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ORIGINAL RESEARCH

Should lactate levels be combined with rapid emergency medicine scores (REMS) to predict outcomes of patients with dyspnea

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Abstract

This study analyzes the effectiveness of adding lactate levels to the Rapid Emergency Medicine Score (REMS) scoring system to better predict short-term mortality and outcomes in patients over 40 years of age who present to the emergency department (ED) with dyspnea. This prospective observational study recruited all consecutive patients with shortness of breath as their chief complaint. Patients were evaluated using REMS and categorized in the ED as low-, intermediate-, or high-risk. In-hospital outcomes and the survival rates of the patients were recorded. The patients' REMS points and lactate levels were analyzed together to elicit the REMS+L scores used to predict mortality and outcomes. A total of 1044 patients were included in the study. The majority (64.8%, n = 677) of the patients received diagnoses related to the respiratory system, 9.9% (n = 103) with the cardiovascular system, and 25.3% (n = 264) with nonspecific diagnoses. A total of 31% (n = 324) of the patients were hospitalized, while the majority (78%, n = 253) were admitted to an intensive care unit. A total of 104 (10%) died within 28 days, with 23 of those deaths (2.2%) occurring within 2 days. The diagnostic accuracies of lactate, REMS, and REMS+L values were calculated using receiver operating characteristics (ROC) analysis and revealed that the REMS+L score ($p < 0.001$) was more accurate than the lactate measurements ($p < 0.001$) and REMS score ($p < 0.001$) in predicting short-term mortality. The REMS+L score ($p < 0.001$) was superior to the REMS ($p < 0.001$) and lactate values ($p < 0.001$) in predicting mortality. Adding lactate measurements to REMS in patients over 40 years of age who present to the ED with shortness of breath appeared to yield more accurate estimates than using REMS and lactate values alone when determining two-day mortality.

Keywords

Emergency department; Triage; REMS; Lactate; Shortness of breath; Dyspnea

1. Introduction

Recent studies have shown that the number of admissions to emergency departments (ED) is increasing and that the length of stay in both EDs and hospitals is prolonged [1]. A number of scoring systems are used to differentiate patients in the diagnosis, treatment, and follow-up stages in an efficient and accountable way to avoid increasingly crowded workspaces [2]. It is postulated that certain classification systems devised to predict the severity of the disease, based on physiological values, routinely obtained in an ED, are important in the early diagnosis of patients and in the prediction of mortality and morbidity. The ideal ED scoring system should include a small number of physiological variables that can be easily collected from the moment of admission to an ED, and should provide clinically important and correct results, such as mortality estimations [3].

Different scoring systems have been used in EDs for many years, especially in predicting the mortality and clinical outcomes of specific groups of patients. The National Early Warning Score (NEWS), Modified Early Warning Score (MEWS), "Confusion, Uremia, Respiratory rate, Blood pressure, age greater than 65 years" (CURB-65) and Rapid Emergency Medicine Score (REMS) are the most commonly used scoring systems [4]. However, new combined scores, such as NEWS-L, have been used to increase the predictive power of these scoring systems by adding a mortality predictor biochemical variable, which is mostly based on vital signs. Studies have shown that these combined scoring systems provide more successful and accurate mortality estimations [5]. Developed by Olsson *et al.* [6] (2004), REMS is one ED scoring system, and is based on the Rapid Acute Physiological Score (RAPS). The RAPS assesses heart rate, respiratory rate, arterial blood pressure, and Glasgow Coma

Scale (GCS). REMS, on the other hand, adds the patient's age and pulse oxygen saturation (SpO_2) readings to known RAPS parameters [6, 7].

Lactate is a product of anaerobic metabolism. The serum lactate level informs the clinician about tissue perfusion [8]. Lactate is the end product released in almost all tissues (skeletal muscle, brain, erythrocytes, and kidneys), even under conditions where oxygen is sufficient, and enters a cycle where it is kept at certain levels in arterial and venous blood, especially by being converted to pyruvate by liver metabolism. In the ED, an abnormal lactate level has been associated with poor outcomes in critically ill patients, such as those with trauma, infection, sepsis, and myocardial infarction. Therefore, it has become a widely used biomarker for predicting patient outcomes in the ED [9].

Dyspnea is a subjective experience reported by the patient as an uncomfortable sensation in breathing. Shortness of breath is among the most common chief complaints in ED admissions. Dyspnea can be encountered in almost every organ pathology in the body, including pneumonia, congestive heart failure, reactive airway disease, and valvular heart disease [10].

Healthcare providers are recommended to routinely apply risk scoring to all patients who present to the ED, although there is controversy over which one is the most useful. This study aims to compare the effectiveness of the REMS scoring system and lactate levels separately in predicting two-day and twenty-eight-day mortality and ED outcomes (admission or discharge) in patients over 40 years of age who presented to an ED with non-traumatic dyspnea.

2. Methods

2.1 Study design and setting

The population of the study included patients aged 40 and over who were admitted to the University of Health Sciences Istanbul Education and Research Hospital's Department of Emergency Medicine between 15 December 2018 and 15 February 2019 with the chief complaint of shortness of breath.

2.2 Selection of participants

A total of 38,315 patients presented to the ED during the two-month study period, with approximately 5.5% of these patients (n = 2107) admitted to the ED with shortness of breath and related complaints. The number of patients aged 40 and over admitted to the ED due to dyspnea in the study period was 1475. All patients admitted to the ED with a complaint of dyspnea during the study period were consecutively assigned to the appropriate division in the ED after the triage category was specified. These patients were informed by the physician responsible for the study. Written and verbal consent was obtained from the patients who volunteered to participate in the study after the information was provided. Consent to participate in the study was obtained from the patient, a first-degree relative, or the person who accompanied the patient to the hospital. As a result, 1044 patients who met the inclusion criteria were recruited for the study.

2.3 Methods and measurement

The vital signs of the patients included in the study, systolic and diastolic blood pressure, mean arterial pressure (MAP), pulse, respiratory rate, and SpO_2, were measured with a vital signs monitor (Carescape, V100, General Electric, Mississauga, ON, Canada) device and recorded in the study data sheets.

2.3.1 REMS calculation

Two hours of theoretical REMS training were given to emergency physicians prior to the study. No changes were made to the diagnosis and treatment processes of the patients due to the study protocol. Based on this information, the REMS scores of the patients were calculated. The patients were categorized using life table analysis according to the patients' total REMS scores as follows: low risk, under 6 points; medium risk, 6–13 points; and high risk, 13 points or more.

2.3.2 Calculation of lactate value and REMS+L

The blood gas sample taken from the patients, as ordered by the treating physician, was studied for lactate level using a blood gas analyzer (RapidLab 1265, Siemens Healthcare Diagnostics Inc., Tarrytown, NY, USA) device, which has a lactate measurement range of 0.3 to 20 mmol/L and was periodically checked by the manufacturer. The effectiveness of measuring the hospital outcome and mortality values of the patients was analyzed by comparing the data obtained from lactate levels. In this study, lactate measurements were analyzed using both venous and arterial blood gas values; therefore, both were included in the study. The REMS+L scores were calculated using both components. The lactate value in mmol/L was added to the calculated REMS value, and a new value was derived.

In this study, hospital outcomes were defined as either discharge or hospitalization (ward or intensive care unit). The two-day and twenty-eight-day survival statuses of the patients were determined by questioning the Identity Sharing System of the General Directorate of National Population and Citizenship Affairs, or by contacting the patients and their relatives by phone.

After clinical evaluation, laboratory, and imaging tests, the possible diagnoses of the patients were divided into three groups in accordance with the presumptive diagnosis of the primary physician:

1. Pulmonary causes: asthma, chronic obstructive pulmonary disease (COPD), smoke exposure, interstitial lung disease, lung infections (pneumonia, acute bronchitis), upper respiratory tract infections (acute pharyngitis, sinusitis, acute laryngitis), pulmonary embolism, spontaneous pneumothorax, and sarcoidosis and pneumoconiosis lung cancers.
2. Cardiac causes: congestive heart failure, hypertensive pulmonary edema, and acute myocardial infarction.
3. Non-specific causes: anemia, acute renal failure, various malignancies (non-pulmonary), and carbon monoxide exposure.

2.4 Exclusion criteria

Patients under 40 years of age or who were admitted to the ED due to trauma were not included in the study. In addition,

patients who were admitted to the critical care area in a case of cardiopulmonary arrest, who underwent resuscitation, trauma patients, patients with an indication for referral due to an urgent operation or need for further treatment, and patients who could not be communicated were excluded from the study. A total of 71 of these patients were excluded from the study because they did not consent, and the remaining 1404 were evaluated for eligibility for inclusion in the study. Of these patients, 282 were excluded from the study because their lactate levels were not requested by their primary physician following admission, vital signs, or examination. Among the patients who were eligible for inclusion in the study, 37 were excluded from the study due to laboratory errors, 12 due to inaccessible death information (*e.g.*, inaccessible identification number, inability to reach patients by phone), and 29 due to an inability to record a whole set of vital signs.

2.5 Statistical methods

Mean, standard deviation (SD), median, range, frequency, and ratio values were used in the descriptive statistics of the data. The distribution of variables was measured using the Kolmogorov-Smirnov test, the Mann-Whitney U test was used to analyze quantitative independent variables, the chi-square test was used to analyze qualitative independent variables, and Fisher's exact test was used when the chi-square test conditions were not met. The effect level was investigated using the ROC curve and univariate analysis. The DeLong method was used for ROC comparison. Statistical Package for the Social Sciences (SPSS) 22.0 (IBM Corp. Armonk, NY, USA) and MedCalc 20.104 (MedCalc Software Ltd., Ostend, Belgium) programs were used to conduct the analyses.

3. Results

A total of 1044 patients were included in the study. The mean age of the patients was 66.6 years (SD 14.71). Most of the patients were female (n = 559, 53.5%). The most common etiological causes were found to be pulmonary entities (n = 677, 64.8%). While the majority of the patients were discharged from the ED (n = 721, 69.1%), 70 patients (6.7%) were admitted to the ward, and 253 patients (24.2%) were followed up in an intensive care unit. Two-day mortality was recorded in 23 patients (2.2%), while 104 patients died within 28 days (10%). The mean REMS score of the patients was 5.78 (SD 3.14), while the mean lactate value was 1.91 (SD 1.22). The mean REMS+L score of the patients included in the study was 7.69 (SD 3.55).

Regarding the figures for mortality within 28 days, when the patients were evaluated, the mean age of the mortality group was 11.12 years higher than the other group (95% confidence interval (CI) 8.76–13.48; Student's *t*-test, $p < 0.001$; see Table 1). There was no significant difference between the patient sexes (Pearson's chi-square test, $p = 0.239$). When the groups were evaluated according to the admission blood pressure levels, mean systolic blood pressure was 15.75 mmHg (95% CI 8.91–22.61) in the mortality group, diastolic blood pressure was 4.58 mmHg (95% CI 1.02–8.13), and mean arterial pressure was 8.3 mmHg (95% CI 4.01–12.59) lower than those of the survivor group (Student's *t*-test: $p < 0.001$, $p = 0.004$, $p < 0.001$, respectively).

The mean oxygen saturation levels (pulse oximetry readings) of the mortality group were 3.1% (95% CI 1.53%–4.67%) lower than those of the survivor group (Student's *t*-test, $p < 0.001$). There was no significant difference between the groups with regard to heart rate and body temperature (Student's *t*-test, $p = 0.11$, $p = 0.393$, respectively). Mean respiratory rate of the non-survivor group was significantly higher than that of the survivor group and the mean difference was 2.62 bpm (95% CI 1.54–3.7) (Student's *t*-test, $p < 0.001$), while the GCS was 0.58 points (95% CI 0.23–0.92) lower than the survivors (Student's *t*-test, $p < 0.001$). The mortality rate of the pulmonary group was lower than that of both the cardiac group and the non-specific group (Pearson chi-square test with Bonferroni correction for both $p < 0.001$). The mortality rate of the hospitalized group (n = 80, 24.7%) was found to be significantly higher than that of the discharged group (n = 24, 3.3%; Pearson's chi-square test, $p < 0.001$).

The mean lactate level of the mortality group was 1.08 mmol/L (95% CI 0.63–1.54) higher than the mean level of the survivors (Student's *t*-test, $p < 0.001$). In the mortality group, the REMS score was 2.53 (95% CI 1.91–3.15), and the REMS+L score was 3.61 (95% CI 2.93–4.3) higher than the mean score of the survivors (Student's *t*-test, both $p < 0.001$).

The mean age of the two-day mortality group was 8.64 years (95% CI 2.57–14.71) higher than that of the other group (Student's *t*-test, $p = 0.005$; see Table 2). There was no significant difference between the groups in terms of sex (Pearson's chi-square test, $p = 0.894$), systolic and diastolic blood pressure, MAP, pulse, body temperature (Student's *t*-test, $p = 0.078$, $p = 0.118$, $p = 0.118$, $p = 0.109$, $p = 0.051$, $p = 0.396$, $p = 0.179$, respectively), or GCS values (Mann-Whitney U test, $p = 0.189$). The mean pulse oximetry level was 4.06% (95% CI 1.44–6.68%) lower in the mortality group (Student's *t*-test, $p = 0.002$), and the respiratory rate was 2.72 bpm (95% CI 0.29–5.14) higher than in the survivor group (Student's *t*-test, $p = 0.03$). The mean blood lactate level was found to be 2.14 mmol/L (95% CI 1.07–3.21) higher in the mortality group than in the survivor group (Student's *t*-test, $p < 0.001$). The mean REMS score was 2.85 points (95% CI 1.56–4.14) higher in the mortality group than in the survivor group, while the corresponding difference in the mean REMS+L score was 4.99 points (95% CI 3.55–6.43) higher (Student's *t*-test, both $p < 0.001$). With regard to the predictions of two-day and twenty-eight-day mortality, the predictive accuracy, sensitivity, and specificity levels of the different REMS+L scores are given in Table 3.

Diagnostic accuracy analysis for two-day mortality *via* ROC curves revealed that the REMS+L score (AUC = 0.844, 96% CI 0.768–0.920) was found to be statistically significant and superior to the REMS score (AUC = 0.738, 96% CI 0.639–0.836) in predicting two-day mortality (difference between areas (DBA) 0.106, $p = 0041$). There was no significant difference between lactate value (AUC = 0.824, 96% CI 0.726–0.922) and REMS+L score ($p = 0.718$), or between lactate value and REMS score ($p = 0.256$) (Table 4).

Concerning mortality prediction, REMS+L score (AUC = 0.758, 96% CI 0.712–0.804) was found to be superior to

TABLE 1. Comparison of demographic variables, ED diagnoses, vital signs, clinical outcomes, lactate values and scoring systems with special regard to twenty-eight-day mortality.

	Survivors	Mortality	Mean difference (95% CI)	*p*
Demographic variables				
Age	65.49 ± 14.64	76.61 ± 11.17	11.12 (8.76–13.48)	<0.001
Female	509 (91.1)	55 (8.9)		
Male	431 (88.9)	54 (11.1)		0.239
Vital signs				
Systolic arterial pressure (mmHg)	141.99 ± 28.29	126.23 ± 34.00	15.76 (8.91–22.61)	<0.001
Diastolic arterial pressure (mmHg)	74.55 ± 14.92	69.97 ± 17.62	4.58 (1.02–8.13)	0.004
MAP	97.03 ± 17.84	88.72 ± 21.29	8.30 (4.01–12.59)	<0.001
SpO_2 (%)	92.76 ± 6.10	89.66 ± 7.83	3.10 (1.53–4.67)	<0.001
Pulse (bpm)	97.39 ± 20.18	102.81 ± 23.98		0.110
Temperature (°C)	36.53 ± 0.86	36.60 ± 0.87		0.393
Respiratory rate (bpm)	16.74 ± 3.70	19.36 ± 5.45	2.62 (1.54–3.70)	<0.001
GCS	14.97 ± 0.27	14.39 ± 1.78	0.58 (0.23–0.92)	<0.001
Diagnosis				
Pulmonary	631 (93.2)	46 (6.8)		<0.001
Cardiac	86 (83.5)	17 (16.5)		
Non-Specific	223 (84.5)	41 (15.5)		
Disposition				
Discharge	697 (96.7)	24 (3.3)		<0.001
Admission	244 (75.3)	80 (24.7)		
Lactate (mmol/L)				
Mean	1.80 ± 0.97	2.88 ± 2.31	1.08 (0.63–1.54)	<0.001
Scorings				
REMS	5.53 ± 3.07	8.06 ± 2.77	2.53 (1.91–3.15)	<0.001
REMS+L	7.33 ± 3.35	10.94 ± 3.71	3.61 (2.93–4.30)	<0.001

CI: Confidence Interval; MAP: Mean Arterial Pressure; GCS: Glasgow Coma Scale; SpO_2: Pulse O_2 Saturation; REMS: Rapid Emergency Medicine Score; REMS+L: Rapid Emergency Medicine Score+Lactate.

REMS score (AUC = 0.722, 96% CI 0.676–0.768) and lactate value (AUC = 0.653, 96% CI 0.588–0.718) (DBA 0.039, p = 0.0053; DBA 0.105, $p < 0.001$, respectively); there was no statistical significance between lactate value and REMS score (p = 0.0710) (Figs. 1,2).

4. Discussion

Although there are many scoring systems for the diagnosis, treatment, and follow-up of patients in work areas where patient care is intense, such as emergency departments (EDs), a useful, practical, and accurate scoring system should be devised that involves just a few easily accessible parameters to retain high power in the estimation of disease severity.

Shortness of breath is one of the most common reasons for admission to the ED. When the ED data for the USA were analyzed, approximately 2.6% of all ED referrals were found to have been caused by dyspnea in 2015 [11]. REMS is viewed as an important measure of the clinical course in patient evaluation and patient status, especially by EMs and EDs. The major advantage of the REMS score is that it can be utilized as a continuous measure of acuity based on objective physiological data and the age of patients [12]. Therefore, patients with dyspnea, whose clinical status can change rapidly, and who have a wide spectrum in terms of underlying etiology, were targeted for participation in this study [13].

In this study, 5.5% of the patients who were admitted to the ED during a two-month study period presented with a complaint of shortness of breath; of these, 70% were over the age of 40. The study was conducted over a two-month period during the winter, when seasonal peaks in the incidence of COPD attacks and pneumonia were anticipated. The reason for this is that the winter environment boosts the spread of various respiratory tract virus infections, as evidenced in the literature [14]. The detection of the higher admissions rate than the figures obtained from other centers in the USA can be attributed to this situation. Considering the annual census, it is possible to determine rates that are more correlated with the Western world. Sepsis studies have revealed that shortness of breath is one of the most common complaints

TABLE 2. Comparison of demographic data, ED diagnoses, vital signs, clinical outcomes, lactate values and scoring systems with special regard to two-day mortality.

	Survivors	Mortality (two-day)	Mean difference (95% CI)	*p*
Demographic variables				
Age	66.41 ± 14.73	75.04 ± 10.82	8.64 (2.57–14.71)	0.005
Female	547 (97.9)	12 (2.1)		0.894
Male	474 (97.7)	11 (2.3)		
Vital signs				
Systolic arterial pressure (mmHg)	140.76 ± 28.91	125.09 ± 40.50		0.078
Diastolic arterial pressure (mmHg)	74.20 ± 15.18	69.17 ± 18.33		0.118
MAP	96.39 ± 18.18	87.81 ± 24.53		0.109
SpO_2 (%)	92.54 ± 6.29	88.48 ± 8.04	4.06 (1.44–6.68)	0.002
Pulse (bpm)	97.68 ± 20.31	108.78 ± 30.97		0.051
Temperature (°C)	36.53 ± 0.85	36.8 ± 1.18		0.396
Respiratory rate (bpm)	16.94 ± 3.92	19.65 ± 5.58	2.72 (0.29–5.14)	0.030
GCS	14.92 ± 0.63	14.70 ± 0.77		0.179
Diagnosis				
Pulmonary	666 (98.4)	11 (1.6)		0.198
Cardiac	99 (96.1)	4 (3.9)		
Non-Specific	256 (97)	8 (3)		
Disposition				
Discharge	718 (99.7)	2 (0.3)		<0.001
Admission	303 (93.5)	21 (6.5)		
Lactate (mmol/L)				
Mean	1.86 ± 1.13	4.00 ± 2.47	2.14 (1.07–3.21)	<0.001
Scorings				
REMS	5.72 ± 3.11	8.57 ± 2.98	2.85 (1.56–4.14)	<0.001
REMS+L	7.58 ± 3.48	12.57 ± 3.52	4.99 (3.55–6.43)	<0.001

CI: Confidence Interval; MAP: Mean Arterial Pressure; GCS: Glasgow Coma Scale; SpO_2: Pulse O_2 Saturation; REMS: Rapid Emergency Medicine Score; REMS+L: Rapid Emergency Medicine Score+Lactate.

of patients diagnosed with sepsis upon presentation to an ED [15]. In another study, including all patients who presented to an ED without distinguishing symptoms and complaints, Olsson *et al.* [7] reported that the median REMS score was 5.5. Similarly, in the present study, the median REMS score was found to be 6, which correlated with the findings of both studies. There are studies in the literature investigating the effectiveness and accuracy of the REMS score in predicting the outcome and mortality of patients. Bulut *et al.* [16] reported mean REMS scores in the short-term outcomes of the patients in a multicenter study: three at discharge, and six on admission to the ward and/or intensive care unit. In the present study, the mean REMS score was found to be 5 at discharge, 7.2 on admission to the ward, and 7.5 on admission to intensive care units. The higher REMS scores found in the present study can be attributed to a higher mean age in this study and a higher number of comorbidities than in the other studies.

The REMS is employed in many areas where patient care is provided, including the pre-hospital field, EDs, critical care, and intensive care units. In a study conducted on patients followed in the intensive care unit, Kennedy *et al.* [17] argued that REMS scores were an appropriate method for determining the high-risk patient group and their in-hospital mortality. However, in this study, the ratio of both moderate- and high-risk patients in the mortality group was found to be significantly higher than in the survivor group. While a small proportion of patients with an REMS score below 6 (low-risk group) died within 28 days, this rate increased in patients in the intermediate-risk category, and almost 50% of the patients in the high-risk category died within 28 days.

It is quite remarkable that in the present study, no patient with an REMS+L score below six was in the two-day mortality group. Although the REMS+L score has been proven to have a better diagnostic value than the lactate and REMS scores, according to the AUC analysis in this study, the sensitivity and specificity values, especially the specific cut-off values, are of greater importance. In other words, since the two-day and twenty-eight-day mortality rates of patients with an REMS+L

TABLE 3. Predictive accuracy, sensitivity and specificity levels of different REMS+L scores in predicting twenty-eight-day mortality and two-day mortality.

Cut-off point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Twenty-eight-day Mortality				
≥6	95.19	33.83	13.73	98.45
≥7	85.58	45.64	14.83	96.62
≥8	75.96	58.30	16.77	95.64
≥9	65.38	69.36	19.10	94.77
≥10	53.85	80.00	22.95	94.00
≥11	43.27	87.34	27.44	93.30
≥12	36.54	92.23	34.23	92.23
≥13	29.81	94.79	38.75	92.43
≥14	25.00	97.02	48.15	92.12
Two-day Mortality				
≥6	100.00	31.64	3.19	100.00
≥7	95.65	43.39	3.67	99.77
≥8	86.96	55.83	4.25	99.48
≥9	78.26	66.90	5.06	99.27
≥10	78.26	77.86	7.38	99.38
≥11	65.22	85.41	9.15	99.09
≥12	60.87	90.50	12.61	99.04
≥13	52.17	93.34	15.00	98.86
≥14	34.78	95.49	14.81	98.48

PPV: Positive Predictive Value; NPV: Negative Predictive Value.

TABLE 4. Comparison of lactate, REMS and REMS+L values in regard to diagnostic accuracies to predict two-day and twenty-eight-day mortality.

	Two-day mortality			Twenty-eight-day mortality		
	AUC	(95% CI)	*p*	AUC	(95% CI)	*p*
Lactate	0.824	(0.726–0.922)	<0.001	0.653	(0.588–0.718)	<0.001
REMS	0.738	(0.639–0.836)	<0.001	0.722	(0.676–0.768)	<0.001
REMS+L	0.844	(0.768–0.920)	<0.001	0.758	(0.712–0.804)	<0.001

AUC: Area Under Curve; CI: Confidence Interval; REMS: Rapid Emergency Medicine Score; REMS+L: Rapid Emergency Medicine Score+Lactate.

score below six were very low, this value can be used for safe discharge from an ED, especially if this study is supported by other multicenter studies. On the other hand, the two-day and twenty-eight-day mortality specificities of patients with an REMS+L score above 11 were above 85%, indicating that this patient group had a high risk of mortality or a poor outcome.

Martin-Rodriguez *et al.* [18] conducted a study of the prehospital area in patients with cardiovascular disease, and investigated the predictive power of a measured lactate level on early mortality. They reported that a lactate level of 4.3 mmol/L and above at hospital admission is an important predictor in estimating early mortality in patients followed in the ED and intensive care units. Similarly, in this study, the lactate level was found to be significantly higher in the two-day mortality group when compared to that of the survivors. Of note, the cut-off value at 2.17 mmol/L for the lactate level was found to be 82.6% sensitive and 75.6% specific for predicting two-day mortality. In addition, all of the patients with lactate levels above 11.5 mmol/L died during the twenty-eight-day period. However, less than one percent of 134 patients with lactate levels below 1 mmol/L died within two days. In other words, this study finds that a low lactate value was a significant factor in ruling out mortality risks, which is similar to the findings of Martín-Rodríguez *et al.* [18].

In another study conducted in an ED setting, researchers investigated the effectiveness of adding a lactate value (mmol/L) to the frequently used NEWS score. They reported that *de novo* NEWS-L proved to be significantly more accurate than NEWS in determining early and late mortality [19]. Similarly, in this study, the effectiveness of REMS+L in predicting two-day

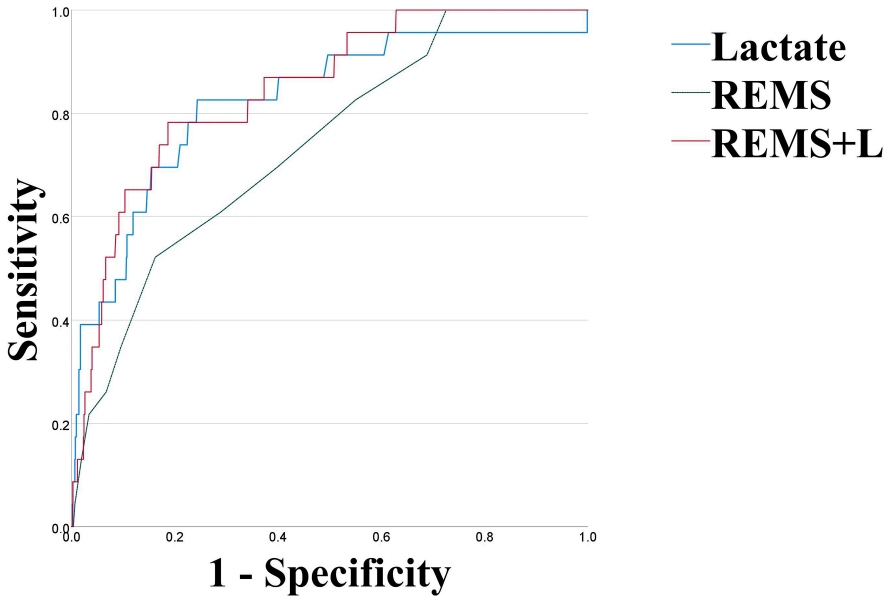

FIGURE 1. ROC curve analysis for sensitivity and specificity to predict two-day mortality. REMS+L: Rapid Emergency Medicine Score+Lactate.

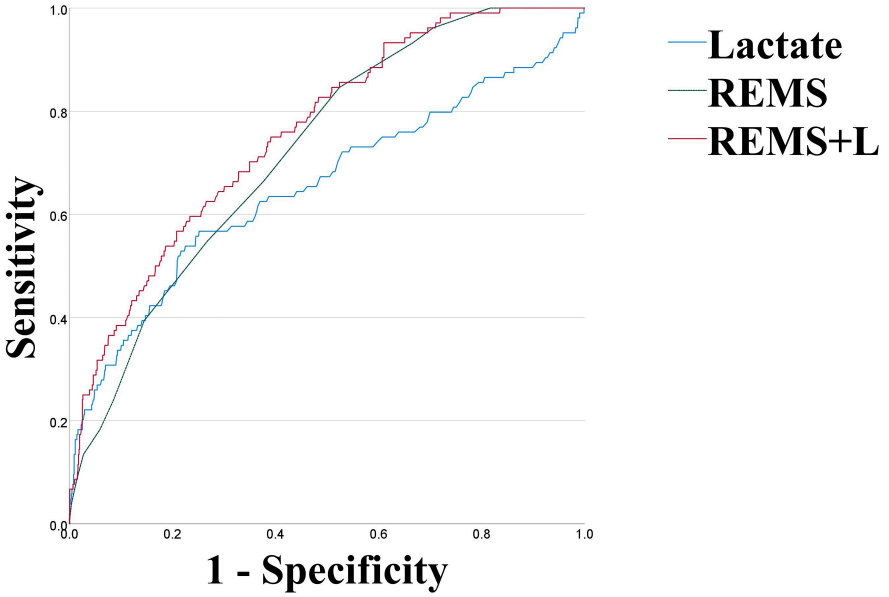

FIGURE 2. ROC curve analysis for sensitivity and specificity to predict twenty-eight-day mortality. REMS+L: Rapid Emergency Medicine Score+Lactate.

and twenty-eight-day mortality was found to be significantly higher than that of REMS and lactate taken separately.

5. Limitations

The single-center observational design is a major limitation of the study, which prevents the generalizability of the findings. In addition, the exclusion of patients younger than 40 years of age should be considered before extrapolating the findings to the general population.

6. Conclusions

It is evident that adding an absolute lactate value (mmol/L) to an REMS score (REMS+L) in patients over 40 years of age, who are admitted to an ED with shortness of breath as the chief complaint, results in higher accuracy when predicting twenty-eight-day mortality than REMS and lactate values do alone. REMS+L can be used in risk stratification processes in ED patients with dyspnea.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

PV and OK—conceived the study, designed the trial; supervised the conduct of the trial and data collection. PV, OK, ACT and SY—undertook recruitment of participating centers and patients and managed the data, including quality control; takes responsibility for the paper as a whole; drafted the manuscript, and all authors contributed substantially to its revision. PV, ACT and SY—provided statistical advice on study design and analyzed the data. OK—chaired the data oversight committee.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This prospective observational study was commenced following Ethics Committee Approval was obtained from University of Health Sciences Istanbul Education and Research Hospital (decision number: 1138). Consent to participate in the study was obtained from the patient, a first-degree relative, or the person who accompanied the patient to the hospital.

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CONFLICT OF INTEREST

The authors declare no conflict of interest. Ozgur Karcioglu is serving as one of the Editorial Board members of this journal. We declare that Ozgur Karcioglu had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to MC.

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