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Research article

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The role of right ventricular volume in the diagnosis of pulmonary embolism and morbidity prediction

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Ethics Committee Approval
Local Ethics Committee of Adnan Menderes University with the decision number of 2018/1292.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Pulmonary embolism is a quite common and usually fatal disease. This study aimed to investigate the predictive value of the right ventricular volume in terms of pulmonary embolism and its laterality using imaging techniques.
Methods: This case-control study included patients who underwent tomography with a pre-diagnosis of pulmonary embolism between January 2016 and January 2018. The study group included patients diagnosed with pulmonary embolism, while the control group consisted of those with an excluded diagnosis of embolism. The gender, age, echocardiography, right ventricular volume, embolism location, computed tomography results, morbidity, and mortality of the patients were recorded. Among 253 patients who underwent chest tomography with a diagnosis of pulmonary embolism, the data of 149 patients were obtained. There were 64 individuals in the control group and 85 individuals in the patient group.
Results: In the study group, the length of hospital stay was 10.0 (range, 15.0-6.0) days, the systolic blood pressure was 125.5 (28.8) mmHg, the diastolic blood pressure was 77.8 (17.8) mmHg, and the heart rate was 103.4 (28.1) min. The ROC analysis of right ventricular volume revealed 81.2% sensitivity and 67.2% specificity (AUC: 0.850; P=0.001; 95% CI 0.789-0.910; cut-off: 103.7) in showing pulmonary embolism. There was a positive correlation between right ventricular volume and D-dimer (r: +0.739, P=0.001) in the control group and no correlation between the two in the study group (r: -0.178, P=0.139).
Conclusion: Measuring the right ventricular volume with the software will contribute to the treatment and referral of patients with suspected pulmonary thromboembolism who underwent chest tomography. Thus, time and financial waste can be avoided by preventing unnecessary patient transfers, and early transfer of real patients can contribute to the reduction of mortality and morbidity.

Keywords: Right ventricular volume, Pulmonary embolism, Mortality

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Introduction

Pulmonary thromboembolism (PTE) is the 3rd leading cause of cardiovascular deaths [1] in the USA with an incidence of 0.5-1.0 per thousand people [2], although its prevalence varies between 3.9% and 16.6% in the analysis of autopsy data [3,4]. Therefore, despite the frequent occurrence of PTE, its diagnosis remains a major clinical challenge, because many diseases present with the same signs and symptoms.

The diagnosis of PTE [2] is based on the following: The D-dimer level, and radiological imaging findings. The imaging techniques currently used for diagnosis are chest x-ray, pulmonary angiography, CT, MRI, V/P scintigraphy [5], and dual-energy computed tomography (DECT). DECT is the most recent method [6].

Large CT companies have been developing volume-based software at high prices, and the major problem with this software is that the calculations have to be done on CT portals, not on personal computers (PCs) [7]. This causes personal and professional limitations for patient images.

Our study aimed to propose an affordable and practical way for measuring right ventricular volume with normal computer software to accelerate the diagnosis of pulmonary thromboembolism.

Materials and methods

This case-control study included patients who underwent tomography with a diagnosis of pulmonary embolism between January 1, 2016, and January 1, 2018. Ethics approval was obtained from the Local Ethics Committee of Adnan Menderes University with the decision number 2018/1292. At least 66 patients were required for medium effect size, alpha=0.05, two-way hypothesis, and 80% power. The study group included patients diagnosed with pulmonary embolism, while the control group consisted of those with an excluded diagnosis of embolism.

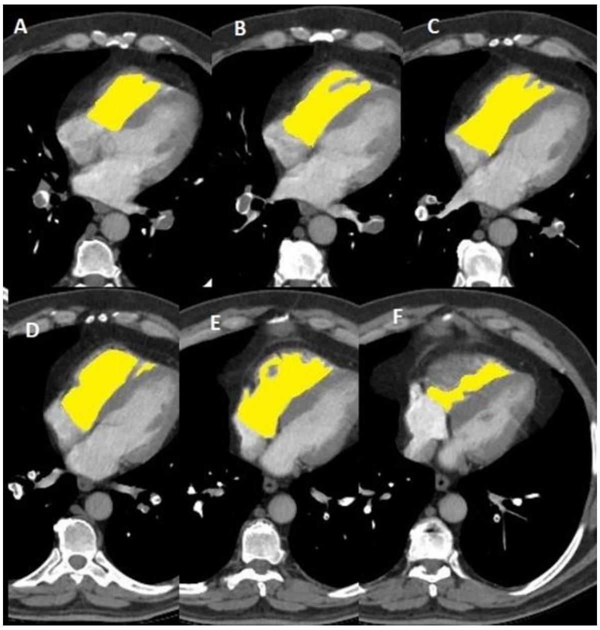
Patients over 18 years of age were included in this case-control study. Those who did not want to participate in the study, those with malignancies, those diagnosed with cor pulmonale and heart failure were excluded. All patients diagnosed with pulmonary embolism by CT were reviewed, the volumes of the right and left heart structures were calculated, and the results of transthoracic echocardiography performed after admission were noted.

Volume measurements were performed using the free-hand technique with Ekinoks advanced CT and MRI imaging Workstation software version 1.7.2017 (Telemed-Ekinoks software, Bogazici University Technopark, Istanbul, Turkey) (Figure 1). The pulmonary regions of interest were measured blinded to the diagnosis of the patients.

Statistical analysis

The data obtained from this case-control study were analyzed with SPSS 20 (SPSS Inc., Chicago, IL, USA). Kolmogorov-Smirnov test was performed to evaluate the distribution of the variables. When evaluating the differences between groups, the Kruskal-Wallis H test was used for the variables that did not conform to normal distribution. ROC curve analysis was performed to investigate the predictive value of right ventricular volume for pulmonary embolism. $P<0.05$ was considered statistically significant.

Figure 1: This image of a 1 mm-thick axial plane shows the sequential CT images (A, B, C, D, E, F) of a patient with pulmonary embolism in the craniocaudal direction. The sum of the area measurements from all sections gives the total right ventricular volume.



Results

Among 253 patients who underwent chest tomography with a diagnosis of pulmonary embolism between January 2016 and January 2018, the data of 149 patients were obtained. There were 64 individuals in the control group and 85 individuals in the patient group. The age, gender, right ventricular volume, and D-dimer distributions of the groups are shown in Table 1.

Table 1: Age, gender, right ventricular volume, and d-dimer distributions of the study groups

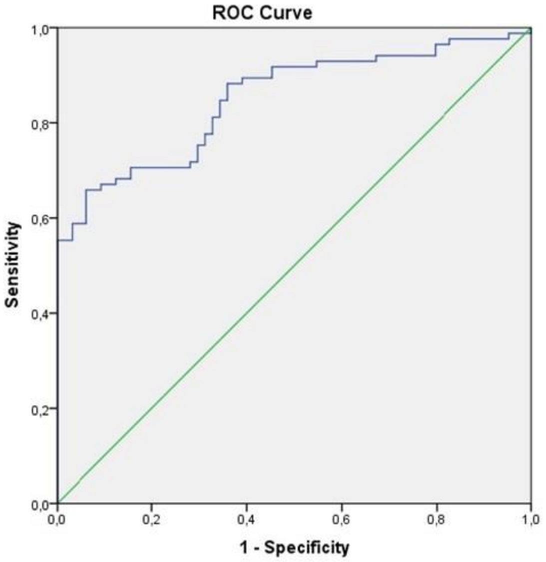
	Control n=64	Patient n=85	*P*-value
Age	69.3(12.5)	69.5(13.8)	0.968
Gender (Female)	15(44.1%)	35(42.2%)	0.755
Right ventricle volume	95.6(18.7)	150.3(51.0)	0.001
D-Dimer	359.3(103.0)	3293.6(1297.2)	0.001

The length of hospital stay (n=83), systolic blood pressure (BP) (n=37), diastolic BP (n=37) and heart rate (n=35) values of our study group were 10.0 (range, 15.0-6.0) days, 125.5(28.8) mmHg, 77.8(17.8) mmHg and 103.4(28.1) min, respectively. The volumes and the demographic data of our patient group are shown in Table 2. The ROC curve analysis between the control group and the patient group revealed a sensitivity of 81.2% and a specificity of 67.2% for right ventricular volume (AUC: 0.850; $P=0.001$; 95% CI 0.789-0.910; cut-off: 103.7) (Figure 2).

Table 2: Echocardiography findings of the patient group, deep venous thrombosis, embolism location, tissue plasminogen activator (tPA) treatment, volume analysis according to the type of embolism

		n(%)	Volume	*P*-value
Right Ventricular Dilatation in ECO	Positive	21(24.7%)	159.1(61.5)	0.285
	Negative	64(75.3%)	141.6(43.3)	
DVT	Positive	12(14.1%)	160.5(44.2)	0.191
	Negative	73(85.9%)	164.8(58.0)	
Side of embolism	Left	10(11.8%)	117.7(39.2)[a]	0.003[b&c]
	Right	30(35.4%)	133.7(42.7)[b]	0.005[a&c]
	Bilateral	45(52.8%)	168.6(51.8)[c]	
Treatment with tPA	Positive	14(16.5%)	166.8(52.3)	0.113
	Negative	71(83.5%)	142.9(48.5)	
Embolism	Massive	29(34.2%)	166.4(57.2)	0.036
	Submassive	56(65.8%)	142.0(45.9)	
Survival	Non-survivors	17(20%)	125.5(45.8)	0.020
	Survivors	68(80%)	157.4(50.4)	

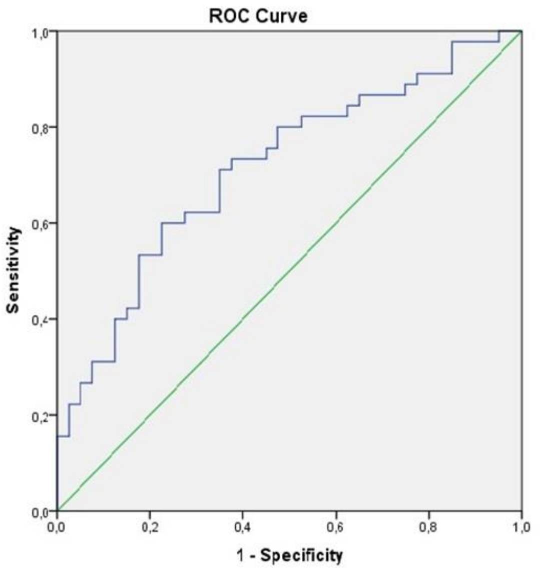
Figure 2: The ROC curve analysis of right ventricular volume (AUC: 0.850; *P*=0.001; 95% CI 0.789-0.910; cut-off: 103.7)



The correlation between volume and D-dimer was analyzed (Pearson's), which revealed r:+0.739 and *P*=0.001 in the control group and r:-0.178 and *P*=0.139 in the patient group.

The ROC curve analysis of right ventricular volume in terms of predicting whether the embolism was bilateral in the patient group revealed a sensitivity of 80% and a specificity of 52.5% (AUC: 0.716; *P*=0.001; 95% CI: 0.607-0.824; cut-off: 124.0) (Figure 3).

Figure 3: The ROC curve analysis of right ventricular volume in predicting whether the embolism was bilateral in the patient group (AUC: 0.716; p = 0.001; 95% CI: 0.607-0.824; cut-off: 124.0)



Right ventricular volume was insignificantly lower among patients with deep venous thrombosis compared to those without (44.2(12.8) vs. 58.0(15.0), p=0.834), while mean D-dimer values were significantly lower among those with deep venous thrombosis than those without (1004.3(302.8), 1186.1(342.4), *P*=0.027).

Discussion

Acute PTE affects at least one in a thousand people, and two-thirds cannot be diagnosed before death due to the nonspecific clinical presentation [8-10]. There are numerous risk factors for PTE, which include trauma obesity, pregnancy, surgery, immobilization, smoking, oral contraceptives, cancer, hormone replacement therapies, and a history of previous PTE or known coagulation disorders. The clinical presentation of PTE ranges from asymptomatic small pulmonary embolism with low mortality to a massive PTE resulting in right ventricular failure (RVF), shock, and/or death [11]. The hemodynamic response in PTE is not only dependent on the size of the embolism and the degree of pulmonary obstruction but also the physiological reaction of the vasoreactive substances released in response to this condition and the individual's cardiopulmonary infrastructure. In individuals without any cardiopulmonary disease, 25-30% of the vasculature must be occluded to increase pulmonary pressure. A normal RV can increase the mean pulmonary artery pressure to 40 mmHg with acute obstruction of 50-75% of the pulmonary vascular network by clot before RV failure occurs [12, 13].

Patients with right ventricular dysfunction have an increased risk of mortality and morbidity according to the guidelines. Pruszczyk et al. [14] found increased PE-related mortality when tricuspid annular plane systolic excursion measurement was ≤15, which indicates right ventricular dysfunction. The study by Ates et al. [15] also found higher mortality in the group with right ventricular dysfunction. A meta-analysis by Barco et al. supports this finding: RV dysfunction at admission was associated with early mortality [16]. In our study, RVF volume increase was significantly related to PE location and laterality.

The incidence of pulmonary embolism is increased among the elderly and causes a higher rate of mortality [17]. In their study, Arseven et al. [18] found no difference between the genders in terms of PE incidence. Sharif et al. [19] examined 1075 patients diagnosed with PE in the emergency department and found that the mean age of the patients was 48 years and 69.9% were female. In the study by Dogan et al. [20], 46.8% of 124 patients were female, with a mean age of 61 years. Although the male gender was more prominent in our study, the mean age was 69 years. There was no difference between the two groups in terms of gender and age.

In the study by Sista et al. [21], 90.8% of 87 patients had submassive or non-massive PE, while 9.2% had massive PE. Another study by Ates et al. [22] reported 218 massive, 235 submassive, and 186 non-massive PE in 639 patients diagnosed with PE. Similarly, of the patients in our study, 29 (34.1%) had massive and 56 (65.9%) had submassive PE.

The volume measurement technique comes to the fore, especially in peripheral hospitals, considering the low sensitivity of unenhanced tomography performed under normal conditions, the difficulty in contrast administration, the risk of nephropathy in contrast-enhanced tomography, and the fact that Dual Energy CT (DECT) cannot be performed everywhere. This technique provides the same sensitivity. An experimental study showed that the sensitivity of detecting PTE was 89% for DECT and 67% for conventional CT [23]. Another study reported per-patient sensitivity and specificity of 100% for detecting PTE (24). However, DECT offers a sensitivity of 60.0-82.9% and a specificity of 99.5-99.8% for detecting segmental and subsegmental PTE [24, 25]. Yet, the contact of the pulmonary segments with the upper mediastinum or heart chambers is considered a limiting factor for the appropriate evaluation of PTE by DECT [26]. In our study, the sensitivity for diagnosing pulmonary thromboembolism with right ventricular volume measurement was 81.2%. Of course, the most sensitive diagnostic technique available should be used in central hospitals, but the measurement of the right ventricle in patients who are considered to have pulmonary thromboembolism will benefit the physician in distant hospitals.

Pulmonary embolism has a mortality rate of 25-30% in cases without early diagnosis and treatment [18]. Kempny et al. [27] examined 464,046 patients hospitalized with a diagnosis of pulmonary embolism in England between 1997 and 2015 in terms of mortality and found that the early mortality (1 month) was 15%. In our study, 17 (20%) patients died.

Limitation

To increase the power of the study, multi-centric studies with more patients are needed. Studies including distant hospitals, technological opportunities in terms of calculation, and patient transfer times will strengthen the results of our study.

Conclusion

The use of volume-measuring software that works in any computer instead of contrast-enhanced chest tomography will contribute to the treatment and referral of patients suspected of having pulmonary thromboembolism. Thus, time and financial waste can be avoided by preventing unnecessary patient transfers, and early transfer of real patients can contribute to the reduction of mortality and morbidity.

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