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Evaluation of the effectiveness of transthoracic echocardiography and compression ultrasonography (echo-cus) in the diagnosis of pulmonary embolism in the emergency department

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ABSTRACT

Aims: The aim of this study was to evaluate the effectiveness of echocardiography and compression ultrasonography in the diagnosis of pulmonary embolism and to investigate the diagnostic power of echocardiography and compression ultrasonography in patients with suspected pulmonary embolism.

Methods: The cross-sectional study was conducted on patients who were admitted to the emergency department between 01.10.2020 and 30.09.2021 with complaints of shortness of breath, chest pain, palpitations, bloody cough, fainting and who were recommended to undergo pulmonary computed tomography angiography according to the YEARS protocol. The study included 52 patients according to power analysis. The patients included in our study were evaluated at the bedside with the ultrasound of the emergency department. The main echocardiographic findings and compression ultrasonography findings of the deep veins of the lower extremities were evaluated. Then pulmonary computed tomography angiography was performed to patients. The right ventricle/left ventricle diameter ratio was recorded from the computed tomography images of the patients. The patients were divided into 2 groups according to pulmonary computed tomography angiography report: pulmonary embolism and non-pulmonary embolism. To see whether pulmonary embolism could be diagnosed, the main echocardiographic findings of the criteria we defined and compression ultrasonography of the deep veins of the lower extremities were evaluated. Statistical analysis of the data was performed in IBM SPSS Statics Version 26 program.

Results: There were 52 patients and 20 (38.5%) patients diagnosed with pulmonary embolism according to computed tomography. Fifty percent of the patients included in the study were male and fifty percent were female. The symptom distribution of the cases according to the diagnosis of pulmonary embolism was examined and no significant difference was found between the symptoms ($p>0.05$). When the distribution of echocardiography and compression ultrasonography findings of the patients according to pulmonary embolism diagnosis was analyzed, a statistically significant difference was found between the groups in terms of tricuspid regurgitation jet flow velocity, right ventricle/left ventricle diameter ratio, D-sign, McConnell's sign and deep vein thrombosis findings ($p<0.05$). When the results of the receiver operating characteristic curve analysis for the power of Wells and Geneva scores, echocardiography, compression ultrasonography and computed tomography findings to diagnose pulmonary embolism were analyzed; the cut-off values calculated for Wells and Geneva scores; the area under curve values calculated for the power of current echocardiography findings of tricuspid regurgitation jet flow velocity, right ventricle/left ventricle diameter ratio, D-sign, McConnell's sign findings and computed tomography right ventricle/left ventricle diameter ratio findings to diagnose pulmonary embolism were found to be statistically significant ($p<0.05$).

Conclusion: The results of our study showed that in patients diagnosed with pulmonary embolism, echocardiography is easily available and can help diagnose pulmonary embolism by showing right ventricular dysfunction. The results suggest that bedside echocardiography may help emergency physicians to make faster decisions in pulmonary embolism by increasing the provider's index of suspicion.

Keywords: Critical care, emergency medicine, echocardiography, ultrasonography, pulmonary embolism, thrombosis

INTRODUCTION

Pulmonary embolism (PE) is a clinical, pathologic and physiologic syndrome in which the pulmonary arteries are blocked by various endogenous or exogenous emboli and in most cases manifests as pulmonary circulatory dysfunction. It is a difficult diagnosis that may be overlooked due to its nonspecific clinical appearance. A 2005 study by Calder et al.[1] showed that the diagnosis is missed in 400000 people each year, of whom 100000 to 120000 die. However, early diagnosis is essential as emergency treatment is highly effective. Evaluation of patients in the emergency department should be prompted to reduce associated morbidity and mortality.

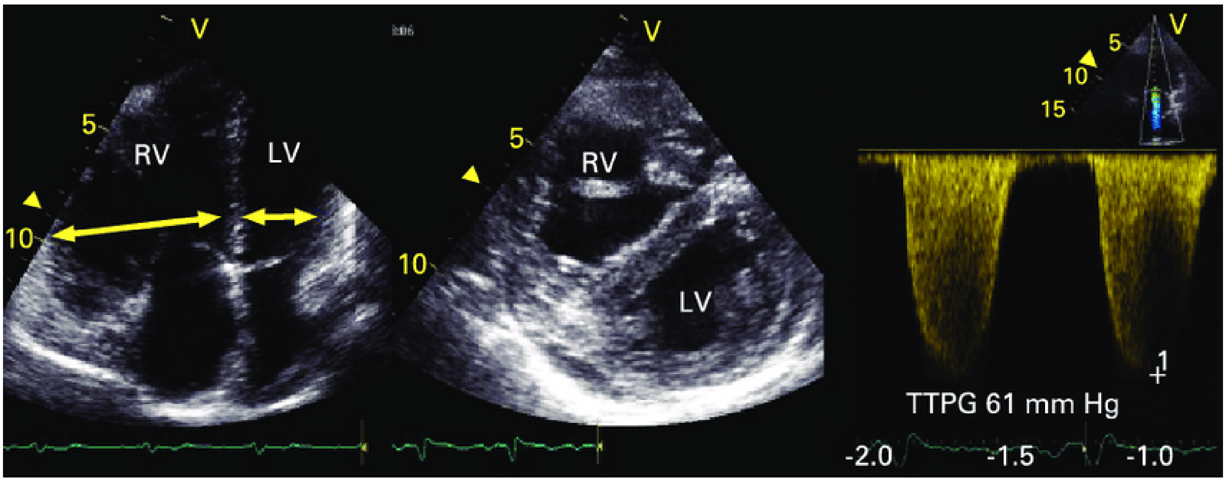

Figure 1. *Images of Right Ventricle Expansion in Pulmonary Embolism from A4 and PSSA view. A: The increase in the diameter of the RV compared to the LV in terms of A4 view. B: The increase in the diameter of the RV compared to the LV in terms of PSSA view. RV: right ventricle, LV: left ventricle, A4: apical four chamber, PSSA: parasternal short axis*

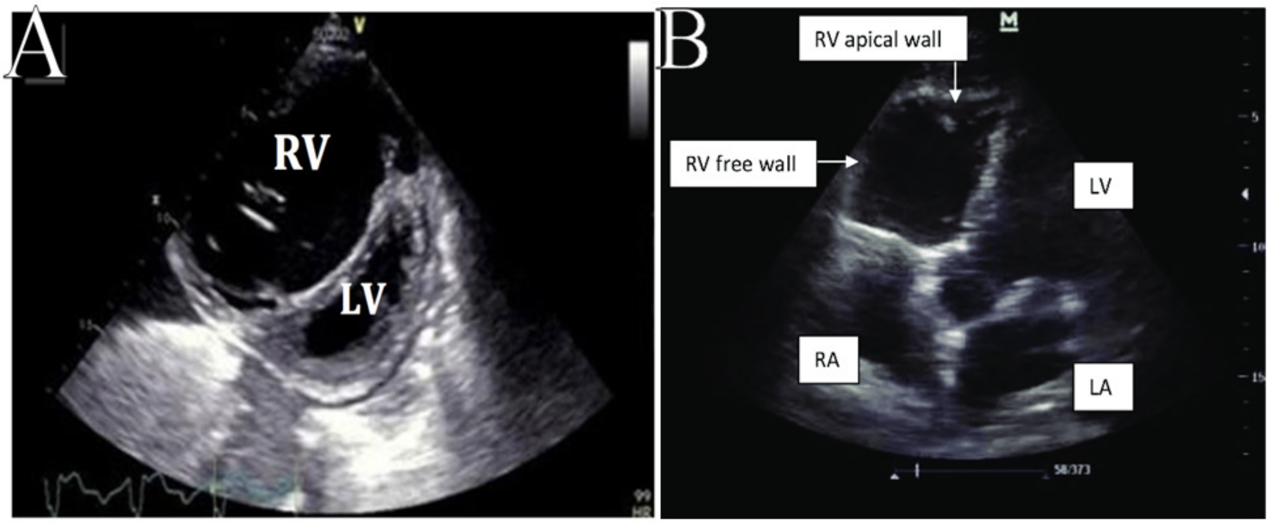

Figure 2*. Images of D-sign and McConnell's sign in PSSA and A4 view. A: D-sign in terms of PSSA view B: McConnell's sign in terms of A4 view RV: right ventricle, LV: left ventricle, RA: right atrium, LA: left atrium, A4: apical four chamber, PSSA: parasternal short axis*

Echocardiography (ECHO) is a rapid, bedside imaging modality in the emergency department. Bedside ECHO is used for emergency management decisions in high-risk patients with suspected PE. Acute PE is defined as high-risk PE when there is hemodynamic instability. According to the 2019 "European Society of Cardiology" (ESC) guideline, hemodynamic instability is characterized by cardiac arrest, obstructive shock or persistent hypotension. Hemodynamically unstable patients show signs of end-organ hypoperfusion such as hypoxia, low GCS, and confusion.[2] In a high-risk patient with suspected PE, echocardiographic evidence of right ventricle (RV) overload and dysfunction is diagnostic and recommends initiation of treatment. PE is caused by deep vein thrombosis (DVT) in the majority of cases and another bedside test recommended by the ESC guidelines for the diagnosis of PE is compression ultrasonography (CUS).[2] DVT is present in 70% of cases with PE.[3] CUS has 90% sensitivity and 95% specificity for DVT. The ESC guidelines state that a simple 4-point (both femoral veins and both popliteal veins) compression test is sufficient for CUS.[2] PE, ECHO and CUS findings were stated in the **Table 1**.[4-11]

In **Figure 1**, the increase in the diameter of the RV compared to the left ventricle (LV) is shown in terms of A4 (apical four chamber) view shown in A. The same finding shown in B is shown from the PSSA (parasternal short axis) view. In **Figure 2**, the D-sign shown in A and McConnell's sign in B are shown from A4 view.[12]

PE is one of the diseases that emergency clinics deal with intensively. It has high mortality and morbidity. In addition to this high frequency and high risk, it is an extremely difficult and challenging pathology to diagnose. Bedside ECHO and CUS methods are used for the diagnosis of PE and are recommended by guidelines. There are not many studies on the extent to which the combined use of these methods (ECHO-CUS) can diagnose PE. We aimed to evaluate the diagnostic power of these bedside methods when used together in our study.

Table 1. Pulmonary Embolism Echocardiographic and Compression Ultrasound Findings

Right Ventricle/Left Ventricle ratio	Pulmonary embolism blocks the right ventricular outflow and increases the right ventricular pressure. As a result, the right ventricle expands and the right ventricle/ left ventricle ratio, which is normally <1/1, increases with right ventricular expansion and becomes >1/1.
D-sign	It is a finding that occurs when the septal wall, which is normally curved to the right due to increased right ventricular pressure, curves towards the left ventricle and takes a "D" shape in the left ventricle.
McConnell sign	Due to increased right ventricular pressure in pulmonary embolism; the outward bulging of the right ventricular wall from the apical 4-chamber view is a finding resulting from normal right ventricular apex wall movement.
Vena Cava Inferior collapsibility index	Increasing right ventricular pressure increases the pressure of the vena cava inferior, one of the vessels entering the right ventricle, and prevents its collapsibility. Physiologically, vena cava inferior collapsibility is >50%.
High tricuspid jet flow velocity	The value considered elevated is ≥2.5 m/sec. Increasing right ventricular pressure causes insufficiency in the tricuspid valve, and the peak velocity of the flow escaping into the right atrium provides information about the right ventricular pressure.
Right ventricle wall thickness	Normal wall thickness is between 3-5 mm. Increased right ventricular wall thickness is an indicator of increased right ventricular work force. Pulmonary embolism may cause an increase in right ventricular wall thickness as it increases the right ventricular afterload by increasing the pulmonary artery pressure. Echocardiography can indirectly provide information about the presence of pulmonary embolism.
Deep Vein Thrombosis	Deep vein thrombosis and pulmonary embolism are part of the venous thromboembolism spectrum. Half of the thrombi in the proximal deep veins of the leg cause pulmonary embolism. Compression ultrasonography is a method of imaging the leg veins and applying pressure to check whether there are clots in them.

METHODS

The study was conducted with the approval of Aydın Adnan Menderes University School of Medicine Scientific Researches Evaluation and Ethics Committee (Date: 01/10/2020, Decision No: 2020/200). We obtained an informed consent form from all patients for the procedure. The procedures were performed in line with ethical rules and the Declaration of Helsinki principles. The cross-sectional study was conducted on patients who were admitted to the emergency department between 01.10.2020 and 30.09.2021 with complaints of shortness of breath, chest pain, palpitations, bloody cough, fainting, and who were recommended to undergo pulmonary computed tomography (CT) angiography according to the YEARS protocol, the criteria of which were specified in the study published by van der Hulle et al.[13] The YEARS protocol includes the criteria for evidence of DVT signs, hemoptysis, and the most likely diagnosis being PE, and helps the clinician to decide on pulmonary CT angiography according to the criteria.[13] The research was conducted in a single center. Patients over the age of 18, who were not pregnant, who were stable in the emergency department and who were subsequently able to undergo pulmonary CT angiography were included in our study. Patients under 18 years of age, pregnant women, and patients who could not undergo pulmonary CT angiography were excluded from the study. In a study conducted by Stefano Grifoni et al.[14] in 1998, the effect size calculated from the table related to PE was calculated as 0.640 and a large effect size of 0.5 was taken for the sample size calculation of our study. With an effect size of 0.5, the sample size was found to be 52 at 95% power with a 5% margin of error and 52 patients were included in the study. Patients were informed about their inclusion in the study and their informed written consent was obtained.

While the patient's examination and treatment for PE was continued by his regular physician without delay, the co-executive of the study evaluated him with ECHO and the necessary data was collected. The patients included in our study were examined by a researcher with a basic and advanced ultrasonography (USG) course certificate given by the Emergency Association of Türkiye, using a Samsung H60 model USG device with doppler features such as pulse wave and continuous wave. Echocardiographic findings of PE were evaluated with the cardiac probe of ultrasound. While the patient was evaluated with a cardiac probe, peak velocity was measured using continuous wave doppler mode on the tricuspid valve from the A4 view in the supine position. Afterwards, RV free wall thickness, McConnell's sign, and the ratio of RV/LV diameters were measured with a cardiac probe. The D-sign and the RV/LV diameter ratio were measured from the PSSA view with the cardiac probe of the ultrasound. The probe was taken to the epigastric area and inferior vena cava (VCI) diameters and collapsibility index were recorded. Then, the linear probe was used and DVT was searched for by compression from 3 different points in both groin and legs, from the femoral vein to the popliteal vein. Afterwards, the patient's regular physician intervened, stabilized him, and pulmonary CT angiography was performed. The RV/LV diameter ratio was recorded from the CT images of the patients. It was recorded whether the patients were diagnosed with PE in their CT angiography reports, and accordingly, the patients were split into 2 groups: PE and non-PE. To see whether PE could be diagnosed, the main echocardiographic findings of the criteria we defined and CUS of the deep veins of the lower extremities were evaluated.

Statistical Analysis

Data were statistically analyzed using IBM SPSS Statistics Version 26 program. For the comparison of categorical data between groups, Pearson Chi-Square statistical analysis was used, and for the comparison of continuous data not conforming to normal distribution between two groups, Mann Whitney U statistical analysis was used. Receiver operating characteristic (ROC) analysis was used to estimate the predictive power of positive pulmonary CT Angiography and $p<0.05$ was considered statistically significant.

RESULTS

The flowchart of the study is presented in **Figure 3**. There were 52 patients and 20 (%38.5) patients diagnosed with PE according to CT. Fifty percent of the patients included in the study were male and fifty percent were female. The median age of the subjects diagnosed with PE was 56 years (18-90) and the median age of the subjects not diagnosed with PE was 64 years (30-91). There was no statistically significant difference between the median ages of male and female patients

Table 4. Results of ROC Analysis for the Power of Wells and Geneva Scores, ECHO, CUS and CT findings to diagnose PE

Cut-off	Sensitivity	95% CI	Specificity	95% CI	AUC	95% CI	p
Wells score	45.0	23.1- 68.5	93.8	79.2- 99.2	0.755	0.616-0.863	**<0.001**
Geneva score	75.0	50.9- 91.3	56.3	37.7- 73.6	0.705	0.563-0.824	**0.004**
High tricuspid jet flow velocity (≥2.5m/s)	60.0	36.1- 80.9	81.3	63.6- 92.8	0.706	0.564-0.824	**0.008**
VCI Collapsibility index (<%50)	90.0	68.3- 98.8	21.9	9.3- 40.0	0.559	0.415-0.697	0.463
RV/LV (PSSA)	75.0	50.9- 91.3	90.6	75.0- 98.0	0.828	0.698-0.919	**<0.0001**
D-shape sign	60.0	36.1- 80.9	96.9	83.8- 99.9	0.784	0.648-0.886	**<0.001**
McConnel sign	35.0	15.4- 59.2	100.0	89.1- 100.0	0.675	0.531-0.798	**0.033**
DVT+ (CUS)	30.0	11.9- 54.3	93.8	79.2- 99.2	0.619	0.474-0.750	0.155
CT RV/LV	70.0	45.7- 88.1	90.6	75.0- 98.0	0.803	0.669-0.900	**<0.0001**

ROC: receiver operating characteristic, ECHO: echocardiography, CUS: compression ultrasonography, CT: computed tomography, VCI: vena cava inferior, RV: right ventricle, LV: left ventricle,
PSSA: parasternal short axis view, DVT: deep vein thrombosis, PE: pulmonary embolism, CI: confidence interval, AUC: area under curve

(p>0.05). When the distribution of ECHO and CUS findings of the patients according to PE diagnosis was analyzed, a statistically significant difference was found between the groups in terms of high tricuspid regurgitation jet flow velocity, RV/LV diameter ratio (PSSA), RV/LV diameter ratio (A4), D-sign, McConnell's sign and DVT (CUS) findings (p<0.05). There was no statistically significant difference between the groups in terms of other variables (>0.05). The distribution of gender, age, ECHO and CUS findings according to the diagnosis of PE is summarized in **Table 2**. When the distribution of symptoms according to the PE diagnosis of the cases was examined in **Table 3**, no significant difference was found between the symptoms (p>0.05).

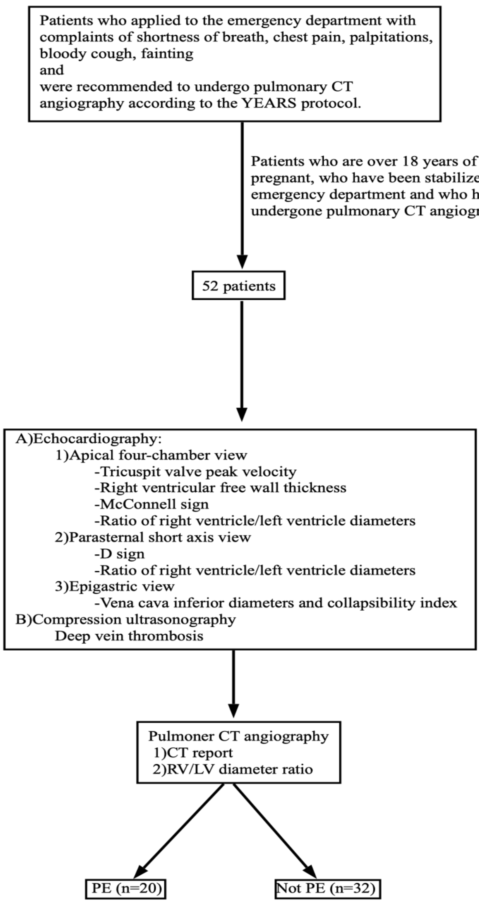

Figure 3*. The flow chart of the study*
CT: computed tomography, PE: pulmonary embolism

Table 2. Distribution of Gender, Age, ECHO and CUS findings according to the diagnosis of PE

		PE(n=20)	Not PE (n=32)	Total(n=52)	p
Age (year)		56(18-90)	64(30-91)	63,5(18-91)	0.257#
Sex	Female, n (%)	11(55.0)	15(46,9)	26(50)	0.569*
	Male, n (%)	9(45.0)	17(53,1)	26(50)	
High tricuspid jet flow velocity (≥2.5m/s), n (%)		12 (60)	6 (18.8)	18 (34.6)	0.002*
VCI Collapsibility index (<%50), n (%)		18 (90)	25 (78.1)	43 (82.7)	0.454*
RV/LV (PSSA) (>0,90), n (%)		15 (75)	3 (9.4)	18 (34.6)	**<0.001***
RV/LV (A4) (>0,90), n (%)		15 (75)	3 (9.4)	18 (34.6)	**<0.001***
D-sign, n (%)		12 (60)	1 (3.1)	13 (25)	**<0.001***
McConnel sign, n (%)		7 (35)	0 (0)	7 (13.5)	**0.001***
RV thickness (>5mm), n (%)		12 (60)	10 (31.3)	22 (42.3)	**0.041***
DVT+ (CUS), n (%)		6 (30)	2 (6.3)	8 (15.4)	**0.043***

* p value for Pearson Chi-Square test, # p value Mann Whitney U analysis
ECHO: echocardiography, CUS: compression ultrasonography, PE: pulmonary embolism, VCI: vena cava inferior, RV: right ventricle, LV: left ventricle, PSSA: parasternal short axis view, A4: apical four chamber view, DVT: deep vein thrombosis

Table 3. Distribution of Symptoms According to Diagnosis of PE

	PE		Not PE		Total		X^2	p
	n	%	n	%	n	%		
Shortness of breath	15	75.0	24	75.0	39	75.0	0.000	1.000
Chest pain	6	30.0	6	18.8	12	23.1	0.878	0.500
Palpitation	4	20.0	3	9.4	7	13.5	1.193	0.408
Bloody cough	1	5.0	2	6.3	3	5.8	0.035	1.000
Fainting	1	5.0	1	3.1	2	3.8	0.117	1.000

Pearson Chi-Square, Fisher's Exact test, PE: pulmonary embolism

When the results of the ROC analysis for the power of Wells and Geneva scores, ECHO, CUS and CT findings to diagnose PE were analyzed; the cut-off values calculated for Wells and Geneva scores; the Area Under Curve (AUC) values calculated for the power of current ECHO findings of high tricuspid regurgitation jet flow velocity, RV/LV diameter ratio (PSSA), D-Sign, McConnell's sign findings and CT RV/LV diameter ratio findings to diagnose PE were found to be statistically significant (p<0.05). AUC values calculated for other variables were not statistically significant (p>0.05). The results of ROC analysis for the power of Wells and Geneva scores, ECHO, CUS and CT findings to diagnose PE are summarized in **Table 4**. The ROC analysis curves of the data with significant AUC values are shown in **Figure 4**. As can be seen in the graph and table, the parameter with the highest specificity was found to be RV/LV diameter ratio.

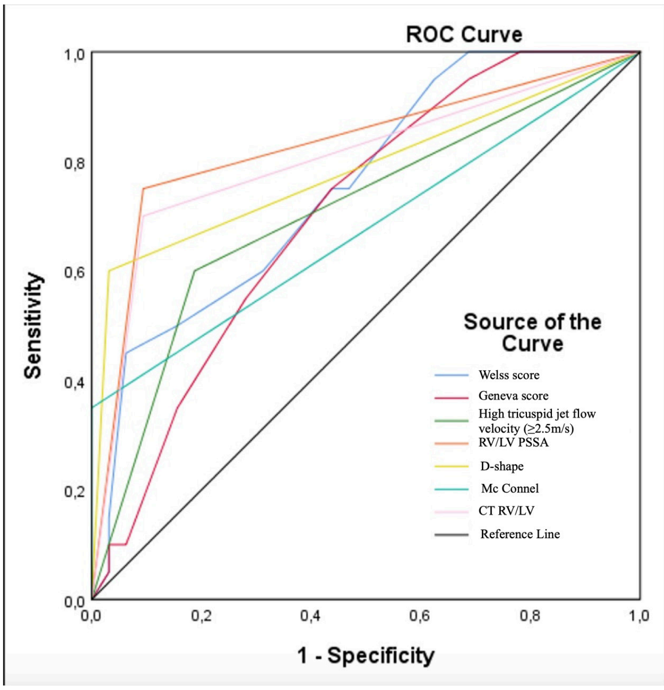

Figure 4. *ROC Curves Plotted for Variables Found Significant in ROC Analysis for the Power of Wells and Geneva Scores, ECHO, CUS and CT findings to diagnose PE*
ROC: receiver operating characteristic, ECHO: echocardiography, CUS: compression ultrasonography, CT: computed tomography, PE: pulmonary embolism, RV: right ventricle, LV: left ventricle, PSSA: parasternal short axis

DISCUSSION

RV function is an important determinant of long-term outcome in patients with acute PE. In these conditions, the RV is subjected to abnormal and increased loading that varies in timing, magnitude and duration. Consequently, RV dysfunction is variably present in the initial presentation of acute PE. Pruszczyk, P. et al.[15] found that the RV/LV diameter ratio was significantly elevated on ECHO. Akhoundi et al.[16] found a significantly higher CT RV/LV diameter ratio in their study. In our study, when the distribution of ECHO, CUS, and CT findings of the patients according to PE diagnosis was examined, a statistically significant difference was found between the groups in terms of RV/LV diameter ratio (PSSA), RV/LV diameter ratio (A4), and CT RV/LV diameter ratio findings. These results indicate that there is a significant clinical need for a simple, reproducible and reliable parameter of RV function in patients with right heart disease. ECHO has an important role in the diagnosis of PE because it is non-invasive, easily accessible, without radiation hazard and without the use of contrast agents.

D-sign is a finding seen in PE, because PE increases RV pressure. In the normal heart, the septum bends towards the RV because the LV pressure is higher. If the pressure in the RV increases as a result of conditions such as PE, the septum bends towards the LV and gives the LV a "D" shaped appearance. This ultrasonographic finding is called "D-sign".[17] In our study, a statistically significant difference was found between the groups in terms of D-sign finding; and the D-sign finding is consistent with the literature.

PE causes morbidity and mortality through RV outflow obstruction, which can lead to increased pulmonary artery pressure, RV failure, LV failure and circulatory collapse. RV dysfunction has been found on ECHO in 27% to 40% of normotensive patients with PE and can predict circulatory collapse.[4] Dresden et al.[4] found that RV dilatation on bedside ECHO is highly specific for PE (98%) but has a low sensitivity (50%). There are also studies proving that the most prominent ECHO finding detected in patients with PE is McConnell's sign.[18,19] The results of our study are consistent with the literature.

The definitive diagnosis of pulmonary hypertension is made by cardiac catheterization, but echocardiographic measurement of tricuspid regurgitation jet stream velocity height can be used to estimate pulmonary artery systolic pressures. Pulmonary hypertension is described as a tricuspid regurgitant jet flow velocity ≥2.5 m/s.[20] Increased jet flow velocity in tricuspid valve regurgitation (≥2.5 m/sec) is one of the echocardiographic findings that lead the clinician to PE in studies. In a study conducted on patients diagnosed with PE, it was found to be elevated in 44 of 46 patients.[21] RV dysfunction may be diagnosed by measuring the peak velocity of the regurgitant jet of the tricuspid valve. Nazeyrollas et al.[22] included a total of 132 cases and showed that peak velocity of the tricuspid valve regurgitant flow ≥2.5 m/s and RV/LV diameter ratio >0.5 were 93% sensitive and 81% specific for the diagnosis of PE. In our study, tricuspid regurgitation jet flow velocity elevation (≥2.5 m/s) and RV/LV diameter ratio elevation was significant and consistent with the literature.

DVT and PE are related diseases covered under the heading of venous thromboembolism. Half of the thrombi that form in the proximal deep leg veins cause PE and DVT is a risk factor for PE. The diagnosis of PE is usually confirmed by pulmonary CT angiography in patients with DVT after CUS.[23] In our study, DVT results were significant and consistent with the literature.

Bedside ECHO is the most popular diagnostic tool in patients with suspected PE, and as the number of PE attending the emergency department rises, the role of ECHO and its results becomes more significant. In a meta-analysis of 24 articles, only RV end-diastolic diameter was found to have a sensitivity of more than 80% for detecting PE, although this is still a low value for a finding to be used in sensitivity. None of the USG findings in this meta-analysis had a specificity lower than 80%. In the studies included in this meta-analysis, the VCI collapsibility index, which was the only finding that was not significant in our study, was not examined and the VCI collapsibility index was not mentioned in the meta-analysis.[24] Yamanoğlu A. et al.[25] grouped the etiologies of patients presenting to the emergency department with dyspnea into cardiac and pulmonary etiologies and examined PE in the pulmonary origin group. They performed ECHO and evaluated the VCI and collapsibility index. The findings of their study have shown that the VCI collapsibility index was normal in pulmonary-induced dyspnea compared to cardiac-induced dyspnea. As a result of our study, we found that the VCI collapsibility index has no place in the diagnosis of PE. Based on these findings, the results of our study are consistent with the literature.

Normal limits of RV wall thickness are 3-5 mm. Exceeding this value indicates thickening of the RV wall, which may indicate RV hypertrophy. The main mechanism of ventricular hypertrophy is increased hemodynamic workload. As a result, increased RV wall thickness is an indicator of increased RV workload. PE may cause increased RV wall thickness because it increases RV afterload by increasing pulmonary artery pressure. In our study, increased RV wall thickness was detected and found to be consistent with the literature.

Limitations

In our study, our results are regional in nature due to the fact that the hospital where the study was conducted was a single center. Larger multicenter studies will be able to provide more objective information. Repeated measurements were not performed in our study, the treatment response of patients can be followed up by performing repeated measurements. The person-dependent nature of the USG performed is also among the limitations of the study.

CONCLUSION

Acute PE is an emergency requiring rapid diagnosis and treatment. ECHO and CUS is a non-invasive, easily accessible, non-radiation hazardous diagnostic tool and were found to be effective in diagnosing PE in our study. Results from our study showed that bedside ECHO and CUS can help emergency physicians to make faster decisions in PE by increasing the provider's index of suspicion.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Scientific Researches Evaluation and Ethics Committee of Aydın Adnan Menderes University (Date: 01/10/2020, Decision No: 2020/200). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Informed Consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declared that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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