column %			Lower	Upper
Low (<13.1)	10	100.0%	9.3%	0	0.0%	0.0%	0.000	0.003	0.000	0.000
Moderate (≥13.1-14)	27	96.4%	25.0%	1	3.6%	2.5%	0.00	0.999	0	0
High (>14-15.6)	39	78.0%	36.1%	11	22.0%	27.5%	0.042	0.003	0.005	0.332
Very high (≥15.6)	32	53.3%	29.6%	28	46.7%	70.0%	0.332	0.008	0.139	0.746

Table 4 Area under the ROC curve for RDW, APACHE II, SOFA to predict mortality of sepsis

Test Variable(s)	Area	Sig.	95% Confidence Interval	
			Lower Bound	Upper Bound
SOFA	0.680	0.001	0.591	0.770
RDW	0.734	0.000	0.649	0.818
APACHE II	0.728	0.000	0.637	0.819

Figures

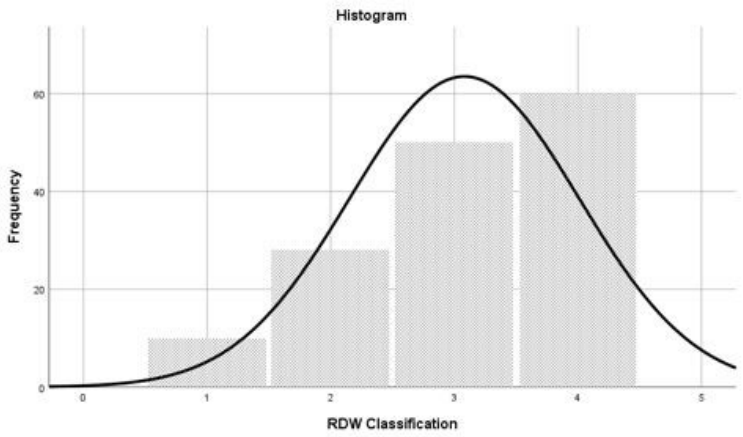

Figure 1

1 histogram of RDW classification; 1=low RDW <13.1, 2= moderate RDW ≥13.1-14, 3= high RDW >14-15.6, 4= very high RDW ≥15.6

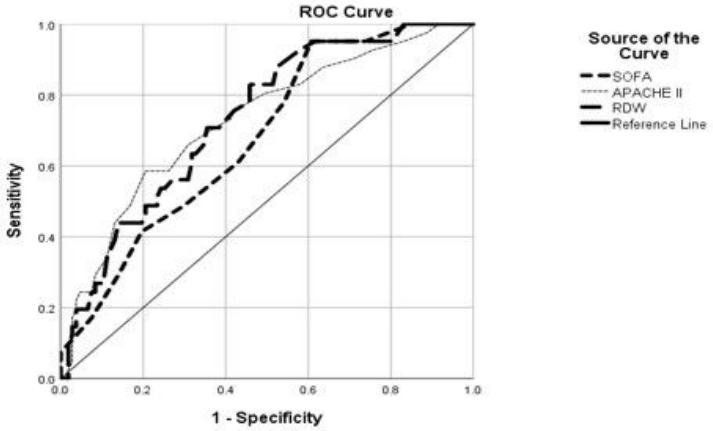

Figure 2

Receiver operating characteristics curve analysis for RDW, SOFA and APACHE II to predict mortality in sepsis