ORIGINAL ARTICLE

The qSOFA score combined with the initial red cell distribution width as a useful predictor of 30 day mortality among older adults with infection in an emergency department

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Abstract

Purpose This study aimed to investigate whether the qSOFA and initial red cell distribution width (RDW) in the emergency department (ED) are associated with mortality in older adults with infections who visited the ED.

Methods This was a retrospective study conducted in 5 EDs between November 2016 and February 2017. We recorded age, sex, comorbidities, body temperature, clinical findings, and initial laboratory results, including the RDW. The initial RDW values and the qSOFA criteria were obtained at the time of the ED visit. The primary outcome was 30 day mortality.

Results A total of 1,446 patients were finally included in this study, of which 134 (9.3%) died within 30 days and the median (IQR) age was 77 (72, 82) years. In the multivariable analysis, the RDW (14.0–15.4%) and highest RDW (> 15.4%) quartile were shown to be independent risk factors for 30 day mortality (OR 2.12; 95% CI 1.12–4.02; $p = 0.021$) (OR 3.35; 95% CI 1.83–6.13; $p < 0.001$). The patients with qSOFA 2 and 3 were shown to have the high odds ratios of 30-day mortality (OR 3.50; 95% CI 2.09–5.84; $p < 0.001$) (OR 11.30; 95% CI 5.06–25.23; $p < 0.001$). The qSOFA combined with the RDW quartile for the prediction of 30 day mortality showed an AUROC value of 0.710 (0.686–0.734).

Conclusion The qSOFA combined with the initial RDW value was associated with 30-day mortality among older adults with infections in the ED. The initial RDW may help emergency physicians predict mortality in older adults with infections visiting the ED.

Keywords Emergencies · Aged · Red cell distribution width · Infection

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Introduction

Older adults are vulnerable to infection, and in individuals with inflammatory diseases, the condition deteriorates rapidly, frequently leading to sepsis and death [1–3]. Due to the aging of society, the number of elderly patients is increasing, and the frequency of visits to the emergency department (ED) is also increasing [4–7]. In addition, many elderly patients with multiple comorbidities are complicated, and accurate diagnosis and treatment are often delayed in the ED [7, 8]. Therefore, it is important to predict 30 day mortality in older adults who visit the ED with an infection as soon as possible to predict the progression of severity and to perform prompt management for the older adult. However, there are few studies assessing the association between prognostic factors and 30 day mortality in older adults with infections who visit the ED.

Red blood cell distribution width (RDW) is a measure of differences in the range of red blood cell (RBC) volume and is mainly used to differentiate the cause of anemia or other conditions [9, 10]. A recent study suggested that a higher RDW value is associated with increased mortality risk in older adults, regardless of age-associated diseases [11].

The quick Sepsis Related Organ Failure Assessment (qSOFA) score was calculated by assigning 1 point each for a respiratory rate greater than or equal to 22 breaths/min, systolic blood pressure less than or equal to 100 mmHg, and any alteration in mental status. The total score was then calculated by adding the individual scores for the 3 elements. The presence of 2 or more of these criteria, which is considered a positive qSOFA score, suggests a high risk of poor outcome in patients with suspected infection [12]. These patients should be more thoroughly assessed for evidence of organ dysfunction in ED. According to the results of a previous study, the qSOFA score showed better predictive validity when comprehensively comparing the SOFA score and the systemic inflammatory response syndrome (SIRS) criteria outside the intensive care unit (ICU) [13–15]. Several studies have reported that a positive qSOFA score is useful for predicting the 30 day mortality of patients who visit the ED, but the sensitivity of the qSOFA score is low [16–18]. Furthermore, studies that predict the 30 day mortality of older adults who visit the ED with infections using the qSOFA and RDW have rarely been conducted. In addition, early recognition and prompt treatment in ED are important because elderly patients with infections can quickly develop sepsis and have high mortality rates.

Therefore, we hypothesized that using two prognostic factors, the qSOFA score and RDW value, which can be determined quickly and easily in the ED, would be useful and more accurate in predicting the 30 day mortality of older adults who visit the ED with infections.

Methods

This study is a retrospective study that was conducted by analyzing medical records. Among subjects over 65 years of age who visited five regional EDs from November 2016 to February 2017 in the Republic of Korea, patients were admitted to a general hospital ward or the ICU via the 5 EDs. To confirm 30 day mortality, the patients were classified into the nonsurvivor group and the survivor group on the basis of 30 day mortality after the date of the visit to the ED. If the patient was discharged within 30 days, the ED and outpatient records of the hospital were reviewed to confirm survival. This study was approved by our institutional review board. As the clinical measurements collected were routine due to the retrospective study, informed patient consent was unnecessary.

We obtained the following demographic and clinical data from the medical records of the study participants: age; sex; hypertension, diabetes, chronic renal disease, cardiovascular disease, and malignancy status; and consciousness at the time of visit [Glasgow Coma Scale (GCS)]. Systolic blood pressure (SBP), diastolic blood pressure, pulse rate, respiratory rate, and body temperature, white blood cell (WBC) count, neutrophil count, hemoglobin, RDW, BUN, creatinine, and total bilirubin were investigated in the initial blood test performed in the ED at the time of the visit. When patients visited the ED, qSOFA was determined based on initial mental status, SBP, respiratory rate, and the use of vasopressors and ventilators in the ED.

Statistical analysis

SPSS version 24.0 (SPSS, Inc., Chicago, IL, USA) was used for the statistical analysis of the collected data. A normal distribution was confirmed for the continuous variables; the median and quartile are expressed, and the data were analyzed using the Mann–Whitney U test. Noncontinuous variables are expressed in terms of frequency and percentage and were analyzed using the chi-square test. RDW was divided into 4 categories using interquartile ranges (IQR) of < 13.0%, 13.0–13.9%, 14.0–15.4% and > 15.4%. Demographic data, qSOFA scores and laboratory data of older adults were analyzed according to RDW quartiles.

To analyze the predictors related to 30 day mortality, a univariable logistic analysis was performed, and then the variables related to 30 day mortality were identified to perform multivariable logistic regression analysis. The results of the multivariable analysis are presented as the odds ratio (OR) and 95% confidence interval (95% CI). The area under the curve was calculated using the receiver operatory characteristic curve (ROC curve), the appropriate cut-off value was selected using the Youden index (J), and sensitivity and specificity were determined. Statistical significance was considered when the p value was less than 0.05.

Results

Characteristics of the study population

Of the 3405 older adults admitted to the general ward or the ICU via the ED with suspected infection during this period, 1959 patients were excluded due to incomplete data or missing initial RDW in the ED. We ultimately included a total of 1446 patients. The most common infection was respiratory infection (616 patients; 42.6%) (Fig. 1).

The median (IQR) age was 77 (72–82) years, and 722 (49.9%) patients were female. Age and sex did not show significant differences between the nonsurvivor and

survivor groups ($p = 0.063$, $p = 0.869$). The most common comorbidities were hypertension (798 patients; 55.2%) and diabetes mellitus (502 patients; 34.7%). However, comorbidities except malignancy did not show significant differences between the two groups. The malignancy frequency was 36 (26.9%) in the nonsurvivors and 167 (12.7%) in the survivors ($p < 0.001$). The rate of reduced mental capacity on admission in the ED (GCS < 15) was more frequent in nonsurvivors (41.0% vs. 18.4%; $p < 0.001$). Forty-four patients had a qSOFA score ≥ 2 in the nonsurvivors (32.8% vs. 11.5%; $p < 0.001$). The non-surviving elderly patients had significantly higher median WBC counts (10^9/L) (11.5 vs. 9.7; $\rho = 0.011$) and neutrophil counts (10^9/L) (8.9 vs. 7.5; $\rho = 0.016$). The markers of renal function, including urea nitrogen and creatinine, were all significantly different between the two groups ($p < 0.001$, $p = 0.003$). The RDW showed a significantly higher median (IQR) in non-survivors (14.8% vs. 13.9%; $p < 0.001$) (Table 1).

The clinical characteristics of the patients according to the interquartile ranges of the initial RDW level in the ED were analyzed and are shown in Table 2. The factors that significantly differed among the four RDW quartile groups included qSOFA, Hemoglobin, BUN and creatinine ($p = 0.038$, $p < 0.001$, $p < 0.001$, $p < 0.001$). Additionally, 30 day mortality, ventilator application and use of vasopressors in the ED were significantly different across the four RDW quartiles ($p < 0.001$, $p < 0.001$, and $p < 0.001$, respectively) (Table 2).

Prediction of 30 day mortality in older adults with infections

In the univariable analysis, the RDW interquartile range (14.0–15.4%, > 15.4%), qSOFA score and BUN were significantly associated with the 30-day mortality of older adults with infections. In the multivariable analysis, the RDW (14.0–15.4%) and highest RDW (> 15.4%) quartile were shown to be independent risk factors for 30-day mortality (OR 2.12; 95% CI 1.12–4.02; $p = 0.021$) (OR 3.35; 95% CI 1.83–6.13; $p < 0.001$). Additionally, patients with qSOFA 3 were shown to have the highest odds ratio of 30 day mortality (OR 11.30; 95% CI 5.06–25.23; $p < 0.001$) (Table 3).

In the prediction of the 30 day mortality of older adults with infections in the ED through ROC curve analysis, the qSOFA score showed an AUROC value of 0.659 (0.634–0.683), and a qSOFA score ≥ 2 had a sensitivity of 32.8% (95% CI

Fig. 1 Flow chart of the study population
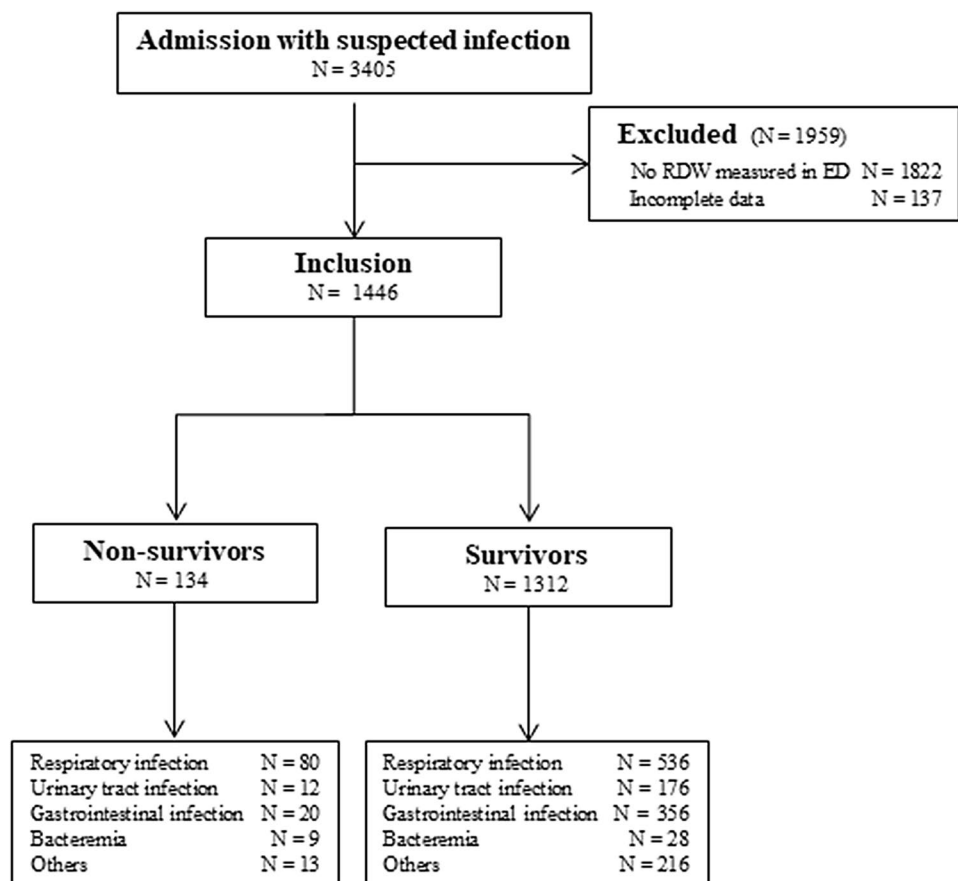
Table 1 Baseline characteristics of older adults with infections visiting the ED

Characteristic	All	Non survivor (n = 134)	Survivor (n = 1312)	p value
Age (years) (IQR)	77 (72–82)	79 (73–83)	77 (72–82)	0.063
Gender, female, n (%)	722 (49.9)	66 (49.3)	656 (50.0)	0.869
Comorbidities, n (%)				
Diabetes mellitus	502 (34.7)	38 (28.4)	464 (35.4)	0.105
Hypertension	798 (55.2)	64 (47.8)	734 (55.9)	0.070
Chronic renal disease	174 (12.0)	14 (10.4)	160 (12.2)	0.567
Cardiovascular disease	123 (8.5)	8 (6.0)	115 (8.8)	0.268
Malignancy	203 (14.0)	36 (26.9)	167 (12.7)	< 0.001
GCS < 15 on admission, n (%)	297 (20.5)	55 (41.0)	242 (18.4)	< 0.001
Initial vital signs				
Systolic BP (mmHg)	130 (110–149)	119.5 (90.0–140.0)	130 (111.0–150.0)	< 0.001
Diastolic BP (mmHg)	72 (60–82)	68 (51.0–80.0)	72.0 (61.0 -83.0)	0.001
Heart rate (beats/min)	94 (79–107)	99 (82–112)	93 (78.0–107.0)	0.009
Respiratory rate (breaths/min)	20 (18–20.3)	20 (20.0–24.0)	20 (18.0–20.0)	< 0.001
Body temperature (°C)	36.8 (36.3–37.5)	36.8 (36.0–37.2)	36.8 (36.3–37.5)	0.033
qSOFA, n (%)				
0	774 (53.5)	42 (31.3)	732 (55.8)	< 0.001
1	477 (33.0)	48 (35.8)	429 (32.8)	
2	164 (11.3)	31(23.1)	133 (10.1)	
3	31 (2.1)	13 (9.7)	18 (1.4)	
Laboratory results, median (IQR)				
WBC count (10^9/L)	9.9 (6.8–14.2)	11.5 (6.9–16.8)	9.7 (6.8–13.9)	0.011
Neutrophil count (10^9/L)	7.6 (4.8–11.5)	8.9 (5.0–13.9)	7.5 (4.7–11.3)	0.016
Hemoglobin (g/dL)	11.3 (9.7–12.8)	10.6 (8.9–12.1)	11.4 (9.8–12.8)	0.001
BUN (mg/dL)	23.1 (15.1–38.7)	30.4 (20.9–50.0)	22.3 (15.0–36.4)	< 0.001
Creatinine (mg/dL)	1.1 (0.8–1.7)	1.3 (0.8–2.6)	1.1 (0.8–1.6)	0.003
Total bilirubin (µmol/L)	0.7 (0.5–1.1)	0.8 (0.5–1.5)	0.7 (0.5–1.1)	0.019
RDW (%)	14.0 (13.0–15.5)	14.8 (13.6–17.3)	13.9 (12.9–15.4)	< 0.001

ED emergency department, *GCS* Glasgow Coma Scale, *BP* blood pressure, *qSOFA* quick Sepsis Related Organ Failure Assessment, *WBC* white blood cell, *RDW* red cell distribution width

25.0–41.5) and specificity of 88.5% (95% CI 86.6–90.2%) for predicting 30 day mortality. The AUROC value of the initial RDW quartile value was 0.630 (0.604–0.655) and the initial RDW value (≥ 14%) had a sensitivity of 67.9% (95% CI 59.3–75.7) and specificity of 51.7% (95% CI 48.9–54.4%) for predicting 30 day mortality. When the qSOFA score was combined with the RDW quartile for the prediction of 30 day mortality, the AUROC value was 0.710 (0.686–0.734). When a qSOFA score ≥ 2 or an RDW value ≥ 14.0% at the ED visit was used as a cut off, the sensitivity was 79.1% (95% CI 71.2–85.6), and the specificity was 46.6% (95% CI 43.8–49.3%) (Fig. 2).

Discussion

In this study, we found that the initial RDW value and qSOFA score were useful prognostic factors in predicting the 30 day mortality of older adults with infections in the ED. The initial RDW quartile showed a stepwise association with 30 day mortality in older adults with infections. Among older adults with infections, the highest quartile of RDW (> 15.4%) was associated with a 30 day mortality rate of 15.1%. In multivariable analysis, a qSOFA score ≥ 2 was a strong independent predictor of 30 day mortality, but it had low sensitivity. The ROC curve analysis showed that the combination of qSOFA score and initial RDW had moderate power to predict 30 day mortality.

RDW is an inexpensive blood test item that can be easily obtained at a low cost in the ED; RDW is the distribution of erythrocyte size, indicating the range of red blood

Table 2 Clinical characteristics stratified according to RDW quartiles

	< 13.0% n = 350	13.0–13.9% n = 371	14.0–15.4% n = 355	> 15.4% n = 370	p value
Age (years) (IQR)	76.5 (71–82)	78 (72–82)	78 (73–82.5)	78 (72–83)	0.144
Gender, female, n (%)	192 (54.9)	170 (45.8)	170 (47.9)	190 (51.4)	0.079
qSOFA score, n (%)					
0	207 (59.1)	205 (55.3)	182 (51.3)	180 (48.6)	0.038
1	115 (32.9)	112 (30.2)	120 (33.8)	130 (35.1)	
2	23 (6.6)	44 (11.9)	47 (13.2)	50 (13.5)	
3	5 (1.4)	10 (2.7)	6 (1.7)	10 (2.7)	
WBC count (10^9/L)	9.6 (6.9–13.7)	10.1 (6.9–14.7)	10.0 (6.9–14.2)	9.9 (6.7–14.1)	0.661
Neutrophil count (10^9/L)	7.4 (4.8–10.9)	7.9 (4.8–12.7)	7.5 (4.8–11.5)	7.5 (4.7–11.3)	0.650
Hemoglobin (g/dL)	12.3 (11.2–13.6)	12.0 (10.4–13.3)	11.1 (9.8–12.4)	9.6 (7.9–11.2)	< 0.001
BUN (mg/dL)	18.5 (13.8–27.6)	22.2 (14.9–35.4)	26.6 (16.4–45.3)	27.1 (18.0–46.5)	< 0.001
Creatinine (mg/dL)	0.9 (0.8–1.2)	1.1 (0.8–1.5)	1.2 (0.8–1.9)	1.2 (0.9–2.1)	< 0.001
Total bilirubin (mg/dL)	0.7 (0.5–1.1)	0.7 (0.5–1.1)	0.7 (0.5–1.1)	0.7 (0.5–1.4)	0.114
30 day mortality, n (%)	15 (4.3)	28 (7.5)	35 (9.9)	56 (15.1)	< 0.001
Vasopressor at ED, n (%)	20 (5.7)	41 (11.1)	53 (14.9)	54 (14.6)	< 0.001
Ventilator at ED, n (%)	16 (4.6)	30 (8.1)	47 (13.2)	29 (7.8)	0.001

RDW red cell distribution width, *qSOFA* quick Sepsis Related Organ Failure Assessment, *WBC* white blood cell

**Table 3** Odds ratios of risk factors for mortality within 30 days

	Univariable analysis (95% CI)	p value	Multivariable analysis (95% CI)	p value
RDW (quartile)				
< 25% (< 13.0%)	(Reference)		(Reference)	
25–50% (13.0–13.9%)	1.82 (0.96–3.48)	0.068	1.57 (0.81–3.05)	0.180
50–75% (14.0–15.4%)	2.44 (1.31–4.56)	0.005	2.12 (1.12–4.02)	0.021
> 75% (> 15.4%)	3.98 (2.21–7.19)	< 0.001	3.35 (1.83–6.13)	< 0.001
qSOFA score				
0	(Reference)		(Reference)	
1	1.95 (1.27–3.00)	0.002	1.87 (1.21–2.89)	0.005
2	4.06 (2.47–6.70)	< 0.001	3.50 (2.09–5.84)	< 0.001
3	12.59 (5.78–27.41)	< 0.001	11.30 (5.06–25.23)	< 0.001
Hemoglobin (g/dL)	1.01 (1.00–1.02)	0.156		
BUN (mg/dL)	1.01 (1.00–1.01)	0.002	1.00(1.00–1.01)	0.132
Creatinine (mg/dL)	1.03 (0.98–1.07)	0.236		

RDW red cell distribution width, *qSOFA* quick Sepsis Related Organ Failure Assessment

cell size. The RDW value increases when the production of red blood cells is less efficient or when more destruction occurs [9, 10]. Several studies have shown that a high RDW value is associated with an increased 30 day mortality risk in different clinical settings, such as in patients with clinically significant cardiovascular disease, stroke, septic shock, bacteremia and community-acquired pneumonia [19–22]. Although the exact reason RDW is high in critically ill or ICU patients is not clearly known, the elevation of RDW value is mainly due to an increase in inflammatory cytokines [23]. Proinflammatory cytokines are activated in critically ill or ICU patients and increase inflammatory cytokines such as tumor necrosis factor α, interleukin 1β, and interleukin 6. Proinflammatory cytokines inhibit erythropoietic factors and affect iron metabolism and bone marrow function. As a result, immature erythrocytes appear in circulating blood and induce an increase in RDW [9, 10, 23–25]. In a previous study, the highest RDW quartile (> 15.6%) was associated with an in-hospital mortality rate of 16.7%, whereas
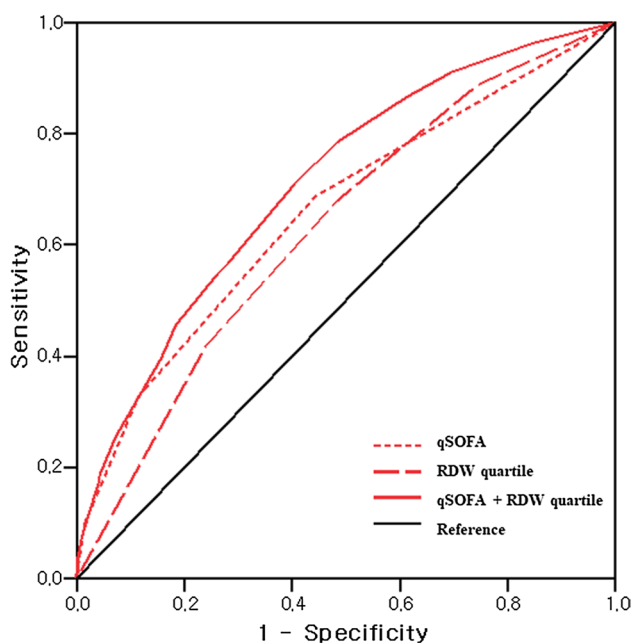
Fig. 2 Receiver operating characteristic curve of the initial RDW quartile and qSOFA score for the prediction of 30 day mortality

the rate in the lowest quartile (< 13.1%) was only 1.6% in septic adults visiting the ED. RDW quartile was found to be an independent predictor of in-hospital mortality in septic adults [20]. In this study, the 30 day mortality rate in the lowest quartile of RDW (< 13.0%) was 4.3%, and an RDW value of ≥ 14% predicted 30 day mortality with a sensitivity of 67.9% and specificity of 51.7% in older adults with infection.

In very elderly patients (≥ 80 years) with bloodstream infections, in-hospital mortality was independently associated with qSOFA ≥ 2 and showed an odds ratio of 4.7 [26]. However, the initial qSOFA score of elderly patients in the ED may be ambiguous, and it may not reflect the physiologic status of the elderly with infections or the possibility of progression to sepsis. A change in mental status in the elderly is a common chief complaint in patients visiting the ED and is often associated with infection [27]. Elderly patients with normal vital signs and altered mental status may not have a high qSOFA score at the time of the ED visit. In a study of 117 elderly patients with sepsis, an initial qSOFA score < 2 was observed in 50% of non-survivors. Nonsurvivors with a qSOFA score < 2 had higher RDW levels (17.0 ± 3.3%) than survivors (15.3 ± 1.4%). They showed that RDW could be a useful parameter of poor prognosis in elderly sepsis patients [28]. In our study, the qSOFA score was less than 2 points in 67.2% of nonsurvivors, and the sensitivity was 32.8% for the prediction of 30 day mortality. This low sensitivity of qSOFA as a screening tool for ED of older adults has been a cause of concern since early-phase recognition and prompt treatment

are the most important aspects of sepsis management. Additionally, the APACHE II and SOFA scores have been validated in several studies to quantify the severity of various illnesses, and the high sensitivity and discrimination ability of SOFA has been revealed, particularly in patients in the ICU. However, these methods have the disadvantage of being complicated to calculate and taking a long time to measure in the ED to obtain multiple values [29, 30]. Therefore, we combined the RDW value with qSOFA, which can be quickly confirmed in the ED. The sensitivity value of predicting 30 day mortality was low when the only qSOFA was used, but it increased by including the RDW value. This combination of qSOFA score and RDW value is thought to be useful for predicting the severity of infections among older adults who visit the ED and helping actively initiate early critical care.

Our study had several limitations. First, this was a retrospective study, which was subject to selection bias and errors of documentation and data entry when the patient information was missing or the medical records were incomplete. Second, although this study is a multicenter study, there is a limit to the generalization of the results because the sample size was small, and the analysis was limited to only patients who died within 30 days. Third, factors that can affect RDW (vit B12, folic acid, zinc, previous erythrocyte values, and the presence or absence of blood transfusions) may affect the results. Thus, this conclusion should be confirmed by a prospective study with a larger sample size, and long-term mortality prediction is also necessary.

In conclusion, we found that the combination of RDW and qSOFA can be considered a practical tool for the early prediction of 30 day mortality in older adults with infections who visited the ED. The initial RDW may be useful for emergency physicians as an inexpensive easily calculable predictor of mortality in older adults with infections visiting the ED.

Compliance with ethical standards

consent was unnecessary, which was confirmed by the Institutional Review Board.

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