

ORIGINAL ARTICLE

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A mortality indicator in acute pulmonary embolism: the inferior vena cava contrast reflux score feasibility

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Abstract: **Objective:** Acute pulmonary embolism (APE) is frequently associated with high morbidity and mortality rates. Numerous studies have investigated the prognostic significance of cardiovascular computed tomography (CT) parameters. This study aimed to investigate potential CT scan predictors of 24-hour mortality in APE and to evaluate the value of the inferior vena cava (IVC) reflux score calculated on CT scan in predicting mortality.

Methods: This study was a single-center, retrospective study. Approval from the local ethics committee (decision no. 2023/76) was obtained before patients' data scanning. Patients who were admitted to the emergency department (ED) of a tertiary education and research hospital in Turkey between January 1, 2019, and December 31, 2021, who were diagnosed with APE at CT scan in the ED and whose treatment was started, and who did not meet the exclusion criteria were included in the study. The relationship between CT scan findings and early and late mortality was evaluated.

Results: The study population comprised 226 patients, meeting the inclusion and exclusion criteria. Of the 226 patients, a total of 39 (17.3%) patients died, 16 (7.1%) within the first 24 hours. In evaluating CT scan parameters, the inferior vena cava (IVC) reflux score showed a statistically significant difference between the groups with and without mortality (24-hour $P=0.001$; 30-day $P=0.001$). Patients who died within the first 24-hour and 30-day after admission showed a reflux grade 3 into IVC more often than survivors (24-hour odds ratio (OR): 14.57, 95% confidence interval (CI): 3.64,58.1; $P=0.001$); 30-day (OR: 6.54, 95% CI: 2.51,16.98; $P=0.001$). However, other CT parameters were evaluated, and no statistical relationship was found between the groups with and without mortality.

Conclusion: The cardiovascular CT scan findings may not be suitable for use as predictors of mortality. However, the IVC reflux score may be a good indicator of both early and late mortality.

Keywords: Inferior Vena Cava Reflux Score; Mortality Indicator; Pulmonary Embolism

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1. Introduction

Acute pulmonary embolism (APE) is a frequently seen entity associated with high morbidity and mortality rates (1-3). A mortality rate as high as 18% has been reported for APE, although the figure in one large meta-analysis was 10.7% (4,5). The diagnosis and treatment of APE are, therefore, critical. However, APE is difficult to diagnose for clinicians due to the absence of a characteristic physical examination finding or symptom (6). Computed tomography pulmonary angiography (CTPA) is the gold standard radiological technique most frequently used to diagnose the disease in clinical practice (7-9). Magnetic resonance imaging (MRI) of the chest, echocardiography, extremity ultrasonography, and nuclear medicine imaging techniques are also employed for diagnosis (10,11). Due to the high mortality rate in APE, performing an emergency risk classification at the time of presentation is very important. Various scoring systems are available for predicting mortality in patients with the condition (12,13). The ma-

majority of these are based on clinical diagnostic and laboratory parameters. Several studies have also evaluated CTPA as an indicator of potential mortality and morbidity in patients with APE. The main right-left pulmonary artery, right-left ventricle, and inferior vena cava (IVC) diameters can be measured in patients with emboli detected at computed tomography (CT) in the pulmonary arteries. Right/left ventricle and IVC anteroposterior/transverse diameter ratios and IVC reflux scores can also be calculated. Some studies have also shown that cardiovascular CT measurements can predict mortality in APE (14-16).

However, another study has reported that these cannot be used as mortality indicators in the APE (17).

Numerous studies have investigated the prognostic significance and association of cardiovascular CT scan parameters with patient outcomes, although inconsistent results have been obtained. However, many studies have evaluated mortality indicators in terms of late (30-day) mortality, and pa-

parameters that can assess early mortality status in APE patients diagnosed in the emergency department (ED) have generally not been adequately examined. Moreover, considering the importance of early treatment intensity, if CTPA can determine mortality risk in APE, CT parameters should determine mortality in the first 24 hours when more intensive treatment is required. Based on this hypothesis, we aimed to investigate potential CTPA predictors of 24-hour mortality in APE and to evaluate the value of the IVC reflux score calculated on CTPA in predicting mortality.

2. Methods

2.1. Study population and design

This single-center, retrospective study examined patients presenting to the ED with differing symptoms and diagnosed with APE. Ethical committee approval was granted prior to data analysis (decision no. 2023/76).

Patients who were admitted to the ED of a tertiary education and research hospital in Turkey between January 1, 2019, and December 31, 2021, who were diagnosed with APE at CTPA in the ED and whose treatment was started, and who did not meet the exclusion criteria were included in the study. Patients under 18 years of age, pregnant women, patients transferred to another institution, patients with a previous history of pulmonary embolism (PE), patients who refused diagnosis and treatment, patients with incomplete CTPA images, patients with a prior history of pulmonary hypertension, patients with a history of severe tricuspid regurgitation by echocardiography, and patients admitted to the ED with arrest were excluded. In addition, artifacts in CTPA images and images that may cause bias in the evaluation due to contrast differences were excluded. Study population (n:226) was formed in the light of the inclusion and exclusion criteria. The patient flow chart is shown in figure 1.

2.2. Study protocol

The study population was formed after the inclusion and exclusion criteria were applied. All data of the patients were obtained from the hospital's digital archive. It was planned to examine the demographic data, comorbidities, clinical outcomes, and CTPA findings included in the study.

The demographic data, comorbidities, and clinical outcomes of the patients included in the study were evaluated by an emergency specialist.

Mortality within the first 24 hours was defined as early mortality, and mortality after 24 hours was defined as late mortality, as CTPA was intended to be used for early mortality. Given the importance of early treatment intensity, if CTPA can determine mortality risk in APE, CT parameters should determine mortality in the first 24 hours when more intensive treatment is required. Therefore, 24-hour was chosen for early mortality. We also chose 30-day for late mortality.

The images of the CTPA were recorded at the time of initial presentation, and a radiologist assessed the imaging modal-

Table 1 The patients' demographic data and baseline characteristics

Characteristics, n=226	Value
Gender, n (%)	
Male	83 (36.7)
Female	143 (63.3)
Age (year), median (IQR)	74.5 (64.0-83.0)
Comorbidities, n (%)	
Hypertension	141 (62.4)
Diabetes	35 (15.5)
Coronary artery disease	44 (19.5)
Atrial fibrillation	18 (8.0)
Stroke	33 (14.6)
Dementia	10 (4.4)
Neoplasia	6 (2.7)
Pulmonary embolism level, n (%)	
Pulmonary artery embolism+	152 (34.6)
Segmental pulmonary embolism	186 (42.3)
Sub-segmental pulmonary embolism	102 (23.1)
CT scan measurements	
PT (mm), mean (min-max)	28.9 (17-43)
RPA (mm), median (IQR)	21.0 (19.0-24.0)
LPA (mm), mean (min-max)	21.8 (12-35)
RV (mm), median (IQR)	47.0 (42.3-52.0)
LV (mm), median (IQR)	43.0 (38.0-47.8)
RV/LV ratio (%), median (IQR)	1.1 (1.0-1.3)
IVC AP (mm), mean (min-max)	21.0 (10-33)
IVC T (mm), mean (min-max)	27.5 (11-42)
IVC AP/T ratio (%), mean (min-max)	0.8 (0.5-1.7)
IVC reflux score, n (%)	
None	107 (47.3)
Grade 1	65 (28.8)
Grade 2	24 (10.6)
Grade 3	30 (13.3)
Mortality, n (%)	
Early period*	16 (7.1)
Late period ^{&}	23 (10.2)

IQR: Interquartile range (25p, 75p); CT: Computed tomography; PT: Pulmonary trunk; RPA: Right pulmonary artery; LPA: Left pulmonary artery; RV: Right ventricle; LV: Left ventricle; IVC: Inferior vena cava; AP: Anteroposterior; T: Transverse; +: Main pulmonary and lobar artery level; *: First 24 hours; &: After the first 24 hours

ities. The radiologist evaluating the images had five years of experience in cardiothoracic CT scan imaging.

2.3. Measurements

All the cases' CTPA scans were obtained with a 16-slice multidetector CT scanner (Toshiba Alexion™; Toshiba medical systems corporation, Nashua, Japanese) with 1 millimeter (mm) thick slices and 120 kVp. In all cases, intravenous administration of an iodine-based contrast medium was achieved through a peripheral venous line at a rate of 2-4 mL/s. Automatic bolus tracking was performed in the pulmonary trunk (PT) with a 100 Hounsfield units (HU) trigger. The radiologist independently evaluated the CTPA scans using the hospital's digital archive picture archiving and communication system (PACS). Images with artifacts that could impact the measurement values were eliminated from the

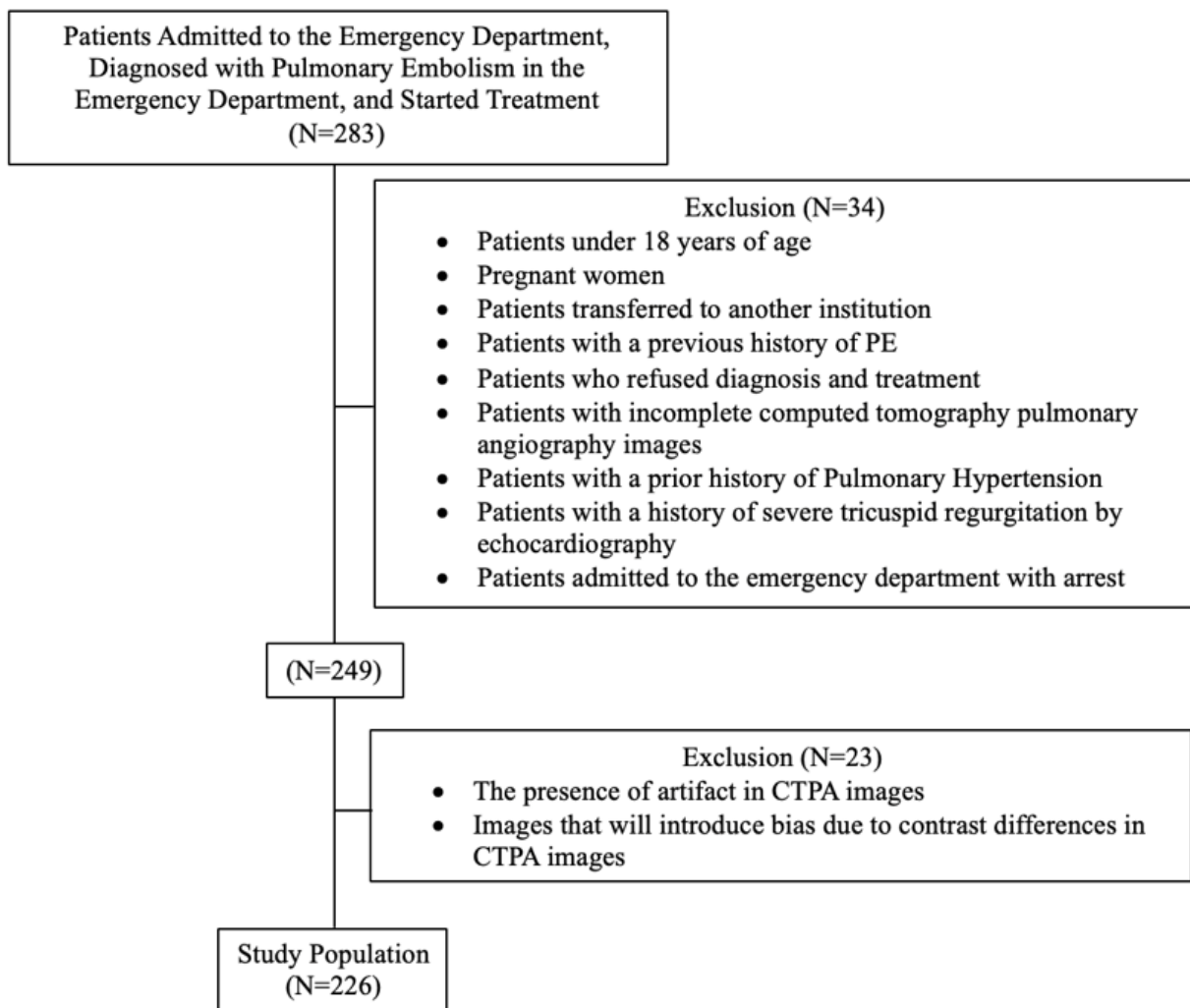


Figure 1 Study flowchart

Table 2 CT scan measurements according to mortality

CT scan measurements	30-day evaluation			24-hour evaluation		
	Surviving (n=187)	Non-surviving (n=39)	P-value	Surviving (n=210)	Non-surviving (n=16)	P-value
PT (mm), mean (min-max)	28.8 (17-43)	29.1 (19-39)	0.745	29.0 (17-43)	27.3 (19-36)	0.148
RPA (mm), median (IQR)	21.0 (19.0-24.0)	23.0 (20.0-26.0)	0.055	21.0 (19.0-24.0)	20.5 (18.0-26.3)	0.960
LPA (mm), mean (min-max)	21.7 (12-35)	22.6 (16-29)	0.192	21.8 (12-35)	22.1 (16-28)	0.818
RV (mm), median (IQR)	47.0 (42.0-52.0)	47.0 (43.0-52.0)	0.973	47.0 (42.0-52.0)	48.0 (44.0-49.8)	0.675
LV (mm), median (IQR)	43.0 (38.0-48.0)	42.0 (37.0-45.5)	0.471	43.0 (38.0-48.0)	40.5 (36.0-44.5)	0.200
RV/LV ratio (%), median (IQR)	1.1 (1.0-1.3)	1.1 (1.0-1.2)	0.950	1.1 (1.0-1.3)	1.1 (1.0-1.5)	0.219
IVC AP (mm), mean (min-max)	21.1 (13-33)	20.8 (10-29)	0.744	21.1 (12-33)	20.7 (10-29)	0.719
IVC T (mm), mean (min-max)	27.7 (11-42)	26.7 (16-42)	0.270	27.5 (11-42)	27.7 (21-42)	0.905
IVC AP/T ratio (%), mean (min-max)	0.8 (0.5-1.7)	0.8 (0.5-1.4)	0.659	0.8 (0.5-1.0)	0.8 (0.5-1.0)	0.428
IVC reflux score, n						
None	96	11		104	3	
Grade 1	55	10	0.001	63	2	0.001
Grade 2	19	5		22	2	
Grade 3	17	13		21	9	

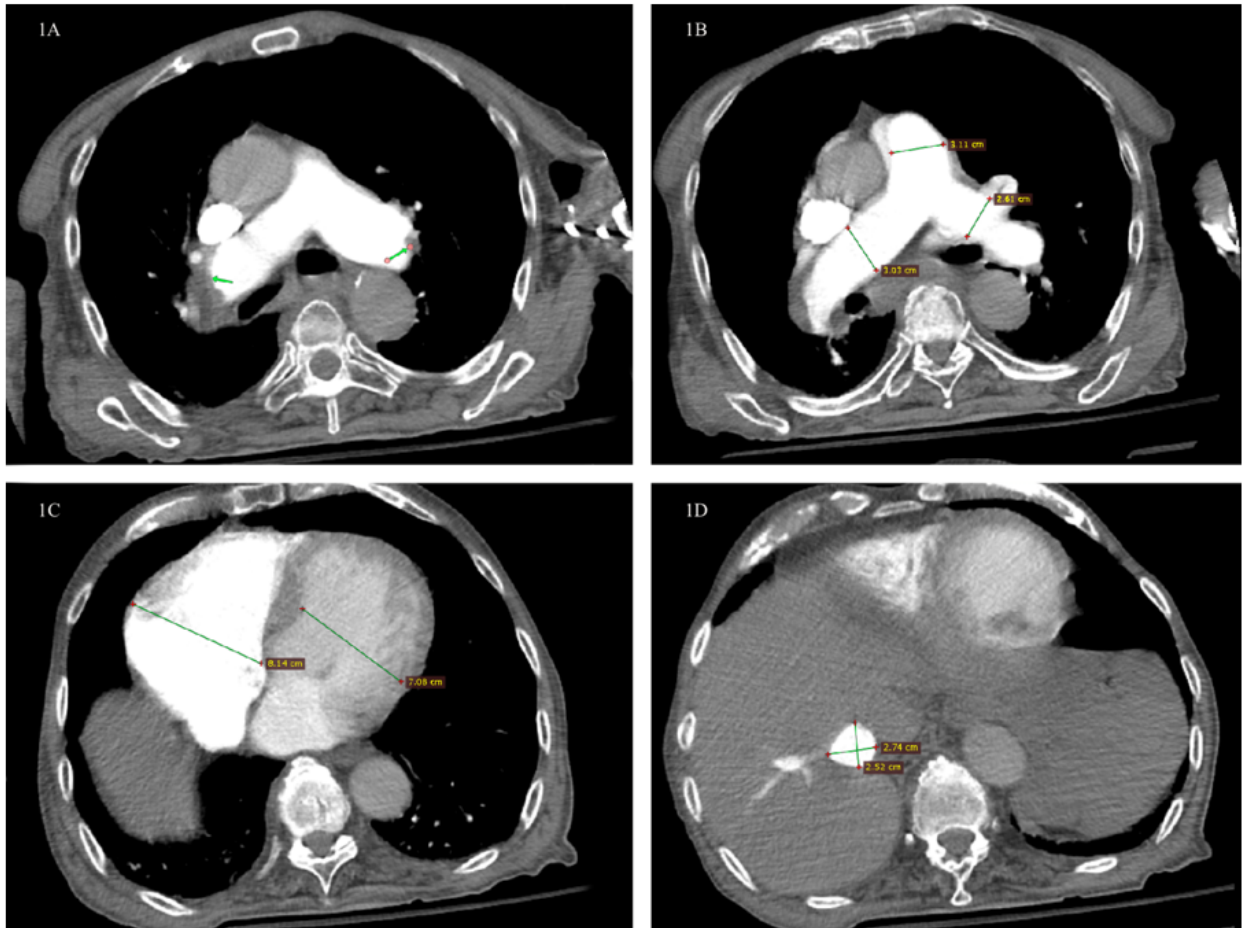


Figure 2 Measurements of CTPA scans

1A) thrombosis in pulmonary arteries; 1B) measurement of pulmonary trunk; right pulmonary artery and left pulmonary artery diameters; 1C) measurement of right ventricle and left ventricle diameters; 1D) measurement of inferior vena cava diameters; CTPA: Computed tomography pulmonary angiography

assessment. Acute embolism was defined as a clot in the pulmonary arteries on CTPA. For this definition, this refers to areas without contrast transmission. Three primary levels were used to express acute embolism: pulmonary (main pulmonary and lobar artery level), segmental, and subsegmental artery levels.

For the present study, the following radiological parameters were measured: diameter of the PT (mm), diameter of the right main pulmonary artery (RPA) (mm), diameter of the left main pulmonary artery (LPA) (mm), diameter of the right ventricle (RV) (mm), diameter of the left ventricle (LV) (mm), diameter of the anteroposterior (AP) and transverse (T) IVC (mm). Each vessel diameter was measured as axial sections' most significant wall-to-wall distance. RV and LV diameters were estimated at the most prominent points between the inner margins of the interventricular septum and the ventricle wall. The PT diameter was measured at its origin, proximal to the branching point. LPA and RPA diameters were measured just after the PT branching. IVC measurements were performed at the intrahepatic level. The purpose of taking measurements at this level is that these points are easy to define

anatomically, which makes them highly reproducible. Furthermore, RV/LV ratio (%) and IVC AP/T diameter ratio (%) were calculated. The CTPA scan measurements are shown in figure 2.

IVC reflux score were evaluated on axial and coronal images in a four-point scale: 0; no reflux, 1; subcardial reflux, 2; intrahepatic reflux, and 3; subhepatic reflux (18). The IVC reflux score evaluation procedure is summarized in figure 3.

2.4. Endpoints

The primary endpoint of this study was to assess the statistical accuracy of IVC reflux score as an indicator of early mortality. The secondary endpoint is to evaluate the statistical accuracy of CTPA measurements as an early and late mortality indicator.

2.5. Statistical analysis

All statistical analyses were performed on Jamovi v. 1.6 software (Jamovi Project Computer Software, versiyon 1.6. Sydney, Australia). Type 1 errors were regarded as 5% for all comparisons. The Shapiro-Wilk test was applied to evalu-

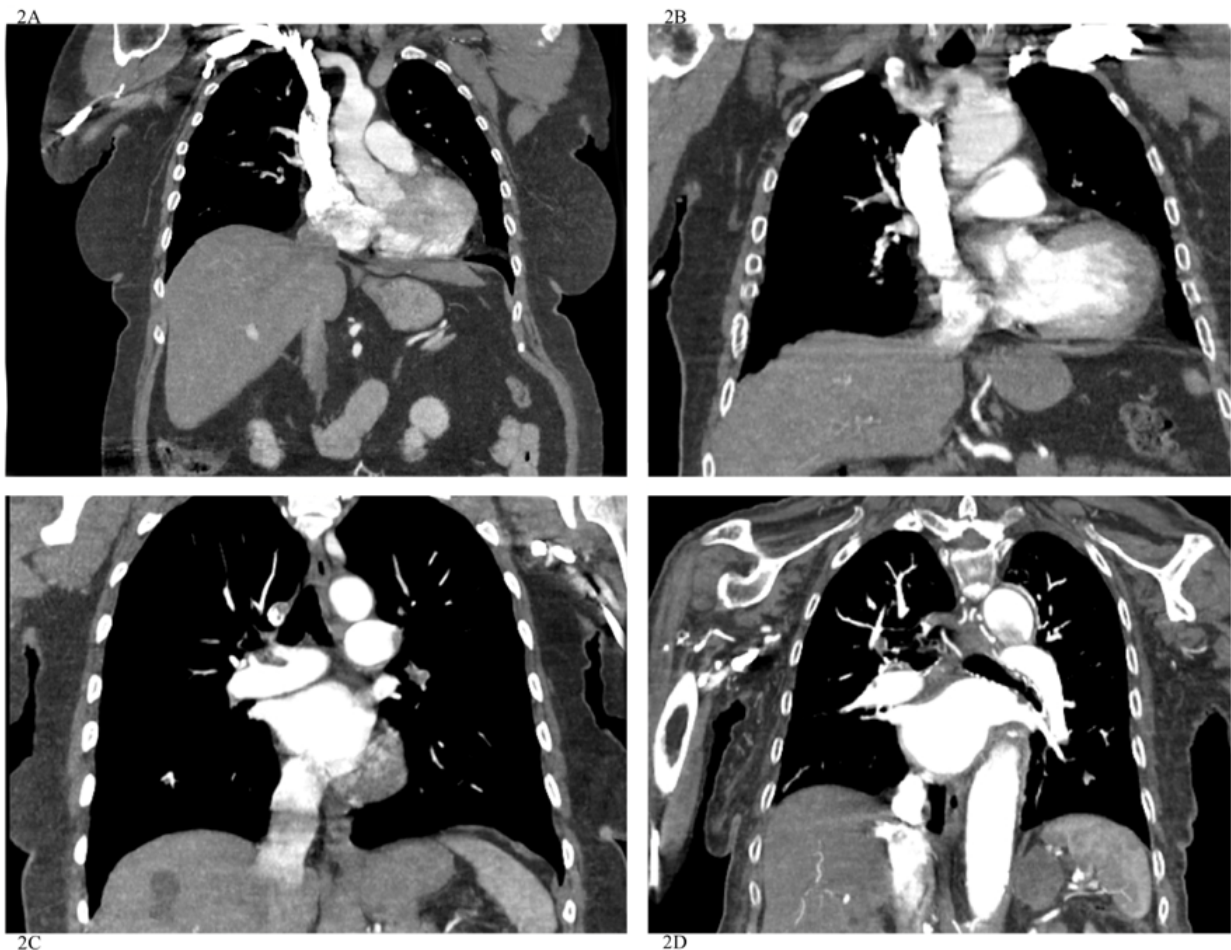


Figure 3 IVC reflux score

2A) grade 0: no reflux; 2B) grade 1: reflux into the suprahepatic; 2C) grade 2: reflux into the intrahepatic; 2D) grade 3: reflux into the subhepatic; IVC: Inferior vena cava

ate normality of data distribution. Non-normally distributed data for continuous variables 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. 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-squared test. Logistic regression analysis was applied for univariate analysis, and odd ratio (OR) and P values were calculated for early- and late-period mortality.

3. Results

The study population consisted of 226 patients meeting the inclusion and exclusion criteria. Eighty-three (36.7%) patients were men and 143 (63.3%) women. The patients' median age was 74.5 years (IQR: 64-83). The most frequent comorbid diseases were hypertension in 141 (62.4%) patients and coronary artery disease in 44 (19.5%). The total number of embolisms detected on the CTPA scans was 440, of

which 152 (34.6%) were in the pulmonary arteries (main pulmonary and lobar artery level), 186 (42.3%) in the segmental branches, and 102 (23.1%) in the sub-segmental branches. The total number of deaths in the study population was 39 (17.3%), of which 16 (7.1%) occurred within the first 24 hours and 23 (10.2%) after the first 24 hours. The mean diameter of the PT was 28.9 mm, with a value of 17-43 mm. The median diameter of the RV and LV were 47 mm (IQR: 42.3-52.0) and 43 mm (IQR: 38.0-47.8), respectively. The mean AP diameter of IVC was 21 mm, with a 10-33 mm. The mean T diameter of IVC was 27.5 mm, with a 11-42 mm. Additionally, an IVC reflux score of 0 was detected in 107 (47.3%) patients, and degrees of 1 in 65 (28.8%), 2 in 24 (10.6%), and 3 in 30 (13.3%). The patients' demographic data, pulmonary embolism levels, mortality rates, and CT scan measurement evaluations are summarized in table 1.

In evaluating CT parameters, the IVC reflux score showed a statistically significant difference between the groups with and without mortality (24-hour (P=0.001); 30-day (P=0.001)). However, other CT parameters were evaluated, and no statistical relationship was found between the groups with and

Table 3 Logistic regression analysis of the acquired parameters for predicting mortality in patients with acute pulmonary embolism

Univariate analysis		Non-surviving (n=39)	
CT scan measurements	OR	95 % CI	P-value
Pulmonary trunk	1.01	0.94,1.09	0.743
Right pulmonary artery	1.10	1.00,1.20	0.058
Left pulmonary artery	1.06	0.97,1.16	0.192
Right ventricle	1.02	0.97,1.06	0.478
Left ventricle	0.99	0.94,1.04	0.622
Right/left ventricle ratio	2.48	0.55,11.08	0.235
IVC AP diameter	0.99	0.91,1.07	0.742
IVC T diameter	0.96	0.90,1.03	0.270
IVC AP/T diameter ratio	1.66	0.18,15.40	0.658
IVC reflux score			
Grade 1	1.55	0.62,3.89	0.347
Grade 2	2.25	0.70,7.22	0.173
Grade 3	6.54	2.51,16.98	0.001
Univariate analysis		Early period* (n=16)	
CT scan measurements	OR	95 % CI	P-value
Pulmonary trunk	0.92	0.82,1.03	0.149
Right pulmonary artery	1.02	0.90,1.15	0.807
Left pulmonary artery	1.02	0.90,1.16	0.817
Right ventricle	1.02	0.96,1.09	0.523
Left ventricle	0.97	0.90,1.04	0.408
Right/left ventricle ratio	7.43	0.98,56.68	0.053
IVC AP diameter	0.98	0.86,1.11	0.718
IVC T diameter	1.01	0.91,1.11	0.904
IVC AP/T diameter ratio	0.21	0.01,9.37	0.422
IVC reflux score			
Grade 1	1.08	0.18,6.64	0.934
Grade 2	3.09	0.49,19.61	0.231
Grade 3	14.57	3.64,58.41	0.001

IVC: Inferior vena cava; AP: Anteroposterior; T: Transverse; *: First 24 hours; OR: Odds ratio; CI: Confidence interval; CT: Computed tomography

without mortality. A statistical summary of the parameters between the groups is shown in table 2.

Of 226 patients, 16 (7.1 %) died in the first 24 hours, totaling 39 (17.3 %) patients. Patients who died within the first 24-hour and 30-day after admission showed a reflux grade 3 into IVC more often than survivor (24-hour OR: 14.57, 95% CI: 3.64,58.41; P=0.001; 30-day OR: 6.54; 95% CI: 2.51,16.98; P=0.001). In addition, the other CTPA parameters had no significant effects in terms of determining either early or total mortality. A logistic regression analysis summary is shown in table 3.

4. Discussion

APE is generally diagnosed in the ED. The most frequently employed radiological imaging method in diagnosing APE in clinical practice is CTPA (7-9). A mortality rate of approximately 18 % has been reported for APE (4), although a large meta-analysis reported a figure of 10.7 % (5). Therefore, an emergency risk classification at the time of presentation is particularly important due to this high mortality. Various scoring systems and cardiovascular CT measurements estimate mortality in patients with APE (12-16). However, there are differences among studies concerning the usefulness of

cardiovascular CT measurements as an indicator of mortality. In addition, several studies have focused on long-term mortality. For these reasons, examining the feasibility of cardiovascular CT measurements as an indicator of early mortality has become particularly important.

Bach et al. investigated CTPA findings predicting 30-day mortality in patients with APE. They concluded that IVC contrast reflux measurement was a novel and reliable method for predicting 30-day mortality in APE (15). The present study investigated whether the IVC contrast reflux score indicates 24-hour and 30-day mortality. Significant differences were determined in IVC reflux score regarding 24-hour and 30-day mortality between the survivors and non-survivors. Given these data, the IVC reflux score may indicate mortality.

In their previous study, Bailis et al. evaluated the predictive ability of the IVC reflux score for both 24-hour and 30-day mortality in 224 cases of APE. Grade 3 IVC reflux was observed more frequently in the exitus cases compared to patients who survived after the first 24-hour (OR: 7.6, 95% CI: 3.3,17.7; P<0.001). In addition, 30-day analysis revealed that Grade 3 IVC reflux was also more frequent in the exitus patients compared to the survivors (OR: 3.4, 95% CI: 1.7,7.0; P<0.001). Those authors concluded that subhepatic contrast reflux (grade 3) is a powerful predictor of 24-hour and 30-day

mortality in patients with APE (19). The present study investigated the use of the IVC contrast reflux score cardiovascular CT finding to indicate 24-hour and 30-day mortality. Grade 3 IVC reflux was more common in both 24-hour and 30-day mortality compared to the surviving patients (OR: 14.57, 95% CI: 3.64,58.41; P=0.001 for 24-hour mortality and OR: 6.54, 95% CI: 2.51,16.98; P=0.001 for 30-day mortality). No significant difference was observed in terms of grade 1 or 2 IVC reflux between either the groups' 24-hour or 30-day mortality and the surviving group (grade 1 IVC reflux OR: 1.08, 95% CI: 0.18,6.64; P=0.934 for 24-hour mortality and OR: 1.55, 95% CI: 0.62,3.89; P=0.347 for 30-day mortality; grade 2 IVC reflux OR: 3.09, 95% CI: 0.49,19.61; P=0.231 for 24-hour mortality, and OR: 2.25, 95% CI: 0.70,7.22; P=0.173 for 30-day mortality). In light of the present study and previous research in the literature, the IVC reflux score may be a good indicator of both early and general mortality. Our study findings support this view.

No statistically significant differences were observed in this study between cases of 24-hour or 30-day mortality and the surviving patients in terms of the cardiovascular CT findings of pulmonary artery diameters, right and left ventricle diameters, right/left ventricle diameter ratio, or IVC anteroposterior and transverse diameters. Morris et al. investigated the relationship between CT findings and long-term mortality. Who examined the CT scan findings of 1105 patients and concluded that CT scan findings could not be used as a predictor of long-term mortality in PE (20). Similarly, Atasoy et al. examined CT scan findings in non-severe PE and reported no significant difference in cardiovascular CT parameters between survivors and non-survivors (21). Comparing our study findings with data from the previous literature, we also conclude that except for IVC contrast reflux score, CT scan findings cannot be used to predict 24-hour or 30-day mortality.

5. Limitations

This study has some limitations. In particular, the study was small in size, conducted in a single center, and was retrospective. Patient data cannot be adequately assessed because of the retrospective design. This raises concerns about the possibility of selection bias, similar to other retrospective studies. However, to address this concern, the study population was constructed by excluding diseases and measurements that could cause bias. Another limitation is that, in line with the aim and methodology of the study, only the effect of CT scan parameters on mortality was evaluated. This made it impossible to assess the confounding effect of many factors on mortality. As a result, in our study, the evaluation of CT scan parameters on mortality was based on univariate analyses. Also, despite the small sample size, IVC reflux score groups were not compared. This limited the evaluation of the relationship between subgroups. Finally, the fact that a single radiologist performed the measurements and used a 16-slice multi-detector CT scanner is also a limitation. Overall, fur-

ther studies with a significant number of patients and more centers are needed to confirm our findings.

6. Conclusion

The cardiovascular CT findings of pulmonary artery diameters, right and left ventricle diameters, IVC anteroposterior and transverse diameters, right/left ventricle diameter ratio may not be suitable for use as predictors of mortality. However, the IVC reflux score may be a good parameter as an indicator of both early and late mortality.

7. Declarations

7.1. Acknowledgement

We would like to express a special thank to Emergency and Radiology Department of Recep Tayyip Erdoğan University Training and Research Hospital.

7.2. Authors' contribution

Initials of the contributing authors were listed in brackets after the relevant parts of the research: Literature search (GA, MMY), Study design (GA, MMY), Legislative applications (GA, MMY, HG), Data collection (MMY, HG), Supervision and quality control (GA), Statistical data analysis (MMY), Data interpretation (HG, MMY), Drafting the manuscript (MMY, GA). All authors were involved in the writing and critical revision of the manuscript and approved the final version. MMY and GA take the whole responsibility for the paper.

7.3. Conflict of interest

None declared.

7.4. Funding

None declared.

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