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Radiological findings and their relationship with mortality in acute pulmonary embolism

F. TAŞÇI[1], İ. ATAŞ[2], M. MURAT YAZICI[3], E. GÜLER[4], Ö. BILIR[3]

[1]Department of Radiology, Recep Tayyip Erdoğan University, Training and Research Hospital, Rize, Turkey
[2]Department of Emergency Medicine, Rize State Hospital, Rize, Turkey
[3]Department of Emergency Medicine, Recep Tayyip Erdoğan University, Training and Research Hospital, Rize, Turkey
[4]Department of Emergency Medicine, Sultan 1. Murat State Hospital, Edirne, Turkey

Abstract. – OBJECTIVE: The aim of the study was to investigate whether sarcopenia had the potential to predict mortality by analyzing epicardial and visceral fat thickness measurements, which are among the radiological findings and scores known to be crucial in determining the prognosis and risk classification of patients diagnosed with acute pulmonary embolism (PE) in the emergency department.

PATIENTS AND METHODS: The study included patients diagnosed with acute PE in the emergency department from January 2019 to December 2022 and involved the retrospective examination of their demographic characteristics, clinical parameters, and radiological data obtained from computed tomography pulmonary angiography (CTPA) [main pulmonary artery (MPA) diameter, pulmonary artery obstruction, right and left ventricular diameters, epicardial and visceral tissue thicknesses, and pectoralis muscle thickness (PMT)]. The primary endpoint was mortality during the hospitalized treatment and follow-up processes, and the secondary endpoint was mortality within 90 days after diagnosis.

RESULTS: Of the 389 patients included in the study, 11.6% had a fatal outcome in the early period following hospitalization for treatment, and 22.6% had a fatal outcome within the 90-day (late) period after diagnosis. In patients with late-period mortality, pleural fluid (30.8%), pericardial fluid (16.7%), and atelectasis (32.6%) were found to be statistically significantly higher. Among the markers obtained from imaging examinations, only PMT – right: 9.4 [interquartile range (IQR): 6.0-14.0]; left: 9.1 (IQR: 5.4-13.8) – was associated with mortality. According to logistic regression analysis, the MPA diameter was associated with early-period mortality, and it was determined that the right ventricular diameter and the right and left PMT values had a predictive effect on late-period mortality.

CONCLUSIONS: To predict mortality, CTPA-based scoring systems that include markers such as PMT, pericardial and pleural fluid, and atelectasis would be more effective; however, large-scale studies are needed to enrich these findings.

Key Words:
Acute pulmonary embolism, Epicardial fat thickness, Visceral fat thickness, Pectoral muscle area.

Introduction

Acute pulmonary embolism (PE) is a potentially fatal cardiovascular disease that requires urgent diagnosis and treatment[1]. Therefore, it is crucial to promptly conduct risk classification at the time of patient presentation. The basic diagnostic strategies include clinical probability scores, D-dimer measurement, and computed tomography pulmonary angiography (CTPA) findings. In particular, CTPA is used as the gold standard diagnostic method, with sensitivity and specificity rates of up to 100%[2]. Many studies[3-5] have suggested that the parameters obtained from CTPA can serve as predictors of mortality and morbidity in this patient group.

Many computed tomography (CT) findings, such as obstruction and percentage of obstruction in the vascular bed, right heart dilatation, and leakage of contrast material into the vena cava, have been used to assess the prognosis and complications that may arise in the acute period of PE[6-8]. Epicardial fat thickness (EFT) and visceral fat thickness (VFT), which have been shown to be the source of proinflammatory cytokines, have been utilized to formulate care strategies and determine mortality risk in patients with critical life-threatening diseases[9,10]. In addition, sarcopenia, a condition that occurs

Corresponding Author: İsmail Ataş, MD; e-mail: drismailatas@gmail.com

as a primary result of aging, has been identified as a marker of mortality in critically ill patients[11]. These findings obtained from CTPA taken at the time of patient presentation have been used to determine mortality and morbidity in patients with acute PE[12-14].

The combination of clinical, laboratory, and radiological parameters evaluated at the time of presentation to the emergency department is effective in determining the risk classification of patients. This study aimed to ascertain whether sarcopenia had the potential to predict mortality by analyzing epicardial and visceral fat thickness measurements, which are among the radiological findings and scores known to be crucial in determining the prognosis and risk classification of patients diagnosed with PE in the emergency department.

Patients and Methods

Study Design

The study was conducted by retrospectively examining patients diagnosed with acute PE in the emergency department of a tertiary hospital from January 2019 to December 2022. Prior to the study, approval was obtained from the local ethics committee (date: November 9, 2023, decision number: 2023/253). Informed consent was obtained from the participants whose images were used in this publication.

The local computer-based hospital information management system, where patient records are kept, was used to collect the clinical and radiological data of the patients with acute PE included in the study. Patients younger than 18 years, those with incomplete clinical and laboratory data, those with non-diagnostic CTPA findings (movement artifacts, no contrast material injection, or injection errors), and those who could not be followed up for 90 days after diagnosis were excluded from the study. A total of 389 patients diagnosed with acute PE in the emergency department were included in the sample (Figure 1). The primary endpoint was mortality during the hospitalized treatment and follow-up processes, and the secondary endpoint was mortality within 90 days after diagnosis.

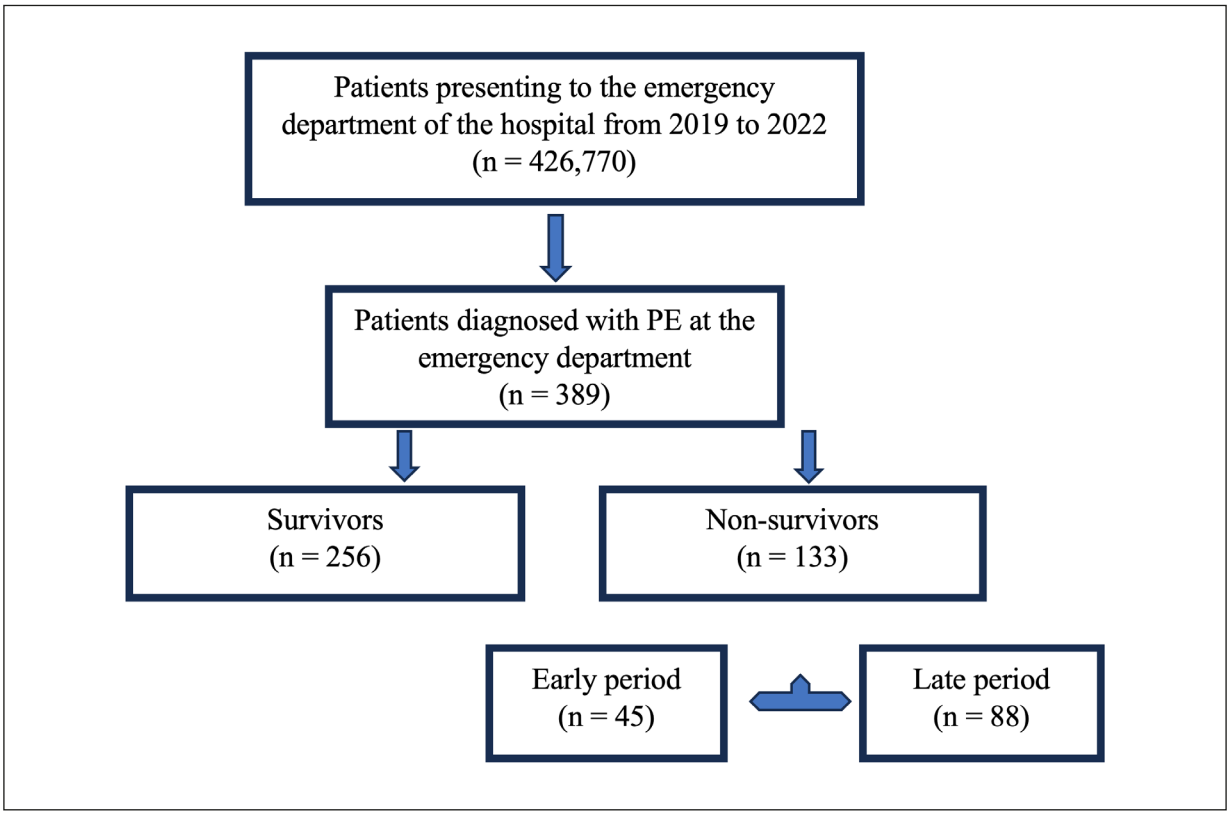

Figure 1. Flow chart of the study.

Clinical Parameters

In addition to the patients' complaints and demographic data at the time of presentation to the emergency department, blood pressure, heart rate, saturation, treatments administered in the emergency department, hospitalized service, and length of hospital stay were recorded. The Wells score[15], the revised Geneva score[16], and the simplified pulmonary embolism severity index (sPESI)[17] were also calculated. Lastly, D-dimer (0-0.5 µg/ml), troponin-I (0-34.2 ng/L), and blood pH and lactate (0.5-1.6 mmol/L) values were collected. Deaths that occurred during inpatient follow-up and treatment after the PE diagnosis were considered early-period mortality, and those that occurred due to any cause during the 90-day period after the PE diagnosis were considered late-period mortality.

Deep venous thrombosis (DVT) was detected using bedside ultrasonography (Fujifilm-Sonosite FC1-FUJIFILM Sonosite, Inc. Bothell, WA 98021 USA, 2015, 7-12 MHz linear transducer) performed during the emergency department management of acute PE. Echocardiography findings (right atrium and ventricle dilatation, thrombus in the right heart, Mc-Connel sign, etc.) were obtained from the patient files.

Imaging Technique

CTPA was performed with a 16-slice CT scanner (Alexion TSX-034A, Toshiba, Shimoishigomi, Otawara-Shi, Toschigi-Ken, Japan). Iodine-based contrast material (Iopromide, Ultravist, 300 mg I/mL, Bayer Schering Pharma, Berlin, Germany) was administered intravenously through peripheral venous access at a rate of 4.0 ml s^{-1}. Contrast material injection was performed as an automatic bolus, triggering 100 Hounsfield units (HU) in the pulmonary trunk. Images were obtained at 100 kVp and 125 mAs with a 1-mm slice thickness under deep inspiration.

Radiological Findings

In the emergency department where the study was conducted, each CT scan is interpreted simultaneously by a radiologist on duty *via* remote access after imaging is completed. In the current study, to ensure standardization in retrospective measurements after the initial evaluation, the CT-PA images of the patients included in the study were re-evaluated by a single radiologist with 20 years of experience. The diagnosis of PE was made based on the detection of a pulmonary artery contrast filling defect in at least two sections. The diameter of the main pulmonary artery (MPA)[18] was measured, and the area of vascular obstruction in the central area (within the main and/or lobar pulmonary artery) or peripheral area (including the segmental and/or subsegmental pulmonary artery branches)[19] were evaluated at 50% or ≥ 50%. Right ventricular (RV) diameter was obtained by measuring the distances from one end of the inner surface of the ventricular wall to the other end at the valve level during the same time of the cardiac cycle on the same axial CT scan without cardiac synchronization (Figure 2)[20].

EFT

EFT was measured using the freely available AW4.6 software (GE, General Electric Company

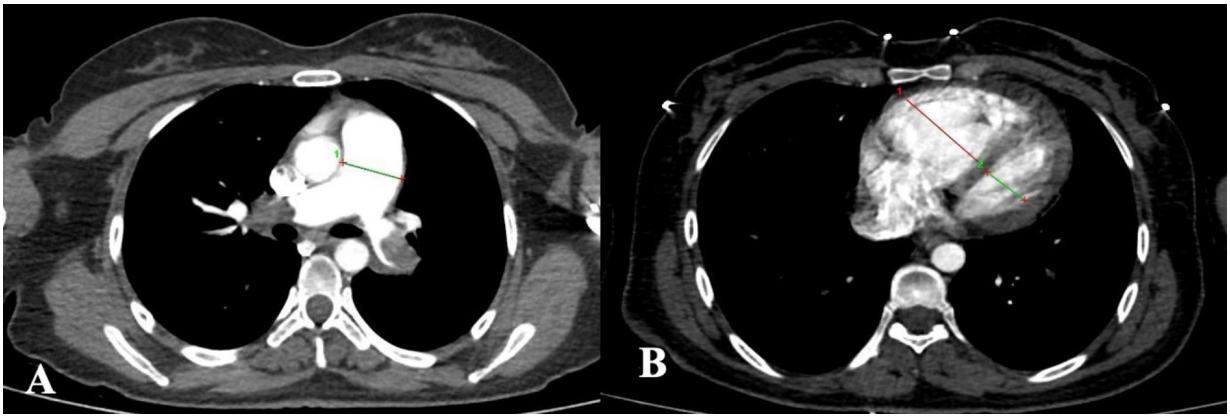

Figure 2. Imaging of the pulmonary artery and determination of ventricular diameters. **A**, Axial measurement of the main pulmonary artery diameter and images of pulmonary artery obstruction obtained from a computed tomography scan of a sample case. **B**, Computed tomography pulmonary angiography image of a sample case showing the measurement of the right and left ventricles separately at the valve level from one end to the other end of the inner surface of the ventricular walls.

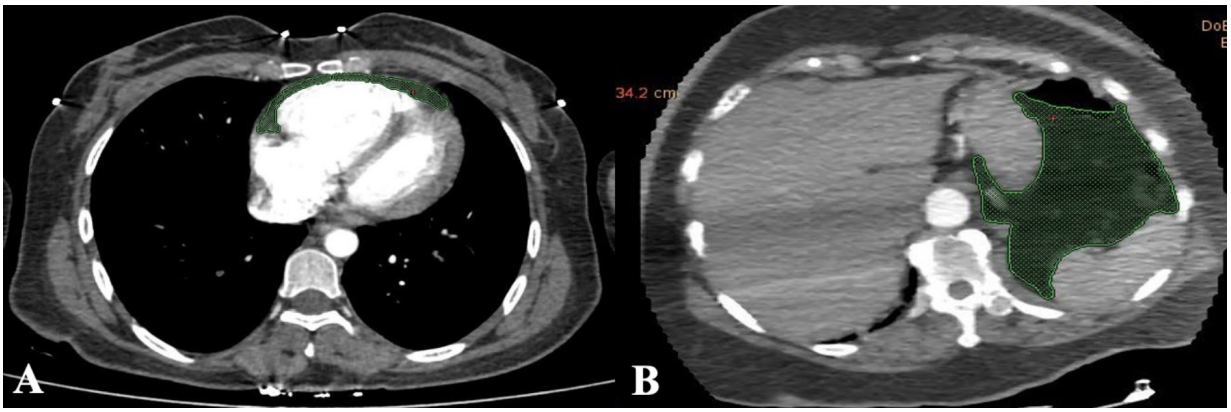

Figure 3. Epicardial and visceral fat thickness measurements. **A**, Epicardial fat thickness measurements obtained from the computed tomography images of a sample case. **B**, Visceral fat thickness measured using the axial section through the middle of the first lumbar vertebra (L1). The green area shows the visceral fat thickness area of a sample case).

Healthcare, Chicago, IL, USA). As in other reference studies in the literature[14,21], the anatomical boundaries were defined as the pulmonary artery bifurcation, left atrium, and aortic root for the upper boundary, and the diaphragm and left ventricular apex for the lower boundary (Figure 3A).

VFT

VFT was measured using the freely available AW4.6 software (GE, General Electric Company Healthcare, Chicago, IL, USA). Area evaluation was performed using an axial section from the middle of the first lumbar vertebra (L1) (Figure 3B), as recommended by similar studies[13,22].

Skeletal Muscle Thickness

Skeletal muscle thickness was measured using the freely available AW4.6 software (GE, General Electric Company Healthcare, Chicago, IL, USA). Bilateral pectoralis muscle thickness (PMT) values were measured on the axial section by anatomically determining the thoracic vertebra 5 (Th5) at the level of the superior arcus aorta in the reformatted images on the sagittal plane in CTPA (Figure 4), as recommended by similar studies[12,23].

Statistical Analysis

All statistical analyses were performed on Jamovi v. 1.6 software (Jamovi Project Computer Software, version 1.6. Sydney, Australia). Type 1 errors were regarded as 5% for all comparisons. The Shapiro-Wilk test was applied to evaluate the normality of the data distribution. For continuous variables, non-normally distributed data were expressed as median and interquartile range (IQR) and normally distributed data as mean and minimum-maximum values. Categorical data were expressed as frequency (n) and percentage (%) values. The comparisons of continuous variables were performed using the *t*-test for normally distributed groups and the Mann-Whitney U test for non-normally distributed groups. Categorical variables were compared using the Chi-square test.

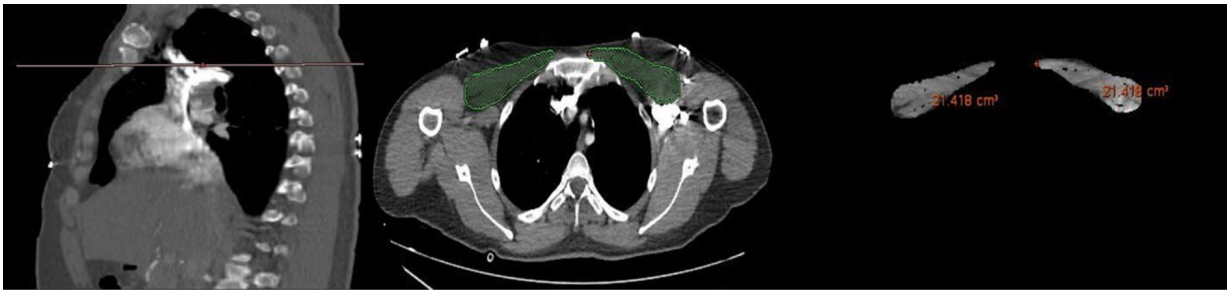

Figure 4. Measurement of pectoral muscle area by determining the Th5 vertebra in a sample case.

Table I. Patients' demographic data and baseline characteristics.

Characteristics, n = 389	Value
Gender	
Male, n (%)	139 (35.7%)
Female, n (%)	250 (64.3%)
Age (years), median (IQR)	73.0 (63.0-82.0)
Comorbidities	
Hypertension, n (%)	316 (81.2%)
Diabetes, n (%)	150 (38.6%)
CAD, n (%)	108 (27.8%)
CHF, n (%)	60 (15.4%)
COPD, n (%)	51 (13.1%)
Asthma, n (%)	7 (1.8%)
Atrial fibrillation, n (%)	113 (29.0%)
Stroke, n (%)	64 (16.5%)
Dementia, n (%)	91 (23.4 %)
Neoplasia, n (%)	76 (19.5%)
History PE, n (%)	38 (9.8%)
History DVT, n (%)	6 (1.5%)
Vital signs	
SBP (mmHg), median (IQR)	130 (110-140)
DBP (mmHg), median (IQR)	80 (70-90)
Pulse (min), median (IQR)	90 (80-103)
Os (%), median (IQR)	91 (88-94)
Laboratory parameters	
Troponin I (ng/L), median (IQR)	15.3 (0.1-74.1)
D-Dimer (µg/L), median (IQR)	3,200 (1,576-5,670)
Lactate (mmol/L), median (IQR)	1.8 (1.4-2.3)
Wells score, median (IQR)	2 (1-2)
sPESI, median (IQR)	2 (1-3)
Geneva score, median (IQR)	3 (2-3)
YEARS score, median (IQR)	1 (0-1)
Mortality	
Early period*, n (%)	45 (11.6%)
Late period&, n (%)	88 (22.6%)

IQR: Interquartile Range (25p-75p), CAD: Coronary Artery Disease, CHF: Congestive Heart Failure, COPD: Chronic Obstructive Pulmonary Disease, PE: Pulmonary Embolism, DVT: Deep Vein Thrombus, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, Os: Oxygen Saturation, sPESI: Simplified Pulmonary Embolism Severity Index. *Early-Period Mortality, &Late-Period Mortality.

Logistic regression analysis was applied for multivariate analysis, and odds ratio and *p*-values were calculated for early- and late-period mortality.

Results

Of the 389 patients included in the study, 64.3% were women, and the median age was 73 (IQR: 63-82) years. At the time of presentation to the emergency department, 13.4% of the patients were hemodynamically unstable, and 11.8% required vasopressors. The main indications for CTPA were high values of calculated PE probability scores and elevated D-dimer levels according to age (median 3,200 µg/L) accompanied by complaints, such as shortness of breath (66%) and chest pain (8.7%), as well as the presence of risk factors, including immobilization (35.2%), cancer (19.5%), and surgery (6.2%). In addition, 35% of the patients had DVT according to the bedside Doppler ultrasonography performed at the time of presentation, 1.5% had a previous history of DVT, and 9.8% had a history of PE. The basic demographic characteristics of the patients are given in Table I. The sPESI score, which indicates 30-day mortality, was determined to have a median value of 2, and this score was found to be ≥ 2 in 51.7% of the patients. Early-period mortality during hospital stay for treatment was observed in 11.6% of the patients, and late-period mortality (within 90 days after diagnosis) occurred in 22.6%.

Table II presents the CTPA findings of the patients. Upon evaluating the localization of the thromboembolism and the degree of occlusion, it was determined that 56.6% of the patients had thromboembolism in both pulmonary arteries, and the percentage of occlusion was < 50% in 66.1% of the cases. Concerning their relationship with mortality, while there was no relationship between the percentage of occlusion and mortality, the presence of occlusion in the right pulmonary artery was associated with early mortality ($p = 0.013$).

Table II. Patients' CT findings and measurements.

Characteristics, n = 389	Value
CT Findings	
Pleural fluid, n (%)	120 (30.8%)
Pericardial fluid, n (%)	65 (16.7%)
Atelectasis, n (%)	127 (32.6%)
Hampton hump, n (%)	164 (42.2%)
CT measurements	
MPA diameter (mm), median (IQR)	29.8 (27.0-32.9)
RV diameter (mm), median (IQR)	43.0 (38.6-47.7)
Right PMT (mm), median (IQR)	9.4 (6.0-14.0)
Left PMT (mm), median (IQR)	9.1 (5.4-13.8)
VFT (mm), median (IQR)	107.0 (69.4-153.0)
EFT (mm), median (IQR)	4.1 (3.2-5.0)
Pulmonary embolism side	
Right, n (%)	116 (29.8%)
Left, n (%)	53 (13.6%)
Bilateral, n (%)	220 (56.6%)
Occlusion percentage	
< 50%, n (%)	257 (66.1%)
≥ 50%, n (%)	132 (33.9%)

IQR: Interquartile Range (25p, 75p), CT: Computed Tomography, MPA: Main Pulmonary Artery, RV: Right Ventricle, PMT: Pectoralis Muscle Thickness, VFT: Visceral Fat Thickness, EFT: Epicardial Fat Thickness.

Pleural (30.8%) fluid, pericardial fluid (16.7%), and atelectasis (32.6%) caused by the effects of PE on the cardiovascular and respiratory systems were identified as potential indicators of late-period mortality (p = 0.010, p = 0.007, and p = 0.008, respectively). Of the markers obtained from imaging examinations, namely PMT [right: 9.4 (IQR: 6.0-14.0), left: 9.1 (IQR: 5.4-13.8)], MPA diameter [29.8 (IQR: 27.0-32.9)], RV diameter [43.0 (IQR: 38.6-47.7)], VFT [107.0 [IQR: 69.4-153.0)], and EFT [4.1 (IQR: 3.2-5.0)], only PMT was found to be associated with mortality (Table III).

According to the logistic regression analysis (Table IV), the MPA diameter had a predictive effect on early-period mortality, while RVD and the right and left PMT values had a predictive effect on late-period mortality.

Discussion

In this study, we found that the PMT measured on CTPA was associated with 90-day mortality in patients diagnosed with acute PE in the emergency department. In studies[24,25] conducted in recent years, body composition characteristics, including muscle and fat thickness areas obtained by CT, have been defined as new imaging markers for predicting the outcomes of both individuals with PE and those with critical diseases, such as malignancy. In a study[26], higher density in subcutaneous fat on CTPA in COVID-19 patients was found to be associated with 28-day mortality. When evaluating the body's muscle area, it is recommended to measure the general skeletal muscle thickness at the L3 level[27]. However, the CT used in the diagnosis of acute PE does not include the L3 level; therefore, in the literature, it is advised to use muscle areas at the T4 or T5 level[12,23]. In the current study, the PMT calculated at the T5 level, considered a reliable area for this measurement, was found to have a relationship with mortality. The PMT was determined to be effective in predicting mortality, as well as length of hospital stay, intubation requirements, mechanical ventilation duration, and airway complications[11,28,29].

VFT and EFT are other parameters acknowledged as new markers of cross-sectional imaging. In particular, they have been reported to be associated with cardiometabolic disorders and lung functions due to secreted pro-inflammatory cytokines in the presence of central obesity, characterized by intra-abdominal fat accumulation[30,31]. However, according to the literature and our study, VFT is not an effective parameter in determining mortality[13]. EFT also plays an active role in determining cardiovascular system and thromboembolism risk[32]. Although it has been evaluated as an effective parameter in studies evaluating disease severity and mortality in critically ill patients, especially during the COVID-19 pandemic[14,33], our results revealed no such relationship. In a study conducted by Rossi et al[14] with patients who were followed up in the intensive care unit due to severe COVID-19, although EFT volume was evaluated to be related to mortality, no significant relationship was detected when age was included in the analysis.

In unstable cases of acute PE accompanied by cardiovascular insufficiency and shock, the amount of embolism and findings of RV dysfunction on CTPA have been found to be associated with mortality[34-36]. Similarly, in the current study, there was a relationship between late-period mortality and the RV diameter. In addition, the presence of pulmonary hypertension in conjunction with an increased RV diameter and RV failure leads to an increase in vascular permeability, which is manifested by pleural fusion[37,38]. This has been reported to be associated with a poor prognosis and a longer hospital stay[39], as also indicated by our study. This situation can also lead to transudative effusion in the pericardial area, and it is established that the presence of pericardial effusion is linked to mortality[40].

Atelectasis is one of the common findings in patients who have undergone CTPA in the emergency department due to suspicion of PE. It is correlated with the degree of hemodynamic disorder, the level of hypoxemia, and the percentage of pulmonary vascular occlusion[41]. In our study, atelectasis was detected in 32.6% of the patients and was associated with late-period mortality.

Limitations

The most important limitation of the study is that it was conducted in a single center using retrospective data obtained from a specific population. In addition, although VFT and PMT depend on population characteristics, such as gender, race, and age, this distinction was not made in the current study. A further limitation concerns the retrospective evaluation of radiological measures acquired using CTPA by a single radiologist to ensure standardization.

Table III. CT measurements according to mortality status.

CT measurements	Survival (n = 187)	Mortality status: Early-period mortality (n = 45)	Mortality status: Late-period mortality (n = 88)	*p*-value*	*p*-value&
Findings					
Pleural fluid, n	83	18	37	0.158	**0.010**
Pericardial fluid, n	42	10	23	0.292	**0.007**
Atelectasis, n	88	20	39	0.073	**0.008**
Hampton hump, n	120	24	44	0.106	0.090
Measurements					
MPA diameter (mm), median (IQR)	29.8 (26.8-32.9)	30.7 (28.7-34.0)	29.9 (28.0-32.9)	0.060	0.411
RV diameter (mm), median (IQR)	42.9 (38.2-47.2)	45.5 (39.3-49.0)	43.9 (39.9-49.1)	0.094	0.057
Right PMT (mm), median (IQR)	9.9 (6.2-14.6)	7.8 (5.5-11.6)	8.1 (5.4-13.2)	0.065	**0.024**
Left PMT (mm), median (IQR)	9.7 (5.9-14.3)	6.9 (3.6-12.1)	6.9 (4.1-11.7)	**0.017**	**0.002**
VFT (mm), median (IQR)	109.0 (73.9-158.0)	109.0 (63.0-134.0)	101.0 (53.4-141.0)	0.344	0.067
EFT (mm), median (IQR)	4.1 (3.2-5.0)	4.0 (3.1-4.8)	4.0 (3.3-5.0)	0.988	0.617
Pulmonary embolism side				**0.013**	0.067
Right, n	86	17	30		
Left, n	36	11	17		
Bilateral, n	179	17	41		
Occlusion percentage				0.212	0.771
< 50%, n	200	26	57		
≥ 50%, n	121	19	31		

CT: Computed Tomography, IQR: Interquartile Range (25p-75p), MPA: Main Pulmonary Artery, RV: Right Ventricular, PMT: Pectoralis Muscle Thickness, VFT: Visceral Fat Thickness, EFT: Epicardial Fat Thickness. &Late-period mortality; *early-period mortality.

Table IV. Logistic regression analysis of the acquired parameters for the prediction of mortality in patients with acute pulmonary embolism.

Univariate analysis	Non-survivors (n = 88)		
CT measurements	**Odds ratio**	**95% CI**	***p*-value**
MPA diameter	1.031	0.979-1.085	0.238
RV diameter	1.034	1.001-1.067	**0.043**
Right PMT	0.955	0.916-0.955	**0.027**
Left PMT	0.945	0.907-0.986	**0.009**
VFT	0.997	0.993-1.001	0.111
EFT	1.064	0.908-1.247	0.442
Univariate analysis	**Early-period mortality (n = 45)**		
CT measurements	**Odds Ratio**	**95% CI**	***p*-value**
MPA diameter	1.072	1.002-1.148	**0.041**
RV diameter	1.036	0.994-1.081	0.087
Right PMT	0.947	0.895-1.002	0.057
Left PMT	0.950	0.899-1.004	0.069
VFT	0.999	0.994-1.003	0.532
EFT	1.118	0.914-1.367	0.276

CT: Computed Tomography, MPA: Main Pulmonary Artery, RV: Right Ventricle, PMT: Pectoralis Muscle Thickness, VFT: Visceral Fat Thickness, EFT: Epicardial Fat Thickness.

Conclusions

In acute PE, CTPA is used not only for the establishment of an emergency diagnosis but also for the evaluation of treatment options and as a mortality predictor. However, this gold-standard method carries the risks of radiation exposure and the development of contrast material-induced nephropathy. Therefore, it is essential to promptly perform risk scoring and determine the necessity of using imaging tests. Given the potentially fatal nature of the disease, it may be more effective to incorporate imaging markers into current scoring systems that are used as mortality indicators as well as diagnostic tools. In particular, PMT presents as a predictor of mortality according to the results of previous studies and the current research. Furthermore, it is important to assess the presence of pericardial fluid, pleural fluid, and atelectasis that occur due to the effects of acute PE on the cardiovascular and respiratory systems. In conclusion, our results indicate that a CTPA-based scoring system to determine mortality may be more effective in diagnosis; however, they need to be confirmed by large-scale studies.

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Authors' Contributions
Literature search (MMY, İA), study design (FT, ÖB), legislative applications (MMY, EG), data collection (FT, İA), supervision and quality control (ÖB, EG, FT), statistical data analysis (MMY), data interpretation (MMY, İA, EG), drafting the manuscript (MMY, İA). All authors were involved in the writing and critical revision of the manuscript and approved the final version. FT, İA, MMY, EG, and ÖB take the whole responsibility for the paper.

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Availability of Data and Materials
The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflicts of Interest
The authors declare they have no conflict of interest.

Informed Consent
Patients' informed consent was obtained before starting the study.

Ethics Approval
This study was approved by the Recep Tayyip Erdoğan University Faculty of Medicine Ethics Committee (date: November 9, 2023, decision number: 2023/253). The research has been conducted by following the Declaration of Helsinki and its later amendments.

ORCID ID
Filiz Taşçı: 0000-0002-8981-171X
İsmail Ataş:0000-0001-6723-8564
Mümin Murat Yazıcı: 0000-0003-1957-7283
Enes Güler: 0000-0003-4926-0332
Özlem Bilir: 0000-0001-9016-1665

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