Correlation of Computerized Tomography Angiographic Pulmonary Artery Obstruction Score with Hematologic Outcome and Mortality in Patients with Acute Pulmonary Embolism

Akut Pulmoner Emboli Hastalarında Pulmoner Arter Bilgisayarlı Tomografi Anjiyografi Obstrüksiyon Skorunun Hematolojik Bulgular ve Mortalite ile Korelasyonu

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ABSTRACT Objective: The aim of this study was to determine the relationship between the computed tomography obstruction score and radiological parameters, biochemical parameters, and mortality. **Material and Methods:** During an 8-month period (January 2011-August 2011), 326 patients with clinically suspected pulmonary embolism (PE) were examined by computerized tomography pulmonary angiography (CTPA). Of these patients, only 95 (49 men and 46 women) were diagnosed with PE. Computerized tomography images were retrieved from the picture archiving and communication system (PACS) for the determination of right ventricle/left ventricle (RV/LV) short-axis ratio, maximum diameter of the pulmonary artery, and vascular obstruction score according to Qanadli method. We investigated the correlation between continuous values of the Qanadli scoring system and mortality, and determined whether there was a significant difference between mortality and CTPA parameters. The values derived from the morphologic changes in the CTPA, hematological findings and gender where then assessed with respect to their impacts on mortality. **Results:** There was a significant correlation between the PE obstruction score and RV/LV short-axis ratio ($r=0.58$, $p<0.001$), RV/LV short-axis ratio, and neutrophil to lymphocyte ratio (NLR) ($r=0.21$, $p=0.035$). Survivors and non-survivors had a statistically significant difference in the NLR and mid–platelet volume (MPV) ($p<0.05$). The mortality incidence in patients with an increased MPV (odds ratio 1.689; 95% confidence interval (CI) 1.06-2.67; $p=0.025$) and older female patients (odds ratio 3.732; 95% CI 1.02-13.65; $p=0.04$) was higher. **Conclusion:** Our results suggest that in patients with acute PE, NLR and MPV may be of value for the estimation of mortality.

Key Words: Pulmonary embolism; multidetector computed tomography

ÖZET Amaç: Bu çalışmanın amacı, bilgisayarlı tomografi obstrüksiyon skoru ile radyolojik, biyokimyasal parametreler ve mortalite arasındaki ilişkiyi belirlemektir. **Gereç ve Yöntemler:** Sekiz aylık periyotta (Ocak 2011-Ağustos 2011), klinik olarak pulmoner emboli kuşkulu 326 hasta bilgisayarlı tomografi pulmoner anjiyografi (BTPA) ile incelendi. Bunların sadece 95'i (49 erkek, 46 kadın) pulmoner emboli tanısı aldı. Bilgisayarlı tomografi imajları sağ ventrikül/sol ventrikül kısa aks oranlarını, pulmoner arter maksimum çapını ve Qanadli obstrüksiyon skorunu saptamak için görüntü saklama ve iletişim sisteminden çağrıldı. Qanadli obstrüksiyon skoru ile mortalite arasındaki ilişki incelendi. Mortalite ve bilgisayarlı tomografi pulmoner anjiyografi parametreleri arasında anlamlı farklılık olup olmadığı araştırıldı. Bilgisayarlı tomografi pulmoner anjiyografideki morfolojik değişikliklerden elde edilen değerler, hematolojik bulgular, cinsiyet ve bunların mortalite üzerindeki etkileri değerlendirildi. **Bulgular:** Pulmoner emboli obstrüksiyon skoru ile sağ ventrikül/sol ventrikül kısa aks oranları arasında ($r=0,58$, $p<0,001$) ve sağ ventrikül/sol ventrikül kısa aks oranları ile nötrofil-lenfosit oranı arasında anlamlı korelasyon vardı ($r=0,21$, $p=0,035$). Sağkalım ve mortalite oranları karşılaştırıldığında, mortalite ile nötrofil-lenfosit oranı ve ortalama trombosit hacmi arasında anlamlı ilişki saptandı ($p<0,05$). Mortalite sıklığı, ortalama trombosit hacmi artmış hastalarda (tahmini rölatif risk 1,689; %95 güven aralığı 1,06-2,67; $p=0,025$) ve ileri yaş kadınlarda (tahmini rölatif risk 3,732; %95 güven aralığı 1,02-13,65; $p=0,04$) daha yüksekti. **Sonuç:** Sonuçlarımız akut pulmoner emboli hastalarında nötrofil-lenfosit oranı ve ortalama trombosit hacmi değerlerinin mortaliteyi öngörmede faydalı olabileceğini öngörmektedir.

Anahtar Kelimeler: Pulmoner emboli; çok tarayıcılı bilgisayarlı tomografi

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Despite modern methods for diagnosis and treatment, pulmonary embolism (PE) continues to have a high mortality rate at 3 months.[1] Clinically, PE ranges from anatomically small and clinically asymptomatic emboli to massive proximal emboli with cardiogenic shock.[2,3] Since early treatment is vital, immediate and correct diagnosis is important.[4] Helical computed tomography (CT) of the pulmonary arteries has become the first-line technique for the detection of emboli in the large and segmental vessels.[3,5,6] The European Society of Cardiology recently included computed tomography pulmonary angiography (CTPA) as the reference standard modality to be used following initial clinical evaluation.[7] PE is diagnosed by demonstrating a filling defect in the pulmonary arteries. The extent of PE is commonly expressed by indicating the anatomic level of the most proximal vessel affected by a clot.[8]

Assessment of the severity of PE plays an important role in determining the management method. Massive PE is described as an obstruction of 50% or more of the pulmonary vascular bed.[9] To assess the severity of PE, a CTPA obstruction index has been proposed that has been formulated by adapting the Qanadli score used for conventional pulmonary angiography.[10] The Qanadli score is related to clinical data, and more specifically to the clinical outcome.[11] The aim of this study was to determine the relationship of CT obstruction score with mortality as well as radiological and biochemical parameters, and to analyze the CTPA findings reflecting PE severity.

MATERIAL AND METHODS

STUDY POPULATION

During an 8-month period (January 2011-August 2011), 326 patients with clinically suspected PE were subjected to CTPA were examined retrospectively. Of these, only 95 patients (49 men and 46 women) were diagnosed with PE. The mean age of the population was 61±17 years (range 15-91), and all were in stable a hemodynamic condition. Underlying cardiopulmonary disease was excluded in all patients. Patients' clinical records were reviewed for mid–platelet volume (MPV), neutrophil to lymphocyte ratio (NLR) and mortality numbers. All patients except one were treated with 5,000 IU of intravenously administered heparin sodium followed by continuous infusion via infusion pump or syringe pump at a dose sufficient to produce a 1.5 to 2.5-fold increase in activated partial prothrombin time compared to normal values. On the day of admission, oral anticoagulation therapy with 5 mg warfarin was initiated to maintain the International Normalized Ratio values between 2 and 3.

CT SCANNING PROTOCOL

All patients were examined with a 64-multidetector CT scanner (Siemens Somatom Sensation 64, Erlangen, Germany) with the following scanning parameters: 0.6 mm collimation, 1.5 mm slice thickness, 1.4 mm increment, 100 kV and 135 mAs, a pitch of 0.9, and a gantry rotation time of 0.33 s. A scout image was acquired while the patient was in the supine position, and the area from the aortic arch level to the diaphragm was identified as the field of examination. All patients were given in 100 ml non-ionic contrast medium (Ultravist 300; Bayer Schering Pharma, Berlin, Germany) through a catheter inserted in the right antecubital vein, at a flow rate of 5 mm/s using an automated injector. The scan was executed 20 s after the start of the injection.

The CT images were retrieved from the picture archiving and communication system (PACS) for diagnosis and determination of the most proximal level of the clot. The RV/LV short-axis ratio was obtained by calculating the ratio between the diameters of the RV and LV short axis in the axial plane (Figure 1). The maximum diameter of the common trunk of the pulmonary artery in the axial plane was identified (Figure 2). The Qanadli obstruction score (0-100%) was defined by the number of obstructed segmental arteries and corrected on the basis of the estimated degree of occlusion of each vessel (1=partial obstruction; 2=complete obstruction). An obstruction >50% was defined as a massive embolism.

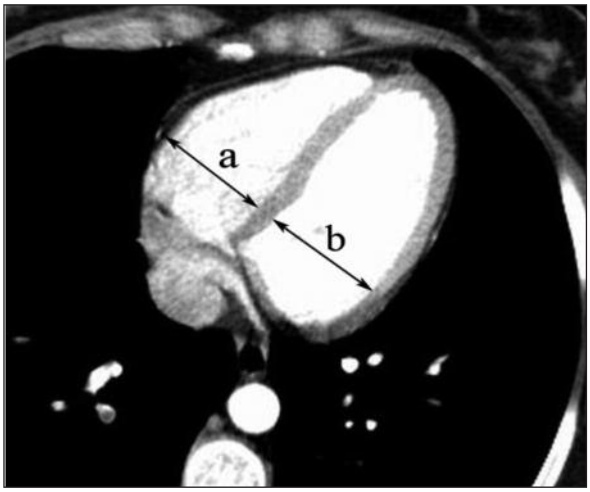

FIGURE 1: Right-to-left ventricular ratio (a/b) was calculated on an axial computerized tomography image.

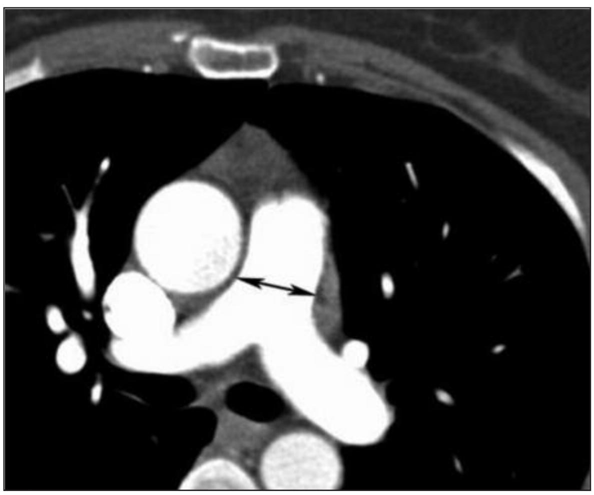

FIGURE 2: The diameter of the common trunk of the pulmonary artery was measured on an axial computerized tomography image.

STATISTICAL ANALYSIS

The statistical analysis was performed using SPSS software package version 16.0 (SPSS Inc, Chicago, IL, USA). A correlation coefficient was used to investigate the correlations between continuous values of the Qanadli scoring system and the clinical parameters. The variables were investigated using visual and analytical methods (Kolmogorov-Simirnov/Shapiro-Wilk's test) to determine if they were normally distributed. Correlation coefficients and significance values were calculated for the association between non-normally distributed and/or ordinal variables by using the Spearman test. Qualitative and quantitative values derived from the morphologic changes in the CTPA as well as gender and their impacts on mortality were assessed using logistic regression analysis. Hosmer-Lemeshow goodness of fit statistics was used to assess model fit. A 5% type-1 error level was used to infer statistical significance (p=0.73). Chi-square tests were used to assess the significance of the association between outcome and clinical parameters. The Mann-Whitney U test was used to determine a significant difference between mortality and CTPA parameters; a p- value of <0.05 was considered to show a statistically significantly result.

RESULTS

The study group included 95 patients with PE diagnosed by unequivocally positive CTPA findings. There was a significant correlation between the PE obstruction score and RV/LV short-axis ratio (r=0.58, p<0.001) (Figure 3), and RV/LV short-axis ratio and NLR (r=0.21, p=0.035). Fifteen of the patients died in a month. Their obstruction scores ranged from 7.5% to 92.5% (Figure 4), their pulmonary artery axial diameter ranged from 23.14 mm to 40.19 mm, their RV/LV short-axis ratio ranged from 0.8 to 2.1, their NLR ranged from 3.11 to 21.77, and their MPV ranged from 5.3 to 10.

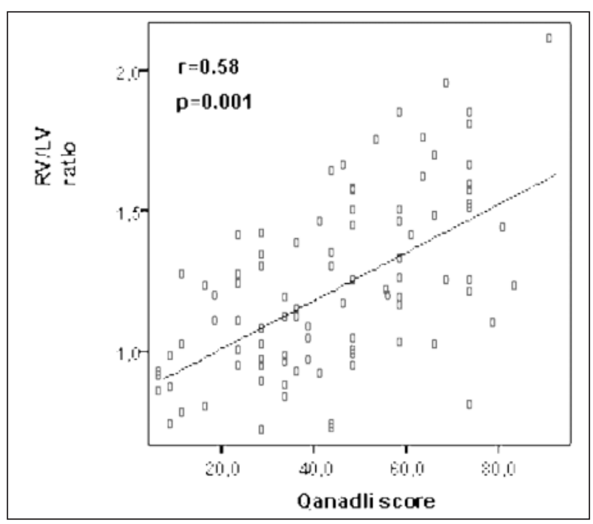

FIGURE 3: Scatter diagrams show a positive correlation between the Qanadli pulmonary artery obstruction index and right ventricle/left ventricle short-axis ratio.

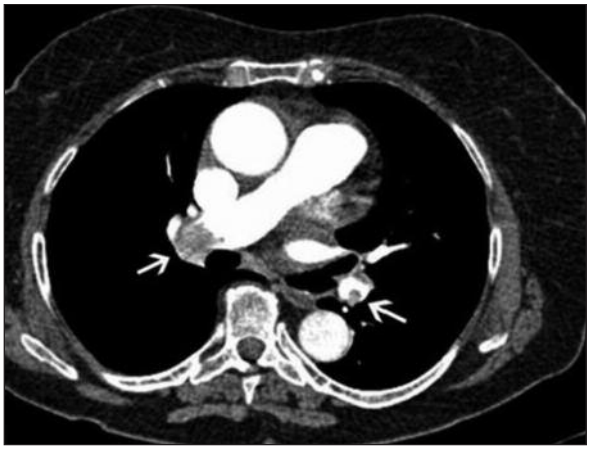

FIGURE4: A 50-year-old female patient with bilateral pulmonary embolism. Total occlusive embolus in the right main pulmonary artery (arrow) and partial occlusive embolus in the left inferior lobar artery (arrow) was seen on pulmonary CT angiography. The pulmonary artery obstruction index (Qanadli method) was calculated as 62.5%.

When survivors and non-survivors were compared, there was a statistically significant difference in the NLR and MPV between the two groups (p=0.014 and p=0.048, respectively) (Table 1). However, the logistic regression model indicated female gender and MPV as significant predictors for mortality (Table 2). The mortality incidence was higher in patients with an increased MPV (odds ratio 1.689; 95% confidence interval (CI) 1.06-2.67; p=0.025) and female patients (odds ratio 3.732; 95% CI 1.02-13.65; p=0.04). No correlation was found between maximum diameter of the pulmonary artery and other parameters.

DISCUSSION

The aim of this study was to determine the relationship of CT obstruction score with radiological parameters, biochemical parameters, and mortality, and to analyze the CTPA findings. Our results suggested that in patients with acute PE, there was a statistically significant difference in the NLR and MPV between survivors and non-survivors. We found a significant correlation between the PE obstruction score and RV/LV short-axis ratio. The logistic regression model indicated female gender and MPV as significant predictors for mortality.

NLR, obtained from a universally available low-cost complete blood count test, has been widely used as a marker of systemic inflammation as well as an indicator to predict cardiovascular outcome.[12-14] However, the prognostic value of NLR in PE patients is still unknown. The findings of our study have indicated for the first time that the NLR is an independent predictor of cardiovascular mortality in PE patients. Patients with a higher NLR showed increased cardiovascular mortality rates compared with patients with a lower NLR. An et al. found that the NLR was an independent predictor of all causes of mortality as well as cardiovascular mortality in peritoneal dialysis patients, and patients with a higher NLR showed significantly increased overall and cardiovascular mortality rates compared to patients with lower NLR.[15] We found a significant correlation between the RV/LV short-axis ratio and NLR in our study.

The MPV is considered as a marker and determinant of platelet function since larger platelets are hemostatically more reactive than platelets of normal size. Increased MPV, a simple marker of platelet activation, was found to predict a fatal outcome.[16,17] Platelet activation has an important role in atherothrombosis and has been reported in ve-

TABLE 1: Significance differences between mortality and computerized tomography pulmonary angiography-biochemical parameters.

	Median	Minimum	Maximum	p value
Qanadli score	45	7.5	92.5	0.170
RV/LV ratio	1.2	0.7	2.1	0.720
PA axial diameter	30.68	21.72	40.19	0.929
NLR	5.22	0.94	61.37	**0.014**
MPV	7.11	4.7	10.7	**0.048**

RV/LV ratio: Right ventricle/left ventricle short-axis diameter ratio; PA: Pulmonary artery; NLR: Neutrophil to lymphocyte ratio; MPV: Mid-platelet volume.

TABLE 2: The logistic regression model indicated female gender and MPV as a significant predictors for mortality.

Risk factor	Odds ratio	p value
Qanadli score		0.126
RV/LV ratio		0.217
PA axial diameter		0.585
NLR		0.408
MPV	1.689	**0.025**
Ref:female	3.732	**0.047**

RV/LV ratio: Right ventricle/left ventricle short-axis diameter ratio; PA: Pulmonary artery; NLR: Neutrophil to lymphocyte ratio; MPV: Mid-platelet volume.

nous thromboembolism.[18,19] Our results suggest that MPV values are significantly related to acute PE. MPV was found to be a significant predictor of mortality, and was elevated in patients with acute PE. Kostrubiec et al. found a correlation between mortality and MPV in acute PE, but MPV was not elevated in patients with acute PE; however, Varol et al. found a correlation between MPV and PE.[20,21] The scoring systems suggested by Qanadli et al. allow quantitative and qualitative evaluation of pulmonary artery occlusions.[10] Our results show a highly significant association between the Qanadli score and RV/LV ratio, which is supported by other reports of a strong positive correlation between the mean obstruction score (calculated with the Qanadli method) and mean RV/LV ratio, a significant correlation between the Qanadli obstruction score and RV/LV ratio, and a correlation between RV/LV ratio and mortality.[22-25] Our results do not confirm those of Araoz et al. who reported no correlation between RV/LV ratio and mortality rate.[24] In 108 consecutive patients, Ozsu et al. showed the correlation of biomarkers and right/left ventricular dimension ratio ≥1.1 on CTPA with mortality.[26]

Several limitations in our study warrant consideration. First, its retrospective design prevented us from producing correlations with findings of other diagnostic clinical parameters. Second, we did not classify patients into subgroups according to proximal level of the PE. Third, we did not correlate Qanadli score with the other scoring methods.

In conclusion, our results suggest that NLR and MPV may be of value for the estimation of mortality in patients with acute PE.

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