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ORIGINAL RESEARCH

Prediction of Mortality Associated with Cardiac and Radiological Findings in Patients with Pulmonary Embolism

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ABSTRACT

Background: In this study, we aimed to compare echocardiography, electrocardiography (ECG) abnormalities, Doppler ultrasonography (USG), and computed tomography pulmonary angiography (CTPA) results in predicting 3-month mortality in patients with acute pulmonary embolism (PE). **Methods:** This retrospective cohort study included 124 patients (72 females, 52 males) with acute PE. Demographics, symptoms, clinical signs, comorbidities, history of surgery, arterial blood gas, liver-renal functions, complete blood count, echocardiography, ECG, Doppler USG, and CTPA results, as well as 3-month mortality were recorded. **Results:** pH ($z = -2.623$; $p < 0.01$), hemoglobin ($z = -3.112$; $p < 0.01$), and oxygen saturation ($z = -2.165$; $p < 0.01$) were significantly higher in survivors. White blood cell ($z = -2.703$; $p < 0.01$), blood urea nitrogen ($z = -3.840$; $p < 0.01$), creatinine ($z = -3.200$; $p < 0.01$), respiratory rate ($z = -2.759$; $p < 0.01$), and heart rate ($z = -2.313$; $p < 0.01$) were significantly higher in non-survivors. Nonspecific ST changes (AUC 0.52, 95% CI 0.43–0.61), p pulmonale (AUC 0.52, 95% CI 0.43–0.61), normal axis (AUC 0.61), right axis deviation (AUC 0.56), right ventricle strain pattern (AUC 0.59), and right pulmonary artery embolism (AUC 0.54) on CTPA showed the highest mortality prediction. **Conclusions:** Nonspecific ST changes, p pulmonale, normal axis and right axis deviation in ECG, RV strain in echocardiography, and right pulmonary artery embolism on CTPA are associated with a higher mortality in patients with PE.

Keywords: echocardiography, electrocardiography, mortality, pulmonary embolism, radiological finding

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INTRODUCTION

Acute pulmonary embolism (PE) is a serious cause of morbidity and mortality occurring as a complication of deep vein thrombosis (DVT), and it is the most serious clinical manifestation of venous thromboembolism leading to sudden cardiac death.[1,2] PE is responsible for approximately 100,000 and 300,000 deaths annually in Europe and the United States, respectively.[3] Obesity, immobilization, cancer, smoking, surgery, trauma, pregnancy, oral contraceptive drug use, hormone replacement therapy, and previous PE are well-known risk factors for DVT

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and a new PE.[1] The clinical picture in PE ranges from asymptomatic to rapid hemodynamic collapse, shock, and death.[4] The prognosis of PE depends on detecting risk factors and rapid diagnosis.[5] It is important to recognize the findings in patients admitted to the emergency department (ED) to predict and reduce deaths from PE. There are studies evaluating mortality in the early period of PE in the literature.[3,4,6]

Estimating mortality in patients with acute PE in the ED is important for patient management. Therefore, we aimed to compare echocardiography, electrocardiogram (ECG) abnormalities, Doppler ultrasonography (USG), and computed tomography pulmonary angiography (CTPA) results in predicting the 3-month mortality of acute PE patients.

MATERIALS AND METHODS

This retrospective cohort study was conducted with approval of Kafkas University Medical Faculty Ethics Committee, between January 2017 and December 2019. All study procedures were in line with the principles stated in the Declaration of Helsinki, and retrospective analysis was based on data on patients who consented for further use of their medical records. The patients who received a diagnosis of PE ICD code in the hospital registry system between these dates were retrospectively analyzed. Patients who were not diagnosed with acute PE, whose ECG, echocardiography, and Doppler USG results were incomplete, and who were under 18 years of age were not included in the study. The study included 124 patients (72 females, 52 males) diagnosed with PE, admitted to the ED. Demographics, symptoms, clinical signs, comorbidities, history of surgery, arterial blood gas, liver-renal functions, complete blood count, echocardiography, ECG, Doppler USG, and CTPA results, as well as 3-month mortality were recorded. The patients were divided into survivor and non-survivor groups according to the 3-month mortality.

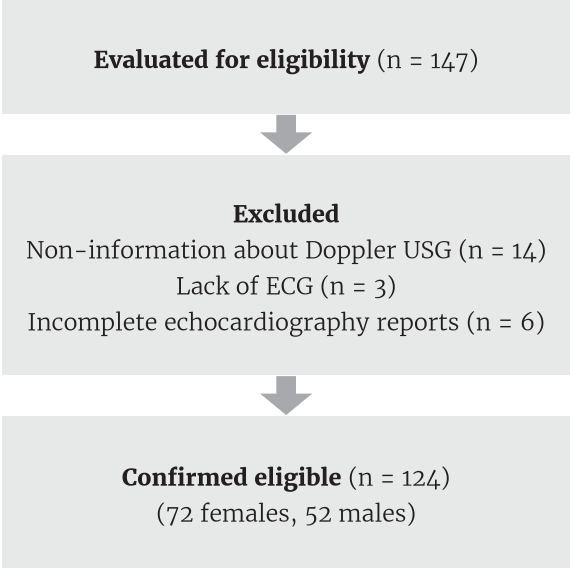

FIGURE 1. CONSORT flow diagram of patients

STATISTICAL ANALYSIS

All statistical calculations were performed with SPSS 23.0 (SPSS for Windows, Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation; categoric variables were defined as percentages (%). The normal distribution was determined by histogram and the Kolmogorov-Smirnov test. Mean values of continuous variables were compared between the groups using the Mann-Whitney U test. Student's t test was used in the comparison of parameters showing normal distribution. Prediction accuracy was assessed using the area under the receiver operating characteristic (ROC) curve. The results were evaluated as 95% confidence interval and p value <0.05, which was considered statistically significant.

RESULTS

Table 1 and Table 2 present the demographics, symptoms, signs and comorbidities of the survivors and non-survivors. Accordingly, 72 (58.06%) of the patients were female and 52 (41.9%) were male. Their ages ranged from 20 to 97 years, with an average of 68.01 ± 15.56 years. The overall 3-month mortality rate was 22.5%. Fifty-eight (60.4%) of the survivors were female and 38 (39.6%) were male; 14 (50.0%) of the non-survivors were female and 14 (50.0%) were male. Dyspnea was the most common symptom of the groups (88.5% of survivors; 92.9% of non-survivors). Hemoptysis and chest pain were observed in 10.9% and 51% of the patients, respectively.

The frequency of comorbidities seen among the patients were: hypertension (46%), diabetes mellitus (10.6%), coronary artery disease (CAD) (12.4%), chronic obstructive pulmonary disease (COPD) (55.8%), asthma (8%), neoplastic disease (9.7%), congestive heart failure (12.4%), cerebrovascular diseases (5.3%), and chronic renal diseases (8%). Confusion was present in 10 (8.8%) cases, and pleural effusion also in 10 (8.8%) cases. Immobilization and leg swelling were observed in 10.4% and 19.8% of survivors, respectively. Massive embolism and non-massive embolism were detected in 35.7% and 60.7% of non-survivors, respectively. Ten (8.1%) patients died on the first admission to the hospital.

TABLE 1. Demographics, symptoms, signs and comorbidities of the survivors and non-survivors

	Survivors		Non-survivors	
	n	%	n	%
Gender, male	38	39.6	14	50.0
Dyspnea	85	88.5	26	92.9
Fever (>38°C)	1	1.0	–	–
Confusion	16	16.7	10	35.7
Hemoptysis	7	7.3	1	3.6
Cough	6	6.3	5	17.9
Flank pain	42	43.8	15	53.6
Palpitation	18	18.8	6	21.4
Chest pain	25	26.0	7	25.0
Leg pain	8	8.3	1	3.6
Grunt	8	8.3	1	3.6
Redness of the leg	3	3.1	–	–
Leg swelling	21	21.9	7	25.0
Cyanosis	15	15.6	10	35.7
History of any disease	11	11.5	3	10.7
Previous PE	9	9.4	1	3.6
Previous DVT	4	4.2	1	3.6
Previous CAD	5	5.2	1	3.6
Previous myocardial infarction	–	–	1	3.6
Previous pneumonia	–	–	1	3.6
Cardiovascular disease	36	37.5	17	60.7
Congestive heart failure	8	8.3	8	28.6
Atrial fibrillation	14	14.6	4	14.3
Hypertension	35	36.5	11	39.3
Diabetes mellitus	6	6.3	6	21.4
Chronic renal failure	–	–	3	10.7
Collagen tissue disease	1	1.0	–	–
Neoplastic disease (non-lung cancers)	3	3.1	5	17.9
COPD	37	38.5	14	50.0
Asthma	14	14.6	1	3.6
Lung cancer	–	–	1	3.6
Major trauma	96	100.0	28	100.0
Orthopedic surgery	5	5.2	3	10.7

TABLE 2. Risk factors, clinical findings and outcomes of the survivors and non-survivors

Clinical parameter	Survivors		Non-survivors	
	n	%	n	%
Immobilization	10	10.4	11	39.3
History of general anesthesia	1	1.0	3	10.7
Pregnancy	1	1.0	–	–
Intercostal withdrawal	13	13.5	12	42.9
Rhonchus	7	7.3	9	32.1
Cyanosis	19	19.8	14	50.0
Leg swelling	19	19.8	5	17.9
Erythema on legs	5	5.2	1	3.6
PE				
Massive	13	13.5	10	35.7
Non-massive	82	85.4	17	60.7
Outcome of first admission				
Discharged	96	100.0	18	64.3
Death	–	–	10	35.7

Table 3 lists the Mann-Whitney U test analysis results of the mean values of pH, platelet, mean platelet volume (MPV), hemoglobin, aspartate aminotransferase (AST), partial pressure of oxygen (PaO2), total bilirubin, direct bilirubin, partial pressure of carbon dioxide (PaCO2), white blood cells (WBC), glucose, blood urea nitrogen (BUN), alanine aminotransferase (ALT), and vital signs including respiratory rate, systolic blood pressure, heart rate, and oxygen saturation. pH ($z = -2.623$; $p < 0.01$), hemoglobin ($z = -3.112$; $p < 0.01$), and oxygen saturation ($z = -2.165$; $p < 0.01$) were significantly higher in survivors. WBC ($z = -2.703$; $p < 0.01$), BUN ($z = -3.840$; $p < 0.01$), creatinine ($z = -3.200$; $p < 0.01$), respiratory rate ($z = -2.759$; $p < 0.01$), and heart rate ($z = -2.313$; $p < 0.01$) were significantly higher in non-survivors.

Several ECG and imaging parameters have been tested in regards to their prognostic value in predicting mortality of patients with acute pulmonary embolism, as shown in Figure 2. Figure 2A shows the accuracy of atrial fibrillation (AF) (AUC 0.53), ectopic beats (AUC 0.53), normal axis, nonspecific ST changes, p pulmonale, and thrombus of main pulmonary artery for predicting mortality. Nonspecific ST changes (AUC 0.52, 95% CI 0.43–0.61) and p pulmonale (AUC 0.52, 95% CI 0.43–0.61) showed the highest mortality prediction. Additionally, normal axis (AUC 0.61 95% CI 0.52–0.70) indicated significantly higher mortality prediction.

Figure 2B illustrates the accuracy of ECG findings including AF, ectopic beats, normal axis, nonspecific ST changes, p pulmonale, and S1Q3T3 in predicting mortality. S1Q3T3 (AUC 0.50, 95% CI 0.41–0.59) and normal axis (AUC 0.61, 95% CI 0.52–0.70) showed the lowest mortality. Figure 2C depicts the accuracy of S1Q3T3, right axis deviation, right bundle branch block (RBBB), sinus tachycardia, pulmonary artery pressure, and paradoxical motion in predicting mortality. Sinus tachycardia (AUC 0.50, 95% CI 0.40–0.61) showed the lowest mortality estimate, while right axis deviation (AUC 0.56, 95% CI 0.46–0.66) showed the highest mortality estimation. Figure 2D reveals the accuracy of right ventricle (RV) strain pattern, right pulmonary artery embolism, right subsegmental PE, left

TABLE 3. Comparison of blood parameters and vital signs of survivors and non-survivors

	Groups	N	Mean rank	U	P
pH	Survivors	86	61.53	771.500	0.009**
	Non-survivors	27	42.57		
Platelet count, cell*106	Survivors	93	57.58	983.500	0.2
	Non-survivors	25	66.66		
Mean platelet volume, fL	Survivors	93	59.07	1122.500	0.7
	Non-survivors	25	61.10		
Hemoglobin, g/dL	Survivors	93	64.58	690.000	0.002**
	Non-survivors	25	40.60		
AST, U/L	Survivors	93	58.68	1086.000	0.4
	Non-survivors	26	64.73		
PaO2, mmHg	Survivors	86	57.43	1124.000	0.8
	Non-survivors	27	55.63		
Total bilirubin, mg/dL	Survivors	88	53.01	748.500	0.055
	Non-survivors	23	67.46		
PaCO2, mmHg	Survivors	86	58.21	1057.000	0.4
	Non-survivors	27	53.15		
WBC, cells*103	Survivors	92	54.58	743.500	0.007**
	Non-survivors	25	75.26		
Glucose, mg/dL	Survivors	87	53.94	864.500	0.06
	Non-survivors	26	67.25		
BUN, mg/dL	Survivors	93	53.58	612.000	0.000**
	Non-survivors	26	82.96		
Creatinine, mg/dL	Survivors	93	54.65	711.500	0.001**
	Non-survivors	26	79.13		
ALT, U/L	Survivors	94	59.11	1091.000	0.5
	Non-survivors	25	63.36		
Respiratory rate/min	Survivors	96	57.77	890.000	0.006**
	Non-survivors	28	78.71		
Systolic blood pressure, mmHg	Survivors	96	64.24	1177.000	0.3
	Non-survivors	28	56.54		
Heart rate, bpm	Survivors	96	58.47	957.500	0.02*
	Non-survivors	28	76.30		
Oxygen saturation, %	Survivors	86	60.74	839.500	0.03*
	Non-survivors	27	45.09		

*p <0.05; **p <0.01

pulmonary artery embolism, DVT of left lower extremity, and DVT of right lower extremity. RV strain pattern (AUC 0.59, 95% CI 0.48–0.69) showed the highest mortality prediction, and DVT of right lower extremity showed the lowest (AUC 0.51, 95% CI 0.41–0.61) mortality prediction. Figure 2E shows the accuracy of right pulmonary artery embolism, DVT of right lower extremity, right subsegmental PE, left pulmonary artery embolism, DVT of left lower extremity, and left subsegmental PE. DVT of right lower extremity (AUC 0.52, 95% CI 0.43–0.61) showed the lowest mortality estimation, and right pulmonary artery embolism (AUC 0.54, 95% CI 0.44–0.63) on CTPA showed the highest mortality prediction. Also, Figure 2F demonstrates the accuracy of PAP, paradoxical motion, and RV strain pattern in predicting mortality. PAP (AUC 0.53, 95% CI 0.42–0.63) showed the lowest mortality prediction, and RV strain pattern (AUC 0.59, 95% CI 0.48–0.69) showed the highest mortality estimation.

DISCUSSIONS

This study demonstrates that clinical parameters, imaging features (echocardiography), ECG and radiological findings (Doppler USG and CTPA) provide relevant infor-

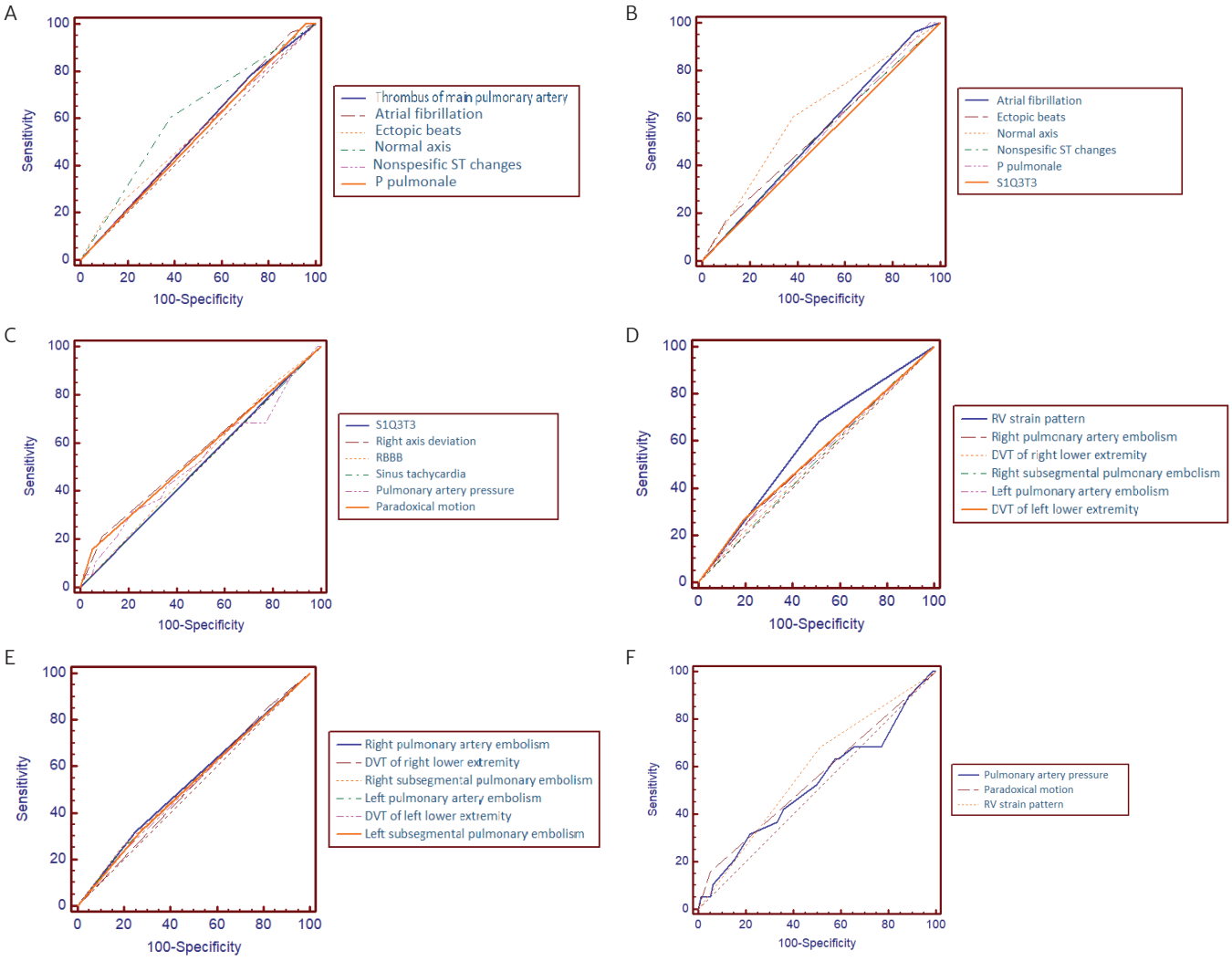

FIGURE 2. The predictive capacity of several clinical and imaging parameters in predicting 3-month mortality in patients with PE

mation about the 3-month mortality risk of patients with acute PE. In our study, serum pH, hemoglobin, and oxygen saturation were lower, and WBC, BUN, creatinine, respiratory rate, and heart rate were higher in non-survivors. Vital signs, such as oxygen saturation, respiration rate, and heart rate, may provide rapid information regarding acute physiological changes in patients in the ED.[7] Decreased intravascular volume, lower hemoglobin level, heart failure, decreased cardiac output, inadequate fractionated oxygen and peripheral blood flow result in increase of heart and respiratory rate, and decrease in oxygen saturation.[6,7] Studies have shown that abnormal vital signs, such as respiratory rate and oxygen saturation, indicating impaired hemodynamics can provide information about intensive care unit admission and in-hospital deaths in patients with PE, sepsis, and shock.[6,8,9] PE can be associated with anemia.[10] Increased release of anti-thrombotic mediators in individuals with anemia and lower blood viscosity may lead to increased clotting.[10] Lower hemoglobin level is a predisposing factor for a new cardiovascular disease, especially in high-risk adults with cardio-cerebrovascular condition, and this condition increases the risk of mortality.[11] In patients with PE, hemodynamic instability affects other organs, including the pulmonary circulation.[12] In these patients, decreased cardiac output, hypoxemia, and increased central venous pressure lead to renal dysfunction.[12] Impaired renal function is an independent risk factor which predicts hospitalization and mortality, especially in patients with heart failure, and this impairment leads to the disruption of bicarbonate homeostasis, decrease of acid load neutralization, and development of acidosis, which are among the normal functions of the kidney.[12,13] Galic *et al.* reported that renal dysfunction causes a decrease in bicarbonate level, acidosis, lower pH, and increased mortality risk in patients with PE who are expected to have respiratory alkalosis.[14]

ECG findings of acute PE are sinus tachycardia, atrial fibrillation, atrial flutter, P wave changes, T wave inversion, S1Q3T3, ST segment depression or elevation, QRS axis or morphology changes, and complete or incomplete RBBB.[15,16] ECG findings in PE are nonspecific and may also be completely normal.[15,16] We found that normal axis (AUC 0.61) and right axis deviation (AUC 0.56) indicated significantly higher mortality prediction. Axis was a stronger predictor of long-term mortality than other ECG findings including atrial fibrillation, ectopic beats, nonspecific ST changes, P pulmonale, S1Q3T3, RBBB, and sinus tachycardia. Geibel *et al*. reported that ECG findings in patients with PE resulting in death are atrial arrhythmias (flutter and fibrillation), RBBB, Q waves in leads III and aVF, ST segment changes, and peripheral low voltage.[17] According to Escobar *et al*., mortality in PE patients was associated with sinus tachycardia and atrial arrhythmias.[18] Shopp *et al*. showed in their meta-analysis that sinus tachycardia, RBBB, S1Q3T3, T wave inversion in V1-V4 leads, ST elevation in aVR, and atrial fibrillation are risk factors for circulatory shock and death in patients with PE.[19] ECG findings and effects on mortality in patients with PE can vary between studies.

In addition to clinical findings showing hemodynamic instability, echocardiography and CTPA are required in order to identify high-risk patients for early death in acute PE.[20] In our study, RV strain pattern (AUC 0.59) and right pulmonary artery embolism (AUC 0.54) showed the highest mortality prediction. RV strain is one of the indicators of RV systolic function, showing myocardial deformation. Also, RV dysfunction and myocardial injury are associated with poor prognosis in patients with acute PE.[3,21,22] Acute PE increases RV afterload, reduces contractility, and changes RV preload and ventricular interdependence, leading to arrhythmias and decompensated acute heart failure, hypotension, with shock and/or death.[1,23] Detecting thromboembolism in at least one segmental level in CTPA indicates RV enlargement and dysfunction.[24] Patients with acute PE who develop RV dysfunction are considered to be at high risk, the circulatory shock develops rapidly, and the risk of mortality in these patients is increased.[24] The presence of embolism in the right pulmonary artery may indicate that these patients are at high risk and that acute decompensated heart failure will develop rapidly, this condition being associated with an increased mortality.

STUDY LIMITATIONS

This single-center study has some limitations. The size of the patient population was relatively small, and we only evaluated 3-month mortality. We did not examine other factors affecting mortality, or other outcomes such as short-term mortality, mean length of hospital stay, and length of stay in the intensive care unit.

CONCLUSIONS

Nonspecific ST changes, p pulmonale, normal axis and right axis deviation on ECG, RV strain on echocardiography, and right pulmonary artery embolism on CTPA are associated with a higher mortality in patients with PE.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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