ORIGINAL RESEARCH

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# Evaluation of The Effects of Laboratory Values, Oxidation Parameters, Scoring Systems, and Ventricular Diameter Measurements on Prognosis in Patients Diagnosed with APE in The Emergency Department

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## Abstract

**Objective:** This study aimed to investigate the role of oxidant and antioxidant levels in the diagnosis of acute pulmonary embolism (APE).

**Materials and Methods:** Participants diagnosed with APE were included in group 1, and healthy volunteers were included in Group 2. In addition, Group 1 was divided into two groups according to 30-day mortality.

**Results:** Sixty-five participants diagnosed with APE were included in Group 1. A total of 52 healthy volunteers were included in Group 2. The total antioxidant capacity (TAC) levels of Group 1 were lower than those of Group 2, and the total oxidant capacity (TOC), oxidative stress index (OSI), and ischemia-modified albumin levels were higher. When receiver operating characteristicanalysis was performed for TAC, TOC, OSI, and ischemia-modified albumin, the highest area under the curve was found for OSI, TOC, and ischemia-modified albumin, respectively. Fifteen (23%) participants in Group 1 died within 30 days of admission to the emergency department (Group 1A), and 50 (77%) survived after 30 days (Group 1B).

**Conclusion:** The oxidant-antioxidant balance is impaired in APE. Therefore, oxidants and antioxidants can be used to diagnose and exclude patients with suspected APE.

**Keywords:** Antioxidant, ischemia, oxidant, oxidative stress, pulmonary embolism

## Introduction

Acute pulmonary embolism (APE) is a potentially fatal disease, with mortality reaching up to 15% in the risk group. Reducing mortality is possible with correct diagnosis and treatment in the early period [1-3]. In the diagnosis of APE, clinical decision rules, such as the WELLS and Revise Geneva scores, electrocardiography (ECG), laboratory tests, and imaging tools, are used together with clinical evaluation [4,5]. Computed tomography (CT)-pulmonary angiography is an imaging tool with high sensitivity in the diagnosis of pulmonary embolism [1,3,4,6]. However, reasons such as excessive exposure to ionizing radiation, complications related to the use of intravenous contrast material, and fetal risks of use in pregnant women limit the use of CT pulmonary angiography scans [7]. The risk of mortality should be determined together with the diagnosis of APE to ensure appropriate treatment management. The risk of mortality is high in patients with unstable clinical findings, hypotension, and shock. In patients with stable clinical findings, a more advanced classification is performed using prognostic criteria. In the prognostic criteria, the participants' comorbidities, clinical findings, laboratory test results, and imaging tools are used. Pulmonary Embolism Severity Index (PESI), Simplified Pulmonary Embolism Severity Index (sPESI), and Bova score are scores that evaluate prognostic parameters

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together and determine the risk of early death associated with pulmonary embolism. Studies have shown that PESI and sPESI can identify high- and low-risk patients for all-cause 30-day mortality [4,8-11].

The formation and removal rates of free radicals are normally in equilibrium in an organism, and this is called "oxidative balance". The imbalance between oxidants and antioxidants leads to the production of extremely reactive oxygen species and can cause oxidative damage. This condition is referred to as "oxidative stress" [12]. Reactive oxygen species, reactive nitrogen species, and sulfur-centered radicals are classified as oxidants. Reactive oxygen species are capable of reacting with biological molecules such as proteins, lipids, and DNA. An increase in reactive oxygen species levels disturbs cellular functions by damaging lipid membranes, enzymes, and nucleic acids [13]. In recent years, the role of oxidative stress in the etiopathological processes of diseases has aroused great interest. Oxidants and antioxidants have been studied in many diseases [13-15].

The aim of this study was to investigate the role of oxidant and antioxidant levels [Total antioxidant capacity (TAC), total oxidant capacity, and Oxidative Stress Index (OSI)] in the diagnosis of APE in the emergency department and to determine the 30-day mortality associated with pulmonary embolism, and to compare oxidant and antioxidant levels with the clinical findings, laboratory test results, CT pulmonary angiography results, and sPESI score of the patients.

## Materials and Method

### Selection of Participants and Ethics Committee Approval

This prospective study was performed in the emergency department of a tertiary hospital after obtaining the University of Health Sciences Antalya Education and Research Hospital Clinical Research Ethics Committee (approval number: 14/15, date: 30.05.2019). Power analysis was performed using G*Power version 3.1.9.7 (2020) for Windows 10 (University of Dusseldorf, Germany) with reference to similar studies in the literature. The sample size was calculated as 49 with 95% power and 0.05 type 1 error rate. Patients who were admitted to the emergency department between June 15, 2019 and March 10, 2020, diagnosed with APE by CT-pulmonary angiography, over the age of 18, and not receiving thrombolytic therapy were included in the study. Patients under 18 years of age, who were using drugs or nutritional supplements that could affect oxidant-antioxidant levels, whose laboratory test results could not be reached or the laboratory tests were not studied as needed in our study, whose CT-pulmonary angiography scans were not performed, who were pregnant, and who did not give consent to participate in the study were excluded from the study. As the control group, healthy volunteers over the age of 18 years who did not use nutritional supplements that could affect oxidant-antioxidant levels, did not have comorbid diseases, and gave consent to participate in the study were included.

Participants were divided into two groups according to whether they were diagnosed with pulmonary embolism or were healthy volunteers. Participants diagnosed with pulmonary embolism were included in group 1, and healthy volunteers were included in Group 2. In addition, Group 1 was divided into two groups according to its 30-day mortality status. Group 1 participants who died within 30 days of admission to the emergency department were included in Group 1A, and those who survived after 30 days were included in Group 1B (discharged from the hospital).

All patients included in the study were evaluated according to the diagnosis and treatment process of "2019 ESC Guidelines for the diagnosis and management of APE developed in collaboration with the European Respiratory Society" [4] and "American College of Cardiology Management of Pulmonary Embolism: an Update on 2020" [16]. This study was conducted in accordance with the code of Ethics of the World Medical Association (Declaration of Helsinki). Informed consent was obtained from all participants and their relatives. An ECG interpretation was made by an emergency physician. All blood samples were analyzed by a medical biochemistry physician at the hospital laboratory. In terms of consistency, ECG comments were interpreted by a single emergency physician, and blood samples were studied by a single medical biochemistry physician.

A standardized data record form was created before the study. Age, gender, comorbidities, smoking habit, ECG findings performed at admission, WELLS score calculated at admission, the test results of high sensitive troponin t, D-dimer, lactate, and CT pulmonary angiography interpretations performed at admission, the values measured at the admission of systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate, $SaO_2$ (measured with a pulse oximeter), and body temperature of participants included in group 1 were recorded in this form. In addition to the laboratory tests taken from the Group 1 participants at the time of admission, the TOC, TAC, and ischemia modified albumin (IMA) levels were studied from the blood taken simultaneously. TAC, TOC, and IMA levels were assessed studied from blood taken from the participants included in Group 2.

### Blood Samples and Laboratory Measurements

Blood samples were placed in biochemistry tubes containing gel and a vacuum cap at the time of participant admission. The blood samples taken from groups 1 and 2 were centrifuged for 10 minutes at 4000 rpm with an uncooled centrifuge device within the first 30 minutes after blood samples were

taken and their serums were separated. In Group 1, highly sensitive troponin t and D-dimer were studied immediately in the emergency department laboratory, and lactate was studied from venous blood gas in the bedside blood gas auto analyzer. In groups 1 and 2, the blood samples separated for the measurement of oxidant and antioxidant levels were transferred to Eppendorf tubes with plastic caps and stored at minus 80 °C until the day of analysis. TAC, TOC, and IMA levels were determined from these stored serum samples.

### Measurement of TAC

It was studied on Abbott Architect ®c16000 auto analyzer using a fully automatic RL0031 RelAssay® (Gaziantep-Türkiye) commercial kit. The results are given as µmol H2O2 Equiv./L [13].

### Measurement of TOC

It was studied on Abbott Architect ®c16000 auto analyzer using a fully automatic RL0031 RelAssay® (Gaziantep-Türkiye) commercial kit. The results are given as µmol H2O2 Equiv./L [13].

### Calculation of OSI

The ratio of TOC level to TAC level was accepted as OSI. The OSI was calculated using the following formula: OSI= [TOC (µmol H2O2 Equiv./L) / TAC (µmoltroloksEquiv./L)]

### Measurement of the IMA

IMA measurements were performed using the albumin–cobalt binding test described by Bar- Tekkanat et. al [13]. The results were recorded in absorbance units.

Oxidant and antioxidant measurements were performed by a single physician. All measurements were performed within 1 day. The centrifugation time of the oxidant and antioxidant blood samples was 10 min. The measurement of serum levels was 15 min in IMA and 7 min in TAC and TOC, and OSI was calculated.

### Measurement of High-sensitivity Troponin T

Analyzed by the chemiluminescence method. Results are presented as ng/mL. The measurement of serum high-sensitivity troponin t level took 45 min.

### Measurement of D-dimer

Measured using a HemosIL D-dimer HS kit. The results were given as µg/L. The measurement of the serum level of D-dimer took 45 minutes.

### Lactate Measurement

Venous blood gas samples were collected from the patients on a bedside radiometer (ABL-800 flex brand) in the emergency department. Results are presented in mmol/L. The measurement of the serum lactate level took 90 s.

### sPESI and Lactate-sPESI (L-sPESI)

The sPESI was developed to classify the risks of pulmonary embolism patients [4]. A sPESI score ≥1 is considered high-risk for 30-day mortality. The L-sPESI score was obtained by adding the lactate value to the sPESI (supplementary material 1). Thus, sPESI used 6 parameters, while L-sPESI used 7 parameters. An L-sPESI score ≥2 is considered a high-risk factor for 30-day mortality.

### Computed Tomography-Pulmonary Angiography and Cardiac Measurements

A 64-slice CT scanner (HITACHI ECLOS) was used for CT pulmonary angiography in the emergency department. For CT-pulmonary angiography, a wide vascular access was made from the antecubital region (16 G or larger), and 80 mL of intravenous contrast material was administered. Imaging was performed in the early arterial phase 10-15 seconds after contrast agent injection. CT and pulmonary angiography scans were interpreted by a radiologist. For the purposes of standardization, a single radiologist interpreted all CT-pulmonary angiography. In CT-pulmonary angiography, pulmonary embolism was grouped as sub-segmental, segmental, and main pulmonary artery emboli according to anatomical localization. In the end-diastolic images, the diameter of the heart chambers was calculated by measuring the distance between the septum and the inner wall of the ventricular cavity. The right and left ventricular diameters (LVD) were measured just below the tricuspid valve, and the left ventricular diameter was measured just below the mitral valve. A longitudinal straight line was drawn at the level of the apex for interventricular septum deviation, and a reference point was established by drawing a vertical line from the inner surface of the right ventricular septum. The measurement was made from this reference point in the presence of septum deviation. Measurements were performed in mm [1,17].

### Outcomes

The primary outcome of this study was to evaluate the accuracy of oxidant and antioxidant levels in the diagnosis and prediction of mortality in the presence of APE. The secondary outcome of our study was to compare the accuracy of oxidant and antioxidant levels in predicting mortality with comorbid diseases, vital signs, D-dimer, high-sensitivity troponin t, lactate, cardiac measurements in CT pulmonary angiography scans, sPESI, L-sPESI, and WELLS scoring.

### Statistical Analysis

All data were analyzed using SPSS Statistics for Windows version 21.0. First, analyses were performed on demographic data (age, sex etc.). For this reason, frequency distributions and chi-square tests were used. The Shapiro-Wilk test was used to determine the distribution of the groups. For comparison of

groups, for paired groups, The Student's t-test was used for parametric distributions and the Mann-Whitney U test for non-parametric distributions. In comparison of more than two groups, the One-way ANOVA test was used for parametric distributions, and the Kruskal-Wallis H test was used for non-parametric distributions. A $p<0.05$ value was considered statistically significant.

## RESULTS

### Primary Results

Sixty-five participants diagnosed with APE were included in Group 1. Of Group 1 participants, 43 (66%) were female and 22 (34%) were male. A total of 52 healthy volunteers were included in Group 2 (Figure 1). Of Group 2 participants, 26 (50%) were female and 26 (50%) were male. There were no statistically significant differences between Groups 1 and 2 in terms of gender ($p=0.091$). The mean age was 65±18 years in Group 1 and 59±12 years in Group 2 ($p=0.112$). The participants included in Group 1 had a medical history of malignancy in 17%, hypertension in 15%, chronic obstructive pulmonary disease in 9%, diabetes mellitus in 6%, and smoking habits in 17%. In Group 1, ECG revealed sinus tachycardia in 29 participants, right bundle branch block in 8 participants, atrial fibrillation in 3 participants, and an S1Q3T3 pattern in 1 participant. The ECGs of the remaining participants were in normal sinus rhythm.

When Groups 1 and 2 were compared, there was a statistically significant difference between TAC, TOC, OSI, and IMA levels. TAC levels in Group 1 were lower than those in Group 2, and TOC, OSI, and IMA levels were higher. When receiver operating characteristic (ROC) analysis was performed for TAC, TOC, OSI, and IMA, the highest area under the curve (AUC) was observed for OSI, TOC, and IMA, respectively. When the cutoff value for OSI was determined to be 3.0, sensitivity was 62%, specificity was 92%, positive predictive value was 94%, and negative predictive value was 92% (Tables 1A, 1B and Figure 2A).

Of the Group 1 participants, 22 (34%) were admitted to the intensive care unit and 43 (66%) to the outpatient unit. Fifteen (23%) participants in Group 1 died within 30 days of admission to the emergency department (Group 1A), and 50 (77%) survived after 30 days (Group 1B).

When Group 1A and Group 1B were compared in terms of comorbid diseases, malignancy was identified as more common in Group 1A (Table 2).

### Secondary Results

When pulmonary embolism was evaluated in terms of anatomical location in the pulmonary arteries, main pulmonary artery embolism was detected in 29 participants, segmental embolism in 18 participants, and sub-segmental embolism in 18 participants in Group 1. When the patients in Group 1A and Group 1B were compared, there was no statistically significant difference in terms of anatomical location of pulmonary embolism ($p=0.330$), age, gender, body temperature, $SaO_2$, TAC, TOC, OSI, IMA, D-dimer, and high-sensitivity troponin t. Compared with Group 1B, SBP and DBP were lower, and heart rate was higher in Group 1A. In laboratory studies, lactate levels were found to be higher in Group 1A (Tables 3A, 3B). When Groups 1A and 1B were compared, there was no difference in the WELLS score. However, the sPESI and L-sPESI scores were higher in Group 1A participants (Table 4A). LVD measured on CT pulmonary angiography were higher in Group 1B than in Group 1A. There were no differences in right ventricular diameters (RVD) and RVD/LVD ratio between Group 1A and Group 1B (Table 4B).

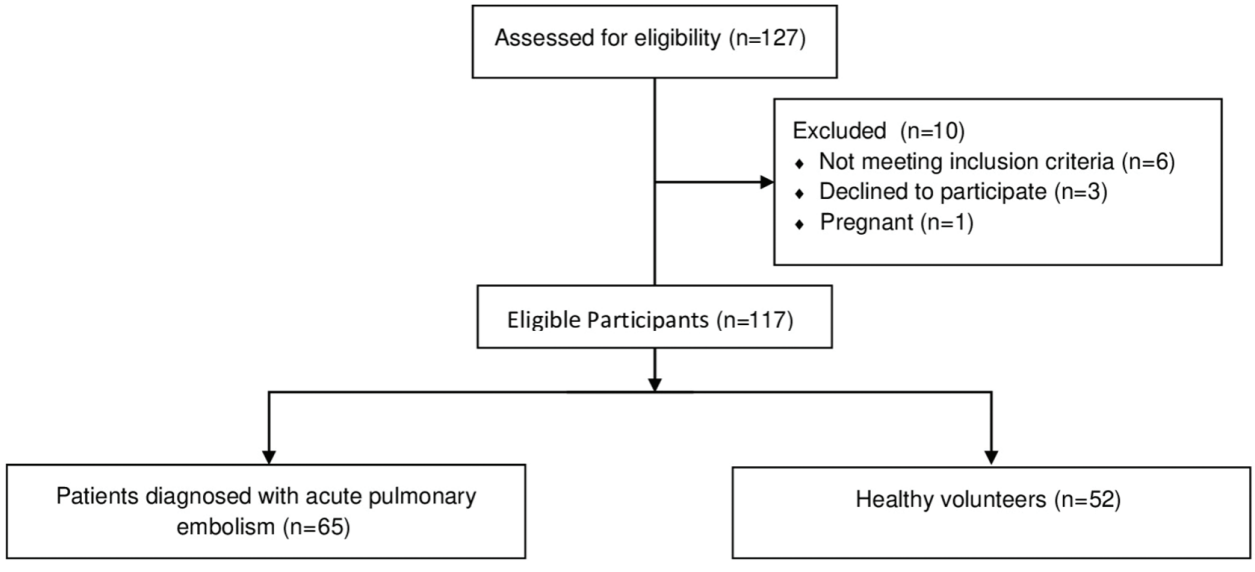


**Figure 1.** Data collection flow chart

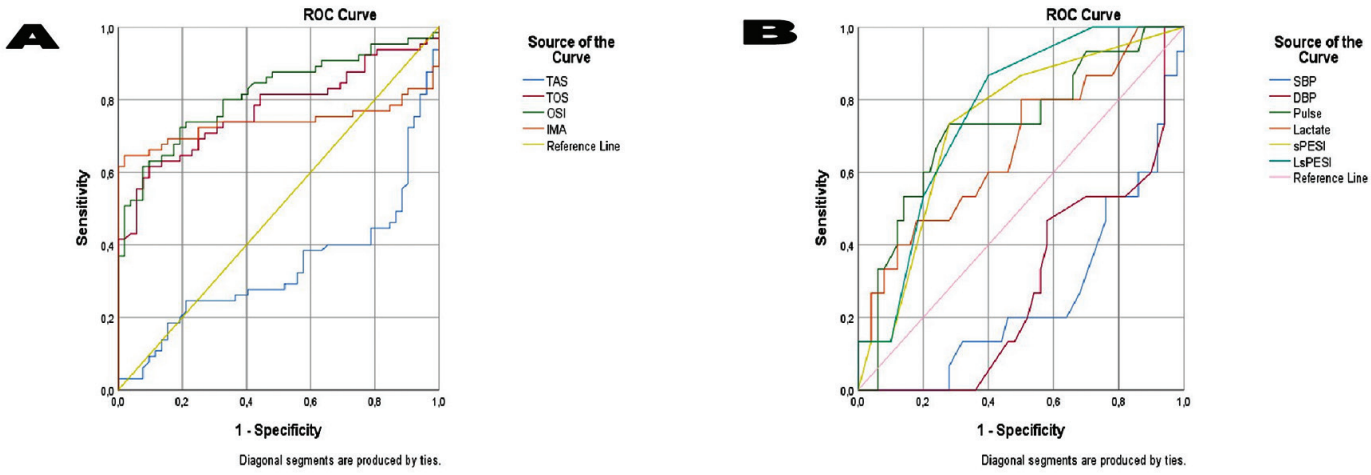


**Figure 2.** A. ROC analysis of TAC, TOC, OSI, and IMA levels in the diagnosis of patients with APE, B. ROC analysis of SBP, DBP, pulse, lactate, sPESI, and L-sPESI values in mortality prediction

ROC: Receiver operating characteristic, TAC: Total antioxidant capacity, TOC: Total oxidant capacity, OSI: Oxidative stress index, IMA: Ischemia modified albumin, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, sPESI: Simplified pulmonary embolism severity index; L-sPESI: Lactate-simplified pulmonary embolism severity index

**Table 1A. Comparison of oxidant and antioxidant levels of participants included in Group 1 and Group 2**

| Oxidant/antioxidant | Patients/ healthy volunteers | Median (min.-max.) | p |
|---|---|---|---|
| TAC* | Group 1 | 1.6 (1.1-2.4) | 0.002 |
| | Group 2 | 1.8 (1.2-2.3) | |
| TOC† | Group 1 | 6.1 (1.7-22.6) | 0.001 |
| | Group 2 | 3.5 (2.1-7.3) | |
| OSI‡ | Group 1 | 3.5 (0.9-13.7) | 0.001 |
| | Group 2 | 1.8 (1.2-4.8) | |
| IMA§ | Group 1 | 0.6 (0.6-0.9) | 0.001 |
| | Group 2 | 0.5 (0.5-0-6) | |

Group 1: Patients diagnosed with acute pulmonary embolism, Group 2: Healthy volunteers, *TAC: Total antioxidant capacity, †TOC: Total oxidant capacity, ‡OSI: Oxidative stress index, §IMA: Ischemia modified albumin, AUC: Area under the curve

**Table 1B. ROC analysis of TAC, TOC, OSI and IMA levels in participants included in Group 1**

| Test Result Variable(s) | AUC | P | Asymptotic 95% Confidence Interval | |
|---|---|---|---|---|
| | | | Lower Bound | Upper Bound |
| TAC* | 0.336 | 0.002 | 0.236 | 0.436 |
| TOC† | 0.773 | 0.001 | 0.688 | 0.859 |
| **OSI‡** | **0.816** | **0.001** | **0.740** | **0.893** |
| IMA§ | 0.738 | 0.001 | 0.638 | 0.838 |

Group 1: Patients diagnosed with acute pulmonary embolism, Group 2: Healthy volunteers, *TAC: Total antioxidant capacity, †TOC: Total oxidant capacity, ‡OSI: Oxidative stress index, §IMA: Ischemia modified albumin, AUC: Area under the curve, ROC: Receiver operating characteristic

**Table 2. Comparison of characteristics of participants included in Group 1A and Group 1B**

| Variables | Group 1A* | Group 1B† | p |
|---|---|---|---|
| Diabetes mellitus | 0 (0%) | 4 (8%) | 0.56 |
| Hypertension | 0 (0%) | 10 (20%) | 0.10 |
| Malignancy | 7 (47%) | 4 (8%) | **0.002** |
| COPD‡ | 0 (0%) | 6 (12%) | 0.32 |
| Smoking habits | 2 (%13) | 9 (18%) | >0.99 |
| Being male | 6 (40%) | 16 (32%) | 0.76 |
| Massive embolism | 7 (47%) | 13 (26%) | 0.20 |

*Group 1A: Participants who died within 30 days of being diagnosed with pulmonary embolism, †Group 1B: Participants who survived after 30 days of being diagnosed with pulmonary embolism,
‡COPD: Chronic obstructive pulmonary disease

When ROC analysis was performed for SBP, DBP, heart rate, lactate, sPESI, and L-sPESI to be used in mortality prediction, the AUC was calculated to be highest for L-sPESI (Figure 2B, Table 5).

## Discussion

APE results in pulmonary circulatory insufficiency, hypoperfusion, hypoxia, and pulmonary ischemia. These conditions cause inflammation and oxidative stress. Therefore, changes occur in inflammatory parameters and oxidant and antioxidant levels [5,17,18]. In this study, we investigated the role of TAC, TOC, OSI, and IMA levels in the diagnosis of APE. The TAC level of patients was lower than that of healthy volunteers,

**Table 3A. Comparison of clinical findings of participants included in Group 1A and Group 1B**

| Group | | Age | SBP‡ | DBP§ | Pulse | Body temperature | SaO2\|\| |
|---|---|---|---|---|---|---|---|
| Group 1B† | Median | 72 | 117 | 78 | 95 | 36.2 | 93 |
| | Min. | 18 | 77 | 47 | 56 | 36.0 | 74 |
| | Max. | 93 | 193 | 129 | 181 | 37.6 | 100 |
| Group 1A* | Median | 65 | 104 | 70 | 124 | 36.0 | 90 |
| | Min. | 23 | 76 | 53 | 70 | 36.0 | 40 |
| | Max. | 98 | 131 | 80 | 148 | 37.0 | 99 |
| p | | 0.42 | **0.004** | **0.01** | **0.008** | 0.32 | 0.11 |

*Group 1A: Participants who died within 30 days of being diagnosed with pulmonary embolism, †Group 1B: Participants who survived after 30 days of being diagnosed with pulmonary embolism,

‡SBP: Systolic blood pressure, §DBP: Diastolic blood pressure, ||SaO2: Oxygen saturation, ¶TAC: Total antioxidant capacity, **TOC: Total oxidant capacity, ††OSI: Oxidative stress index, ‡‡IMA: Ischemia modified albumin, Min.: Minimum, Max.: Maximum

**Table 3B. Comparison of laboratory results of participants included in Group 1A and Group 1B**

| Group | | TAC¶ | TOC** | OSI†† | IMA‡‡ | Lactate | High sensitive troponin t | D-dimer |
|---|---|---|---|---|---|---|---|---|
| Group 1B† | Median | 1.6 | 5.9 | 3.1 | 0.6 | 2.5 | 20 | 737 |
| | Min. | 1.1 | 1,7 | 1.4 | 0.5 | 0.8 | 0 | 112 |
| | Max. | 2.3 | 14.4 | 9.0 | 0.8 | 8.6 | 307 | 19872 |
| Group 1A* | Median | 1.6 | 6.4 | 4.2 | 0.6 | 3.2 | 37 | 970 |
| | Min. | 1.2 | 2.1 | 0.9 | 0.5 | 1.4 | 10 | 354 |
| | Max. | 2.4 | 22.5 | 13.8 | 0.9 | 12.0 | 137 | 11820 |
| p | | 0.57 | 0.20 | 0.28 | 0.74 | **0.044** | 0.067 | 0.061 |

*Group 1A: Participants who died within 30 days of being diagnosed with pulmonary embolism, †Group 1B: Participants who survived after 30 days of being diagnosed with pulmonary embolism,

‡SBP: Systolic blood pressure, §DBP: Diastolic blood pressure, ||SaO2: Oxygen saturation, ¶TAC: Total antioxidant capacity, **TOC: Total oxidant capacity, ††OSI: Oxidative stress index, ‡‡IMA: Ischemia modified albumin, Min.: Minimum, Max.: Maximum

and the TOC, OSI, and IMA levels were found to be higher. In a study investigating the parameters of inflammation and oxidative stress in pulmonary embolism, significant increases were found between the TOC and OSI ($p<0.0001$ for both parameters) levels of the patient and control groups. However, no difference was observed between the TAC ($p=0.800$) levels [5]. In a similar study, TOC (p:0.080) and OSI (0.024) levels were found to be higher and TAC levels were found to be lower (p:0.011) in patients compared with the control group [18]. The results of our study were found to be compatible with the literature. These results show that the TOC and OSI levels increase and the TAC levels decrease or remain unchanged in patients with APE. TAC and OSI levels increase in the presence of APE; thus, they provide an advantage in the diagnosis of APE.

Elevated plasma troponin concentrations on admission may be associated with worse prognosis in the acute phase of pulmonary embolism [4]. In our study, high-sensitivity troponin t levels of participants who survived and died were compared to predict 30-day mortality. There was no difference between the high-sensitivity troponin t levels of the two groups. Lactate is a marker of an imbalance between tissue oxygen supply and demand, and consequently of severe pulmonary embolism. with overt or imminent hemodynamic compromise. Elevated arterial plasma levels of >2 mmol/L can predict PE-related complications, both in unselected and initially normotensive pulmonary embolism. patients. [4]. In a study, lactate levels of the high-risk pulmonary embolism patients were statistically higher than those of the other patients (3.7 vs. 1.9 and 1.3). In our study, the lactate levels of participants who survived and died were compared to predict 30-day mortality. On the other hand, lactate levels were higher in participants who died. This result is important because it indicates that the lactate level measured in a very short time at the bedside in the emergency department is a strong predictor of mortality.

In addition to laboratory parameters for predicting 30-day mortality due to pulmonary embolism, PESI and sPESI were investigated [19]. Studies have indicated that PESI and sPESI, which are frequently used in the emergency department, can identify high- and low-risk patients for all-cause 30-day

**Table 4A. Comparison of sPESI, L-sPESI and WELLS scores of participants included in Group 1A and Group 1B**

| Group | | sPESI‡ | L-sPES§ | WELLS score |
|---|---|---|---|---|
| Group 1B† | Median | 1 | 1 | 2 |
| | Min. | 0 | 0 | 0 |
| | Max. | 4 | 4 | 6 |
| Group 1A* | Median | 2 | 3 | 2 |
| | Min. | 0 | 1 | 1 |
| | Max. | 4 | 5 | 7 |
| p | | **0.004** | **0.001** | 0.42 |

*Group 1A: Participants who died within 30 days of being diagnosed with pulmonary embolism, †Group 1B: Participants who survived after 30 days of being diagnosed with pulmonary embolism,

‡sPESI: Simplified pulmonary embolism severity index, §L-sPESI: Lactate-simplified pulmonary embolism severity index, ||RVD: Right ventricle diameter, ¶LVD: Left ventricle diameter, Min.: Minimum, Max.: Maximum

**Table 4B. Comparison of cardiac chamber diameters measured on computed tomography of participants included in Group 1A and Group 1B**

| Group | | RVD|| | LVD¶ | RVD/LVD |
|---|---|---|---|---|
| Group 1B† | Median | 39 | 38 | 1.2 |
| | Min. | 20 | 18 | 0.5 |
| | Max. | 60 | 54 | 2.8 |
| Group 1A* | Median | 33 | 35 | 1.05 |
| | Min.. | 21 | 18 | 0.4 |
| | Max. | 50 | 51 | 2.4 |
| **p** | | 0.58 | **0.02** | 0.41 |

*Group 1A: Participants who died within 30 days of being diagnosed with pulmonary embolism, †Group 1B: Participants who survived after 30 days of being diagnosed with pulmonary embolism,

‡sPESI: Simplified pulmonary embolism severity index, §L-sPESI: Lactate-simplified pulmonary embolism severity index, ||RVD: Right ventricle diameter, ¶LVD: Left ventricle diameter, Min.: Minimum, Max.: Maximum

mortality [4,8-11]. In a study conducted in patients diagnosed with sub-segmental pulmonary embolism, a high WELLS score was associated with mortality or new venous thromboembolism [20]. In this study, the WELLS score and sPESI were evaluated as predictive of mortality. Among the laboratory studies, L-sPESI was created by adding lactate level (Lactate >2.5 mmol/L) to sPESI because lactate levels are studied at the bedside in emergency department patients. The L-sPESI was evaluated for mortality prediction. Although no difference was observed between the WELLS scores of participants who survived and died, there was a statistically significant difference in sPESI and L-sPESI. The AUC was higher for L-sPESI when ROC analysis was performed. It was concluded that L-sPESI would be a better predictor of mortality.

**Table 5. ROC analysis of SBP, DBP, pulse, lactate, sPESI and L-sPESI values in mortality prediction**

| Test Result Variable (s) | AUC†† | p | Asymptotic 95% Confidence Interval | |
|---|---|---|---|---|
| | | | Lower Bound | Upper Bound |
| SBP* | 0.255 | 0.004 | 0.118 | 0.393 |
| DBP† | 0.289 | 0.01 | 0.154 | 0.425 |
| Pulse | 0.725 | 0.009 | 0.573 | 0.878 |
| Lactate | 0.672 | 0.045 | 0.512 | 0.832 |
| sPESI‡ | 0.731 | 0.007 | 0.592 | 0.871 |
| **L-sPESI§** | **0.765** | **0.002** | **0.646** | **0.885** |

‡sPESI: Simplified pulmonary embolism severity index, §L-sPESI: Lactate-simplified pulmonary embolism severity index, *SBP: Systolic blood pressure, †DBP: Diastolic blood pressure, ††AUC: Area under the curve, ROC: Receiver operating characteristic

In addition to CT pulmonary angiography, which is used in the diagnosis of APE, RVD, LVD measured in CT pulmonary angiography images, and the RVD/LVD ratio were investigated in the risk classification. In one study, the RVD/LVD ratios of low-, intermediate-, and high-risk patients diagnosed with pulmonary embolism were found to differ [1]. A previous study indicated that increased RVD was associated with an increase in 30-day mortality due to APE [21]. In another study, an increase in 3-month mortality was observed with an RVD/LVD ratio of ≥0.9-1 [22]. In our study, unlike other studies, there was no difference in the RVD/LVD ratio between participants who survived and died. In most of the studies, right ventricular dilation was assessed as the right-to-left ventricular ratio. In a meta-analysis (21), 34 studies reported on the right-to-left ventricle short-axis diameter ratio, four studies on the right-to-left ventricle volume ratio, and one study on the right-to-left ventricle area ratio. The right-to-left ventricle short-axis diameter ratio was assessed in transverse bi-dimensional images in 28 studies and in reconstructed 4-chamber images in 16 studies. The cutoff values for right-to-left ventricular ratios differed among the studies. In another study (22), the scans were evaluated by measuring the minor axes of the right and left ventricles of the heart in the transverse plane at their widest points between the inner surface of the free wall and the surface of the interventricular septum. In our study, we assessed RVD and LVD by measuring the distance between the septum and the inner wall of the ventricular cavity. Right ventricular diameter was measured just below the tricuspid valve, and left ventricular diameter was measured just below the mitral valve. The assessment of right ventricular dilation was different from that of other studies in our study. The difference in our study results can be attributed to this factor. Additionally, 15 (23%) of the Group 1 participants died within 30 days of admission to the emergency department in our study. The limited number of participants who died in our study

could have also contributed to the results. However, the RVD/LVD ratio was >1 in both groups, and the patients were at high risk of mortality. In this case, LVD was evaluated as the second parameter, and LVD was found to be lower in participants who died than in those who survived. It was thought that low LVD contributed to decrease in cardiac output, hypotension, and hemodynamic instability in patients with an RVD/LVD ratio >1, leading to increased mortality. This result is important because it indicates that LVD is an important parameter as a mortality predictor in patients with an RVD/LVD ratio >1.

### Study Limitations

In this observational study, only patients who were not given thrombolytic drugs were included. Thus, the number of patients was limited. This is a limitation of our study.

### Conclusion

As a result, the oxidant-antioxidant balance is impaired in APE. Therefore, oxidants and antioxidants can be used to diagnose and exclude patients with suspected APE. However, oxidants and antioxidants are insufficient to predict 30-day mortality. Lactate, sPESI, and L-sPESI can be used to predict 30-day mortality. LVD can be used to predict 30-day mortality in patients with an RVD/LVD ratio>1. However, larger studies are needed to support these findings.

### Ethics

**Ethics Committee Approval:** This prospective study was performed in the emergency department of a tertiary hospital after obtaining the University of Health Sciences Antalya Education and Research Hospital Clinical Research Ethics Committee (Approval number: 14/15, date: 30.05.2019).

**Informed Consent:** Informed consent was obtained from all participants and their relatives.

### Footnote

### Authorship Contributions

Surgical and Medical Practices: M.A., N.J., Concept: M.A., N.J., Design: M.A., N.J., Data Collection or Processing: M.A., Analysis or Interpretation: M.A., N.J., Literature Search: M.A., N.J., Writing: M.A., N.J.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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**Supplementary Material 1. Simplified pulmonary embolism severity index and Lactate- Simplified pulmonary embolism severity index**

| Predictors | sPESI* | L-sPESI† |
|---|---|---|
| Age >80 years | +1 | +1 |
| History of malignancy | +1 | +1 |
| Chronic cardiopulmonary disease | +1 | +1 |
| Heart rate ≥110 beats/min | +1 | +1 |
| Systolic blood rate ≥110 mmHg | +1 | +1 |
| Arterial oxyhemoglobin saturation <90% | +1 | +1 |
| Lactate >2.5 mmol/L | - | +1 |

*sPESI: Simplified pulmonary embolism severity index, †L-sPESI: Lactate- Simplified pulmonary embolism severity index