

A New Approach to Acute Pulmonary Embolism: Coronary Sinus Diameter to Inferior Vena Cava Diameter Ratio

Akut Pulmoner Embolide Yeni Bir Yaklaşım: Koroner Sinüs Çapı - Inferior Vena Kava Çapı Oranı

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Abstract

Objective: This study aimed to explore whether the coronary sinus (CS) diameter to the inferior vena cava (IVC) diameter (CS/IVC) ratio measured by computed tomography pulmonary angiography (CTPA) can be used to predict pulmonary embolism (PE) and its relationship with worse clinical outcomes.

Methods: Our study included 198 patients. Study patients were divided into groups according to the presence of PE. CS and IVC diameters were measured using CTPA. While PE was not detected in 132 patients, it was detected in 66 patients.

Results: The CS/IVC ratio ($78.3 \pm 18.8\%$ and $49.3 \pm 17.2\%$, $p < 0.001$) was higher in the PE group. The CS/IVC ratio was established as a predictor of PE (odds ratio: 4.189, 95% confidence interval: 1.990-8.819, $p < 0.001$). The cut-off value for the CS/IVC ratio value was ≥ 60.8 (sensitivity: 86.4%, specificity: 77.3%, positive predictive value: 66.67%, and negative predictive value: 94.44%) in PE. It was observed that clinical outcomes were higher in patients with CS/IVC ratio $\geq 60.8\%$.

Conclusion: The CS/IVC ratio was predictive of PE in patients diagnosed with acute PE. The CS/IVC ratio may be useful in estimating patients hospitalized for PE who require close monitoring.

Keywords: Pulmonary embolism, coronary sinus, computerized tomographic, diameter

Öz

Amaç: Bu çalışmada bilgisayarlı tomografi pulmoner anjiyografide (BTPA) ölçülen koroner sinüs (KS) çapının inferior vena kava (İVK) çapına (KS/İVK) oranının pulmoner emboliyi (PE) öngörmede kullanılıp kullanılmayacağı ve bunun daha kötü klinik sonuçlarla ilişkisi araştırılmıştır.

Yöntem: Çalışmamıza 198 hasta dahil edildi. Çalışma hastaları PE varlığına göre gruplara ayrıldı. KS ve İVK çapları BTPA kullanılarak ölçüldü. PE 132 hastada saptanmazken, 66 hastada saptandı.

Bulgular: KS/İVK oranı ($78,3 \pm 18,8$ ve $49,3 \pm 17,2$, $p < 0,001$) PE grubunda daha yüksekti. KS/İVK oranı PE'nin öngörücüsü olarak belirlenmiştir (olasılık oranı: 4,189, %95 güven aralığı: 1,990-8,819, $p < 0,001$). PE'de KS/İVK oranı değeri için kesme değeri $\geq 60,8$ (duyarlılık: %86,4, özgüllük: %77,3, pozitif prediktif değer: %66,67 ve negatif prediktif değer: %94,44) idi. KS/İVK oranı $\geq 60,8$ olan olgularda klinik sonuçların daha yüksek olduğu gözlenmiştir.

Sonuç: KS/İVK oranı akut PE tanısı konan hastalarda PE için öngörücüdür. KS/İVK oranı, PE nedeniyle hastaneye yatırılan ve yakın izlem gerektiren hastaların tahmin edilmesinde yararlı olabilir.

Anahtar Kelimeler: Pulmoner emboli, koroner sinüs, bilgisayarlı tomografi, çap



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Introduction

Pulmonary embolism (PE) is a common cardiovascular emergency⁽¹⁾. The following heart attack and stroke, PE is the third major cardiovascular cause of death⁽²⁾. PE can have various clinical manifestations in patients, ranging from asymptomatic cases to cases presenting with right ventricular dysfunction and life-threatening clinical outcomes, depending on the severity of the obstruction in the pulmonary artery (PA). D-dimer, transthoracic echocardiography (TTE), and computed tomography pulmonary angiography (CTPA) are some tests used to diagnose PE^(3,4). CTPA is the diagnostic imaging technique that is generally used worldwide for the diagnosis of PE because of its high accuracy rate, as well as its easily accessible and non-invasive nature. Moreover, CTPA provides vital prognostic information; hence, it remains useful for the physicians⁽⁵⁾.

The coronary sinus (CS) is an intrapericardial vein that drains into the right atrium (RA). It has a tubular structure and is located in the atrioventricular groove in the posterior part of the heart⁽⁶⁾. Extracardial veins, which are involved in the body's essential venous circulation, drain into the RA along with the intrapericardial veins⁽⁷⁾. Because the RA receives a large portion of the venous circulation in a normally functioning heart, clinical conditions involving primary or secondary cardiac involvement, such as right heart failure and pulmonary hypertension, which can cause increased pressure in the RA, will result in impaired venous drainage and a change in CS and inferior vena cava (IVC) diameter^(8,9). In cases of PE, where the PA bed is fully or partially blocked, increased pulmonary artery pressure (PAP) and pressure in the right ventricle (RV) afterload develops⁽¹⁰⁾. Invasively measured systolic PA and RA pressures were shown to be correlated with CS and IVC diameters in studies^(11,12).

Based on this information, we believe that full or partial obstruction of the PA bed causes secondary changes in the right cardiac cavities and associated anatomical structures in patients with PE and that these changes can help detect the PE. Therefore, the current study investigates the CS/IVC ratio, which compares the CS diameter to the IVC diameter measured in CTPA, to determine whether this ratio can be used to predict PE and its relationship with worse clinical outcomes (in-hospital mortality and hospital stay duration).

Materials and Methods

Patients and the Study Design

Our study encompassed patients eligible for inclusion who underwent contrast-enhanced thoracic computed tomography (CT) and received a preliminary diagnosis of

PE at a tertiary health center between January 1, 2015, and July 1, 2021. A total of 3,310 patients who were prediagnosed with PE upon admission to our hospital were retrospectively reviewed. A total of 198 patients were included in our study, comprising 66 patients who had recently been diagnosed with PE and 132 patients who met the age- and gender-related inclusion criteria but were not diagnosed with PE. CTPA was performed on the patients when they were admitted to the emergency department. The PE diagnoses and types were determined using current guidelines⁽¹³⁾. Obstruction of the PA branch and blockage of blood flow to the distal pulmonary section were defined as PE.

The exclusion criteria were as follows: Chronic kidney disease (epidermal growth factor receptor <30 mL/min/1.73 m²), stroke, active infection, diagnosed malignancy, history of PE or pulmonary hypertension, history or previous treatment for congenital valvular heart disease, diagnosed chronic obstructive pulmonary disease, cardiac tamponade, permanent pacemaker, moderate to severe valvular disease, severe pulmonary disease, intubation, anomalies (such as duplication and persistent left superior vena cava), documented left ventricular systolic dysfunction (left ventricular ejection fraction <50%), and diastolic dysfunction, along with a history of right ventricular dysfunction and age 18 years.

The hospital's electronic medical records were used to obtain data on patients' information and laboratory values.

This study received Çanakkale Onsekiz Mart University's Ethical Committee approval (decision no: 2011-KAEK-27/2021-2100135640) and was conducted in accordance with the Declaration of Helsinki.

Image Data

Thoracic vascular examinations were performed by the same radiologist. The images, which were taken with 320-slice MSCT (Aquilion One Vision Edition, Toshiba Medical Systems, Nasu, Japan), were analyzed. The CT scan was 5-mm slice thick and featured 1.5 steps. Contrast agent was used for thoracic images during the full inspiratory phase of the CT scan (an injection rate: 2 to 2.5 mL/s). CS diameter was calculated from a distance of 1 cm from the CS ostium⁽¹⁴⁾. While measuring the diameter of the IVC, the short axis of the vein is evaluated. The IVC diameter was measured between the right atrial orifice and hepatic vein. A sample image showing the CS and IVC measurements is presented in Figure 1.

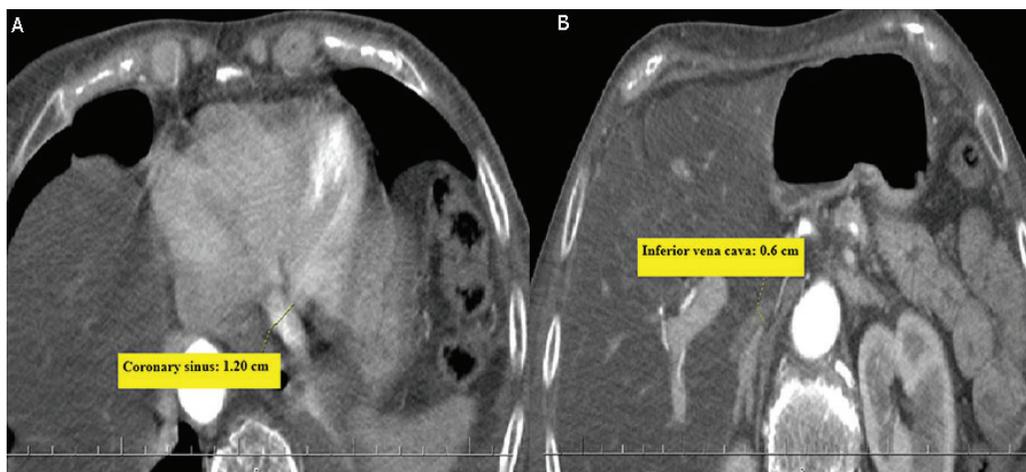


Figure 1. Measurement of the coronary sinus and inferior vena cava diameters

Statistical Analysis

SPSS 19.0 (SPSS Inc, Chicago, IL, USA) software was used for statistical analysis. Continuous variables were analyzed using the Kolmogorov-Smirnov test. The data were presented as mean \pm standard deviation or median (interquartile range). Numbers and percentages are used to express categorical variables. The t-test and Mann-Whitney U test were used to compare normally and non-normally distributed parameters. Chi-square tests were used to compare the odd ratios of categorical variables. Pearson's test was used for correlation analysis. Receiver operating characteristic (ROC) curves were created for the CS/IVC ratio, and their cut-off values were determined. PE predictors were analyzed using multivariate logistic regression. P-values of <0.05 were considered statistically significant.

Using G*Power (effect size: 0.50, alpha error: 0.05, and power 95%), the sample size for our study was calculated to be 66 patients in group 1 and 132 patients in group 2.

Results

The study included 198 patients, with 66 patients diagnosed with acute PE (29 males, 37 females) and 132 patients in the control group (60 males, 72 females). The D-dimer and cardiac troponin (Tn) values were statistically and numerically higher in the PE group. CS diameter (12.70 ± 3.40 mm and 8.87 ± 2.60 mm, $p < 0.001$), IVC diameter (18.57 ± 4.47 mm and 17.01 ± 4.52 mm, $p = 0.023$), CS/IVC ratio ($78.3 \pm 18.8\%$ and $49.3 \pm 17.2\%$, $p < 0.001$), and CS/IVC/body surface areas (BSA) ($41.4 \pm 9.9\%$ and $25.9 \pm 9.9\%$, $p < 0.001$) were higher in the PE group (Table 1).

CS diameter was positively correlated with D-dimer, sPAP, and cardiac Tn. IVC diameter was correlated with sPAP. CS/IVC ratio was positively correlated with D-dimer, sPAP, and cardiac Tn (Table 2). The correlation analysis between the CS/IVC ratio and sPAP was performed using Pearson's test and presented using Scatter dot analysis (Figure 2).

According to the analysis performed on the variables to determine their predictive value for PE, the model had a coefficient value of 93.3%. The CS/IVC ratio was established as the predictor of PE [odds ratio (OR): 4.189, 95% confidence interval (CI): 1.990-8.819, $p < 0.001$] (Table 3).

According to the analysis performed on the CS/IVC ratio to determine its predictive value in PE, the cut-off value was ≥ 60.8 . According to the analysis performed on the CS/IVC/BSA ratio to establish its predictive value in PE, the cut-off value was ≥ 30.3 (Table 4). Receiver operating characteristic (ROC) curve analysis was performed to assess CS [area under the curve (AUC): 0.813, 95% CI: 0.751-0.876, $p < 0.001$], CS/IVC ratio (AUC: 0.865, 95% CI: 0.815-0.916, $p < 0.001$) and CS/IVC/BSA (AUC: 0.869, 95% CI: 0.818-0.919, $p < 0.001$) for their predictive value in PE (Figure 3).

When patients with PE were analyzed as two groups according to CS/IVC ratio (%) ≥ 60.8 and CS/IVC ratio (%) < 60.8 , differences were observed between the groups in terms of hospital stay and mortality [7.24 ± 2.32 and 5.84 ± 1.49 days, respectively, $p < 0.001$; hospital stay duration] and [5 (5.6) and 0 (0) n (%), respectively, $p = 0.017$; in-hospital mortality] (Table 5).

Table 1. Demographic, echocardiographic, and laboratory findings of patients with pulmonary embolism and the control group

	Pulmonary embolism group (n=66)	Control group (n=132)	p-value
Age (years)	67.2±15.9	69.8±13.6	0.231
Gender (n)			0.840
Male	29	60	
Female	37	72	
Smoking (n)	14	23	0.519
Hypertension (n)	6	22	0.149
Diabetes mellitus (n)	11	24	0.792
Body mass index, (kg/m ²)	24.75±1.45	24.76±1.44	0.972
Heart rate (beats/min)	84.48±12.16	81.91±13.24	0.188
SBP (mmHg)	117.69±5.89	119.64±7.78	0.075
DBP (mmHg)	81.03±7.03	83.18±7.14	0.160
Glucose (mg/dL)	118.92±40.75	118.23±48.78	0.921
Creatinine (mg/dL)	0.93±0.16	0.96±0.14	0.235
Hemoglobin (g/dL)	13.16±2.27	13.16±2.30	0.990
D-dimer, ng/mL	77 (55-88)	3 (2-4)	<0.001
Cardiac Tn, ng/L	9.5 (2.5-36)	6 (2-7)	0.003
LVEF (%)	57.96±3.68	58.77±3.48	0.144
LA diameter (mm)	31.45±5.22	30.25±5.24	0.131
RA diameter (mm)	29.45±4.62	25.37±5.03	<0.001
sPAP (mmHg)	35 (25-50)	21 (20-25)	<0.001
CS (mm)	12.70±3.40	8.87±2.60	<0.001
IVC (mm)	18.57±4.47	17.01±4.52	0.023
CS/IVC ratio (%)	78.3±18.8	49.3±17.2	<0.001
CS/IVC/BSA (mm/m ²) (%)	41.4±9.9	25.9±9.0	<0.001

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, Tn: Troponin, LVEF: Left ventricular ejection fraction, LA: Left atrium, RA: Right atrium, sPAP: Systolic pulmonary artery pressure, CS: Coronary sinus, IVC: Inferior vena cava, BSA: Body surface areas

Table 2. Correlation of variables with computed tomography-derived measurements in patients with pulmonary embolism

	CS		IVC		CS/IVC ratio	
	r value	p-value	r value	p-value	r value	p-value
BMI	0.040	0.576	0.039	0.585	0.131	0.066
SBP	0.008	0.916	0.026	0.711	0.004	0.959
DBP	0.025	0.725	0.081	0.256	0.059	0.407
sPAP	0.507	<0.001	0.159	0.025	0.605	<0.001
Cardiac Tn	0.153	0.031	0.036	0.611	0.223	0.002
D-dimer	0.421	<0.001	0.139	0.050	0.339	<0.001

BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, sPAP: Systolic pulmonary artery pressure, Tn: Troponin, CS: Coronary sinus, IVC: Inferior vena cava

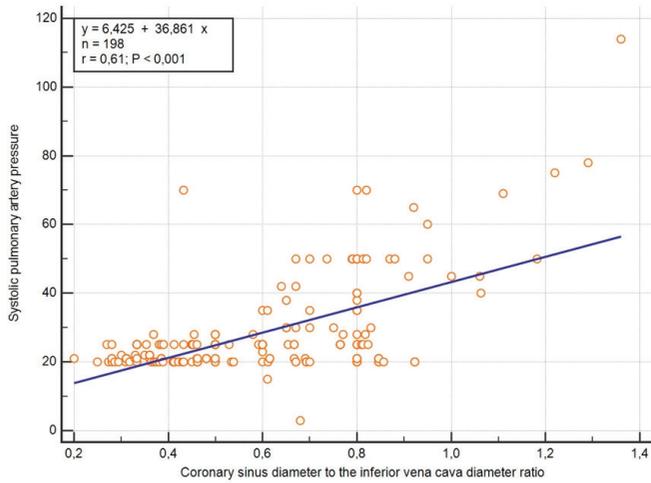


Figure 2. Correlation analysis of CS/IVC ratio and sPAP
 CS: Coronary sinus, IVC: Inferior vena cava, sPAP: Systolic pulmonary artery pressure

Discussion

We demonstrated that the CS/IVC ratio was predictive of PE on CTPA imaging in patients who were diagnosed with acute PE for the first time compared with healthy individuals. Second, in cases of PE, the increased CS/IVC ratio may lengthen the duration of hospitalization and increase in-hospital mortality.

Table 3. Predictors of pulmonary embolism

	p	OR	(95% CI)
D-dimer	<0.001	2.814	(0.956-1.021)
CS/IVC ratio	<0.001	4.189	(1.990-8.819)
sPAP	0.003	1.141	(1.044-1.246)
Cardiac Tn	0.458	0.988	(0.956-1.021)

CS: Coronary sinus, IVC: Inferior vena cava, sPAP: Systolic pulmonary artery pressure, Tn: Troponin, OR: Odds ratio, CI: Confidence interval

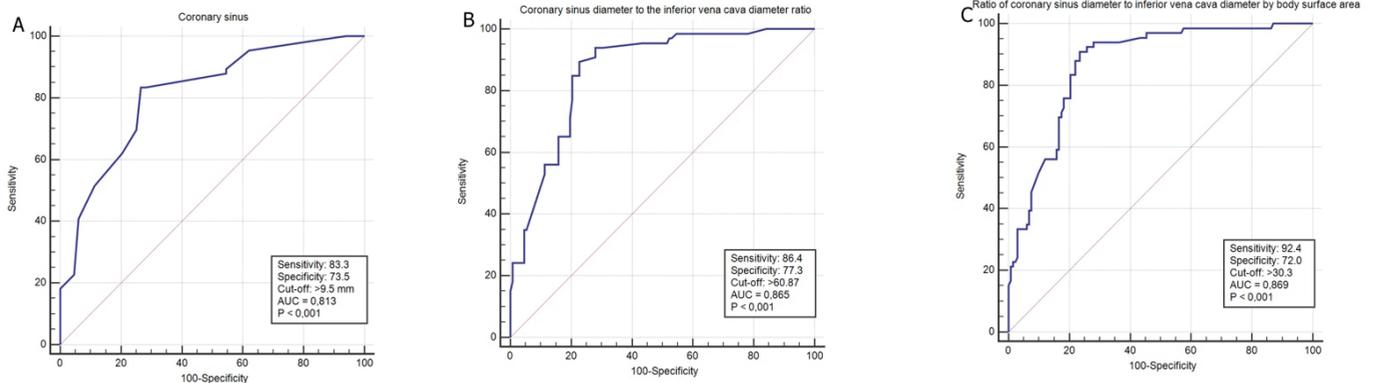


Figure 3. Receiver operator characteristic (ROC) curve analysis of CS, CS/IVC ratio, and CS/IVC/BSA to predict pulmonary embolism

AUC: Area under the curve, CS: Coronary sinus, IVC: Inferior vena cava, BSA: Body surface areas

Table 4. Diagnostic performance results of the CS/IVC ratio in pulmonary embolism

	Cut-off value	Sensitivity	Specificity	PPV	NPV
CS (mm)	≥9.5	83.3	73.5	59.34	88.79
CS/IVC ratio (%)	≥60.8	86.4	77.3	66.67	94.44
CS/IVC/BSA (mm/m ²) (%)	≥30.3	92.4	72.0	65.56	93.52

CS: Coronary sinus, IVC: Inferior vena cava, BSA: Body surface areas, PPV: Positive predictive value, NPV: Negative predictive value

Table 5. Clinical outcomes of patients

	All (n=66)	CS/IVC ratio (%) ≥60.8	CS/IVC ratio (%) <60.8	p
In-hospital mortality, n (%)	5 (7.6)	5 (5.6)	0 (0)	0.017
Hospital stay duration (days)	6.47±2.03	7.24±2.32	5.84±1.49	<0.001

CS: Coronary sinus, IVC: Inferior vena cava

Acute PE is an important cardiovascular disease with a mortality rate ranging from 15% to 20%. The severity of RV dysfunction that develops because of PA obstruction has an adverse effect on survival⁽¹⁵⁾. Vasoconstriction caused by mechanical obstruction in the pulmonary bed results in increased right ventricular afterload⁽¹⁶⁾. An acute increase in right ventricular afterload can lead to various clinical symptoms, such as dilatation in the tricuspid annulus, elevated RA pressure, increase in right ventricular end-diastolic volume, impairment of left ventricular functions, and hemodynamic instability⁽¹⁷⁾. Specific treatments, such as early reperfusion therapy, are required for survival in patients with PE, particularly in the presence of hemodynamic instability⁽¹⁸⁾. Therefore, early detection and treatment of PE will be highly beneficial in avoiding poor clinical outcomes.

CTPA, in addition to being the gold technique for the diagnosis of PE, has the benefit of allowing intrapericardial and extrapericardial structures, such as the CS and IVC, to be easily detected⁽¹⁹⁾. Imaging of the coronary venous system is overshadowed by that of the coronary artery. Along with their widespread use in the current clinical world, such as stem cell therapy, left ventricular pacemakers have been implanted in an increasing number of cases and studied in an increasing number of electrophysiological studies, emphasizing their connection to clinical diseases^(20,21). Because CS has a thin wall structure, it is easily dilated in clinical diseases, including right heart failure and pulmonary hypertension, which can result in increased pressure in the RA and ventricles⁽²²⁾. Previous studies have shown that CS dilatation can be used to predict the severity of heart failure and poor functional capacity; another study has shown that CS diameter correlates with RA size and pressure of the RA^(23,24). In a study investigating the prognostic value of CTPA parameters in acute PE, it was observed that a dilated CS (>9 mm) carries an additional prognostic value when associated with echocardiographic signs of right heart dysfunction and elevated Tn-I levels⁽²⁵⁾. These findings may hold clinical significance in assessing the severity of PE and aiding in the risk stratification and management of patients in emergency departments and intensive care units. CS diameters in patients with PE were found to be significantly higher both numerically and statistically than those in healthy individuals in our study. In our study, CS diameter exceeding 9.5 mm demonstrated reasonable diagnostic performance for PE. In addition, D-dimer, sPAP, and cardiac Tn were substantially correlated with CS diameter. Because CS reflux and increased coronary venous pressure have previously

been associated with coronary slow flow, it is possible that this explains why cardiac Tn levels rise in some patients without the right ventricular pressure or volume load⁽²⁵⁾.

Moreover, IVC (unlike CS) is the main channel that provides venous rotation to the RA from the lower extremities and internal abdominal organs⁽²⁷⁾. In the non-contrast post-mortem CT study in PE, it was stated that increased IVC may suggest PE. However, the study emphasizes that IVC distension may be a finding that may suggest PE rather than being used as a radiological finding alone⁽²⁸⁾. Considering our study and literature findings, we believe that hemodynamic results, especially in the right heart, may be related to IVC dilatation. Our study concluded that sPAP and IVC diameter were significantly correlated. The increases in both CS and IVC diameters, as seen in the study data, indicate the impact of right ventricular volume elevations on indirect venous structures. When considering the literature reviews and our study results together, the potentially more significant contribution of CS dilation compared with IVC dilation to the increase in the CS/IVC ratio may be attributed to various underlying factors.

RV differs from the left ventricle in several ways. Pulmonary circulation pressures are much lower than systemic circulatory pressures in patients without pulmonary vascular disease. Because RV is formed of a thin layer of myofibrils extending parallel to the long axis of the heart, it will be severely affected by sudden changes in PAP⁽²⁹⁾. In patients with PE, a reduction in RV reserve is likely to affect filling pressures, resulting in a high pressure in the right cardiac cavities and a change in the anatomical structures around them. Our hypothesis is supported by a previous study that used invasive methods to show that higher pressure in the RA was related to CS and IVC diameters⁽³⁰⁾.

In addition to CTPA, the use of bedside transthoracic echocardiography (TTE) (presence of right ventricular strain findings, such as D-sign and McConnell's sign) may help in diagnosis⁽³¹⁾. Although TTE may seem more advantageous than CTPA because it does not contain radiation, alternative findings are needed because the parameters have low sensitivity for PE⁽³²⁾. According to studies in the literature, CTPA has become more often used in cases with suspected PE, whereas diagnostic efficiency has decreased^(33,34). However, the proficiency level of clinicians who choose CTPA is also important for the diagnostic efficiency of CTPA. In addition, according to recent studies, CTPA is used for screening purposes rather than for diagnostic

testing^(35,36). This statement is also supported at the low PE detection rate (range: 6-25%) of CTPAs reported in the literature^(37,38). To make the diagnosis, auxiliary examinations should be considered before opting for advanced imaging examinations, risk of developing cancer due to radiation, and risk of nephropathy in CTPA^(39,40). The CS/IVC ratio had acceptable sensitivity, specificity, and normalized pulse volume values for the diagnosis of PE, according to the data obtained in our study.

In this study, we evaluated the effectiveness of a new algorithm for PE diagnosis using CTPA imaging. Despite the availability of advanced diagnostic and treatment methods, PE remains an important health issue. Death often occurs during the period following the diagnosis. The current guidelines contain no information about the utility of the CS/IVC ratio in patients newly diagnosed with PE, although, as shown in our study, this ratio may be a useful parameter for early diagnosis in acute patients with PE. According to our study results, the CS/IVC ratio may be a useful clinical algorithm for predicting PE patients requiring close follow-up.

Study Limitations

The diameters of the CS and IVC can be easily determined using contrast CT imaging. Patients with poor image quality were eliminated from the study, and measurements were taken with patients during the inspiration phase. The respiratory phase may affect the diameters of the CS and IVC. Although it is anticipated that the use of electrocardiography may help obtain optimal diameter measurements, the current guidelines exclude any information about the use of electrocardiogram (ECG) in CTPA in patients with PE. The use of ECG-assisted procedures in cases such as PE, which require emergency diagnosis and treatment, remains controversial due to the risk of patients being exposed to more radiation. Although our aim is to evaluate these patients using a routine practical approach, new prospective studies are needed to address these shortcomings.

Conclusion

We demonstrated that the CS/IVC ratio on CTPA imaging was predictive of PE in patients diagnosed with acute PE for the first time. Although CTPA is commonly used in many patients who have been prediagnosed with PE, PE is only diagnosed in some cases. According to the results of our study, the CS/IVC ratio is understood to be a strong predictor of worse clinical outcomes in PE. Our novel findings may provide physicians

with useful information on worse clinical outcomes in the diagnosis of PE, and they may also serve as a guide for future studies, including CS/IVC measures using various diagnostic tools.

Ethics

Ethics Committee Approval: This study received Çanakkale Onsekiz Mart University's Ethical Committee approval (decision no: 2011-KAEK-27/2021-2100135640) and was conducted in accordance with the Declaration of Helsinki.

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: U.K., E.A., A.K., Concept: U.K., E.A., A.K., Design: U.K., E.A., A.K., Data Collection or Processing: U.K., E.A., A.K., Analysis or Interpretation: U.K., E.A., A.K., Literature Search: U.K., E.A., A.K., Writing: U.K., E.A., A.K.

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