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Predictive role of pretest probability scores and risk factors of contrast-induced acute kidney injury in patients who underwent CT pulmonary angiography for the suspicion of pulmonary embolism

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Abstract:

BACKGROUND AND AIM: The use of computed tomographic pulmonary angiogram (CTPA) without determining pretest probability leads to overuse and morbidities as contrast-induced acute kidney injury (CI-AKI). We aimed to assess the predictive role of Wells' rule and revised Geneva scores together with the D-dimer test in patients who underwent CTPA for the suspicion of pulmonary embolism (PE) and to investigate the frequency of CI-AKI.

METHODS: This single-center study was conducted as a retrospective analysis of patients who underwent CTPA. Demographic and clinical variables, risk factors, pretest probability score (PPS), and biomarkers were recorded from written or electronic medical records.

RESULTS: A total of 1259 CTPA scans performed for suspicion of acute PE were screened. After exclusion, we analyzed 895 CTPAs. PE rates in the emergency department and in-patient wards were 9.1% and 13.9%, respectively. Immobility, high Wells' rule, and Geneva scores were found to be predictors of PE. The [OR (95% CI)] were [12.92 (4.38–38.14)], $p < 0.001$; [7.55 (1.96–28.61)], $p < 0.001$; and [1.25 (1.07–1.39)], $p = 0.003$, respectively. The diagnostic sensitivity of Wells' rule and Geneva score for PE was 24.6% and 68.1%, respectively, while the diagnostic specificity for PE was 91.4% and 42.7% for Wells' rule and revised Geneva score, respectively. CI-AKI was detected in 99 (20.7%) of 479 patients, and the history of myocardial infarction within 3 months was the only predictor of CI-AKI [OR (95% CI)] [6.30 (1.46–27.90)], $p = 0.014$.

CONCLUSIONS: D-dimer test and usage of PPS for patients considered PE may reduce overuse of CTPA and thereby CI-AKI prevalence.

Keywords:

Acute kidney injury, computed tomography, D-dimer, Geneva score, pulmonary embolism, Wells' rule

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Introduction

Pulmonary embolism (PE) is one of the leading causes of cardiovascular death.^[1] Because PE presents with nonspecific signs and symptoms and a wide range of clinical spectrum from asymptomatic presentation to shock, it is difficult to diagnose or rule out PE by signs and symptoms alone.^[1] In response to this concern, diagnostic algorithms combining pretest probability scores (PPSs) and D-dimer test have been developed. Diagnosis of PE can be safely excluded with the combination of low clinical PPS and D-dimer negativity. In cases with high clinical pretest probability or those with low pretest probability with positive D-dimer, diagnostic imaging is needed.^[2] According to guidelines, computed tomographic pulmonary angiogram (CTPA) is recommended as the first choice imaging method for the diagnosis of PE.^[3,4] However, the use of CTPA without determining pretest probability does not only lead to overuse of the test but also increase in financial costs, length of stay, lifelong radiation-related cancer risk, risk of contrast-induced acute kidney injury (CI-AKI), and anaphylaxis.^[5-9] Although there is no exact definition of the overuse of CTPA in guidelines, a diagnostic yield of CTPA less than 10% has been suggested as overuse of CTPA.^[10,11] Easy availability and low invasiveness of CTPA are the other factors for the overuse of this test.^[12] Implementation of PPSs before CTPA order is strongly recommended in recent guidelines and by expert opinions.^[2-4] The most valid PPSs are Wells' rule and the revised Geneva score.^[13] Overuse of CTPA might lead to increased CI-AKI, which has been reported to be at least in 10% of patients, and is associated with increased risk of severe outcomes including severe renal failure and death, observed in 16% of patients who developed CI-AKI after CTPA.^[9]

In this study, we aimed to assess the predictive role of Wells' rule and revised Geneva score together with the D-dimer test in patients who underwent CTPA for the suspicion of PE. We also aimed to investigate the frequency and risk factors of CI-AKI.

Materials and Methods

Study design and patients

In this study, we conducted a retrospective analysis of all consecutive patients who underwent CTPA for a 12-month period from May 15, 2015, to May 15, 2016,

in Hacettepe University Faculty of Medicine, Adult Hospital. The CTPAs performed in the adult emergency department (ED) or in in-patient wards including intensive care units (ICUs) were eligible for the study. The exclusion criteria were age below 18 years, CTPAs ordered from outpatient areas, CTPAs with indeterminate results or suboptimal quality and repeated CTPAs for follow-up, and CTPAs interpreted as chronic PE or as PEs due to air, fat or tumor rather than thromboembolism. Demographic and clinical variables including age, gender, place of admission, symptoms and signs, risk factors [malignancy, major surgery within 3 months, chronic heart failure (CHF), chronic obstructive pulmonary disease (COPD), estrogen use or postpartum state, previous cardiovascular disease (CVD), immobility, previous deep venous thrombosis (DVT) or PE, travel, myocardial infarction within 3 months and lower limb fracture], PPS (Wells' rule, revised Geneva score), biomarkers, echocardiographic findings, type of surgical procedure, and malignancy, as well as drugs known to be nephrotoxic [angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), diuretics, nonsteroidal anti-inflammatory drugs (NSAIDs), acyclovir and cisplatin], were recorded from written or electronic medical records. The study was approved by the local ethics committee of Hacettepe University Faculty of Medicine (no: GO 16/399-22).

PPSs, D-dimer, troponin, and B-type natriuretic peptide

As PPSs, we used two-level Wells' rule and revised Geneva score to evaluate the pretest clinical probability of PE. Patients were categorized as "PE likely" or "PE unlikely" groups according to their PPS (Table 1). The D-dimer threshold level for negativity was 500 ng/mL. We used an age-adjusted D-dimer cutoff value ($\text{age} \times 10 \text{ ng/mL}$) for patients above 50 years of age. Higher reference limits for serum high sensitive cardiac troponin I levels and B-type natriuretic peptide (BNP) were 0.02 ng/mL and 100 pg/mL, respectively.

Imaging protocol for PE

Patients in this study underwent CTPA using a 64-row multidetector scanner (SOMATOM Definition, 140 kV, Siemens Healthcare GmbH, Erlangen, Germany). In the vast majority of cases, CT venography (CTV) was added to CTPA for the evaluation of lower extremity veins for diagnosing DVT.

Table 1: Comparison of demographic and clinical variables between patients with PE and No PE

Variables	All patients (n=895)	PE (n=92)	No PE (n=803)	p
Age, median (IQR)	63 (48–74)	62 (50–74)	63 (47–74)	0.740
Male gender, n (%)	406 (45.9)	36 (39.1)	370 (46.1)	0.205
Place of admission, n (%)				0.122
Emergency department	680 (76.0)	62 (67.4)	618 (77.0)	
Medical wards	101 (11.3)	12 (13.0)	89 (11.1)	
Surgical wards	78 (8.7)	11 (12.0)	67 (8.3)	
ICUs	36 (4.0)	7 (7.6)	29 (3.6)	
Symptoms and signs, n (%)				
Dyspnea	590 (65.9)	67 (72.8)	523 (65.1)	0.140
PaCO ₂ <35 mmHg; n=707	400 (56.6)	53 (69.7)	347 (55.0)	0.014
HR ≥100 bpm; n=524	257 (49.0)	31 (45.6)	226 (49.6)	0.541
Chest pain	275 (30.7)	30 (32.6)	245 (30.5)	0.679
Cough	163 (18.2)	17 (18.5)	146 (18.7)	0.964
Unilateral swollen leg	87 (9.7)	14 (15.2)	73 (9.1)	0.060
Altered mental status	46 (5.1)	3 (3.3)	43 (5.4)	0.389
Hemoptysis	38 (4.2)	4 (4.3)	34 (4.2)	0.959
MAP <65 mmHg; n=490	31 (6.3)	5 (7.1)	26 (6.2)	0.762
Syncope	20 (2.2)	5 (5.4)	15 (1.9)	0.028
Risk factors, n (%)				
Malignancy	292 (32.6)	39 (42.4)	253 (31.5)	0.035
Major surgery within 3 months	123 (13.7)	33 (35.9)	90 (11.2)	<0.001
CHF	118 (13.2)	10 (10.9)	108 (13.4)	0.488
COPD	106 (11.8)	73 (5.4)	99 (12.3)	0.184
Estrogen use/postpartum n=489	56 (11.5)	40 (7.6)	16 (3.7)	0.545
Previous CVD	81 (9.1)	15 (16.3)	73 (9.1)	0.028
Immobility	69 (7.7)	19 (20.7)	50 (6.2)	<0.001
Previous DVT or PE	30 (3.4)	3 (3.3)	27 (3.4)	0.959
Travel within 3 months	21 (2.3)	1 (1.1)	20 (2.5)	0.400
MI within 3 months	11 (1.2)	3 (3.3)	8 (1.0)	0.062
Lower limb fracture	9 (1.0)	3 (3.3)	6 (0.7)	0.022

Statistically significant p values are represented in bold. PE: Pulmonary embolism, IQR: Interquartile range, ICUs: Intensive care units, HR: Heart rate, bpm: Beats per minute, MAP: Mean arterial pressure, CHF: Chronic heart failure, COPD: Chronic obstructive pulmonary disease, CVD: Cardiovascular disease, DVT: Deep venous thrombosis, MI: Myocardial infarction

Assessment of PE severity

Patients were classified on the basis of early mortality risk. Patients presenting with shock or hypotension were at high risk; the remaining hemodynamically stable patients were at intermediate risk or low risk according to the simplified pulmonary emboli severity index (sPESI) score and cardiac damage indicators. Echocardiographic findings and cardiac biomarkers were used to determine cardiac impairment as such, right ventricular (RV) dilatation (RV >26 mm) or RV/LV (left ventricular) ratio for echocardiographic evidence; and elevated cardiac biomarkers for laboratory evidence (troponin level >0.02 ng/mL or BNP >100 pg/mL). The intermediate-risk group was also stratified as intermediate high and intermediate low in itself according to the degree of cardiac dysfunction. Accordingly, all patients were divided into 4 groups as follows:

1. PESI 1: High risk–patients with hypotension or shock at admission;
2. PESI 2: Intermediate high risk–patients with sPESI ≥1 and with evidence of cardiac impairment identified by both echocardiography and laboratory;
3. PESI 3: Intermediate low risk–patients with sPESI ≥1 and with either one or no evidence of cardiac impairment, or patients with sPESI of 0 and any evidence of cardiac impairment;
4. PESI 4: Low risk; patients with sPESI of 0 and with no evidence of cardiac impairment.^[4]

Assessment of CI-AKI

Pretest and posttest creatinine levels, if available, were recorded for the detection of CI-AKI. As defined in KDIGO (Kidney Disease: Improving Global Outcomes) guidelines, an increase in creatinine by 0.5 mg/dL or a 25% increase from baseline value, assessed at 48 h to 5

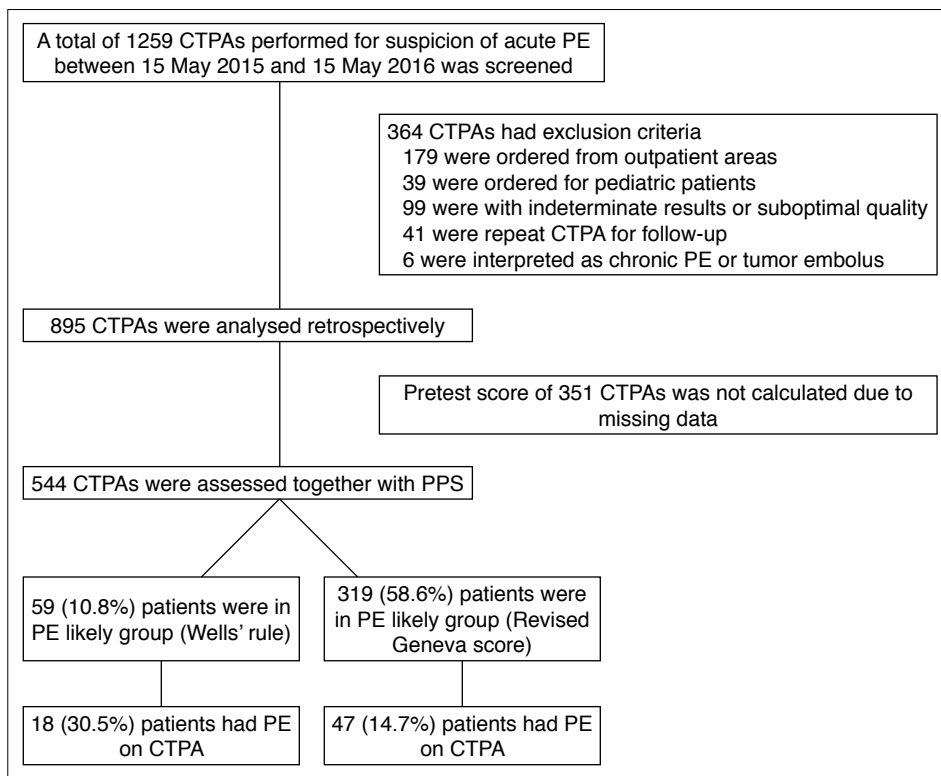


Figure 1: Flow chart of the study. After excluding 364 CTPAs, 895 CTPAs were analyzed, which were performed consecutively during a 1-year period for suspicion of acute PE in an adult university hospital. Due to missing data, 544 of these CTPAs were evaluated in combination with PPS. Of these PPSs, 10.8% of patients were matched with PE likely in Wells' rule but 30.5% of them had PE on CTPA, on the other hand, 58.6% of patients were matched with PE in the revised Geneva score but 14.7% of them had PE on CTPA

CTPA: Computed tomographic pulmonary angiogram, PE: Pulmonary embolism, PPS: pretest probability score

days after a radiological procedure was considered as CI-AKI.^[14] Nephrotoxic drugs such as ACEIs, ARBs, diuretics, NSAIDs, acyclovir, and cisplatin were recorded for CI-AKI evaluation. Patients with chronic kidney disease, whether or not on hemodialysis, were not included.

Statistical analysis

Continuous variables were presented as median and interquartile range (IQR) due to non-normal distribution, whereas categorical variables were presented as frequencies and percentages. Nonparametric Mann-Whitney U test was used to compare the continuous variables, and X² and Fisher's exact test were used to compare categorical variables. The Wilcoxon test was used to compare the change in creatinine levels between pre- and postexposure to contrast. Logistic regression analysis was used in multivariate analysis. In constructing the model, all factors found to be associated with PE in binary analysis were included. Final models were obtained using "Enter" command, to construct the most explanatory model for study-

ing the association between the pre-test score and PE. (Wells' rule or revised Geneva score were included in the model separately.) The predictive role of Wells' rule and revised Geneva score in predicting the diagnosis of PE were analyzed using receiver operating characteristics (ROC) curve analysis. Statistical analyses were performed with SPSS 23.0 (Chicago, IL) software. A p-value of less than 0.05 was considered to indicate a statistically significant result.

Results

We screened a total of 1259 consecutive CTPA scans performed for suspicion of acute PE during the period of 12 months. After the exclusion of 364 CTPAs, we analyzed 895 CTPAs retrospectively [Fig. 1]. CTPA examination was performed for 680 cases (76.0%) in the ED, 101 cases (%11.3) in the medical wards, 78 cases (8.7%) in the surgical wards, and 36 cases (4.0%) in ICUs. Of all patients, 92 (10.3%) had PE diagnosed by CTPA. PE rates in ED and in-patient wards including ICUs were 9.1% and

Table 2: Comparison of scores and laboratory and echocardiographic findings between patients with PE and No PE and sPESI of PE patients

Variables	All patients (n=895)	PE (n=92)	No PE (n=803)	p
Scores, median (IQR)				
Wells' rule, n=544	1.5 (1.0–2.5)	2.5 (1.5–4.25)	1.5 (1.0–2.5)	<0.001
Revised Geneva, n=544	6 (5–7)	7 (5–8)	6 (4–7)	0.001
Biomarkers, n (%)				
D-dimer; n=268*				
<500 ng/mL	19 (7.1)	0 (0)	19 (8)	0.142
<Age adjusted cutoff value	27 (10.1)	0 (0)	27 (11.4)	0.053
Troponin I, n=721				0.002
<0.04 ng/mL	516 (71.6)	42 (55.3)	474 (73.5)	
>0.04 ng/mL	205 (28.4)	34 (44.1)	171 (26.5)	
BNP, n=517				0.058
<100 pg/mL	228 (44.1)	35 (56.5)	193 (42.5)	
≥100 pg/mL	289 (55.8)	28 (44.4)	261 (57.5)	
Cardiac impairment in echocardiography, n=175	140 (80.0)	32 (84.2)	108 (78.8)	0.463

Statistically significant p values are represented in bold. *We used an age-adjusted D-dimer cutoff value ($\text{age} \times 10 \text{ ng/mL}$) for patients more than 50 years, PE: Pulmonary embolism, sPESI: simplified pulmonary emboli severity index, IQR: Interquartile range, BNP: Brain natriuretic peptide

13.9%, respectively. In evaluating PE severity, we found only 5.4% of PE patients had high mortality risk (PESI 1). Eighteen (19.6%) patients had intermediate high risk (PESI 2), 49 (53.3%) patients had intermediate low risk (PESI 3), and 20 (21.7%) patients had low risk (PESI 4).

Comparison of demographic and clinical variables between PE and no PE are shown in Table 1. The most common presenting symptoms and signs in all patients were dyspnea, hypoxemia, tachycardia, and chest pain. In patients with PE, hypoxemia and syncope were significantly higher than in those with no PE. For risk factors, malignancy, major surgery within 3 months, immobility, CVD, and lower limb fracture were significantly more frequent in patients with PE.

The most common cancer types were gastrointestinal (39%) and central nervous system (CNS) tumors (15.3%). PE was detected most commonly in patients who had abdominopelvic (39.4%) and CNS (21.4%) surgeries. Fourteen percent of patients were found to have received anticoagulant treatment in advance for various reasons other than PE and 35% of the PE patients had concurrent acute DVT in CTPA.

Clinical pretest probability was assessed based on Wells' rule and revised Geneva score in 544 (60.8%) patients. Wells' rule and revised Geneva score were higher in patients with PE (Table 2). According to Wells' rule, 59 (10.8%) patients were in the "PE likely" group, while 319 (58.6%) patients were in the "PE unlikely" group according

to the revised Geneva score. Among patients being considered "PE likely" according to the revised Geneva score, 14.7% had PE in CTPA, while this ratio was 30.5% according to Wells' rule [Fig. 1]. The proportion of patients with PE in the PE unlikely group was 10.7% and 9.8% for Wells' rule and revised Geneva score, respectively.

D-dimer was ordered in 268 (30%) patients (Table 2). The frequency of D-dimer testing, which was requested for PE unlikely patients, was 27% (130/485) and 38% (85/225) for Wells' rule and revised Geneva score, respectively.

While high troponin level was observed more in patients with PE compared with the non-PE group ($p=0.002$), there was no difference in BNP levels and echocardiographic findings between groups ($p=0.058$ and $p=0.463$, respectively) (Table 2).

In multivariate analysis, we included the factors found to be associated with PE in binary analysis in contracting model, but we put Wells' rule and revised Geneva score separately to the model because of their high correlation (correlation coefficient=0.70). Immobility, high Wells' rule, and Geneva scores were found to be predictors of PE. The [OR (95% CI)] was [12.92 (4.38–38.14)], $p<0.001$ for immobilization; [7.55 (1.96–28.61)], $p<0.001$ for Wells' rule; and [1.25 (1.07–1.39)], $p=0.003$ for Geneva score.

The sensitivities of Wells' rule and Geneva score for diagnosis of PE were 24.6% and 68.1%, respectively, whereas the specificities of Wells' rule and revised Geneva score

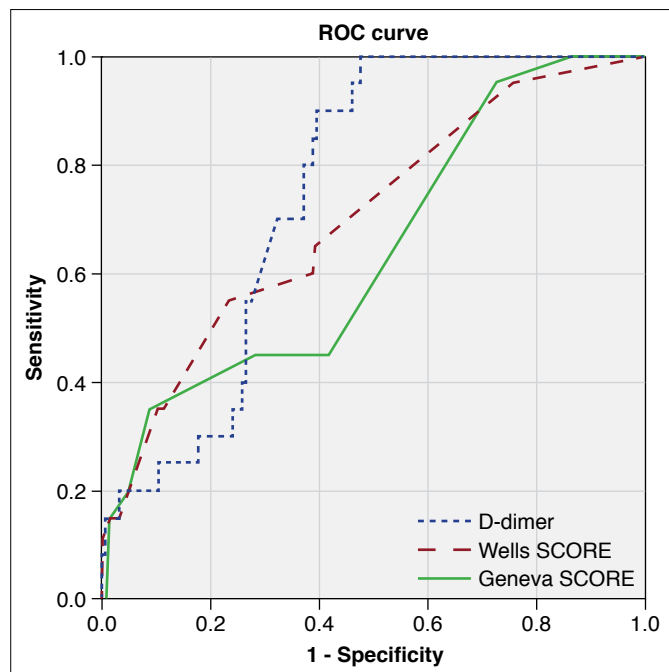


Figure 2: Area under curve (AUC) and p-values for age-adjusted D-dimer, Wells' rule, and Geneva score (AUC=0.751, $p=0.04$; AUC=0.699, $p=0.06$; and AUC=0.643, $p=0.07$, respectively). The sensitivities and specificities of Wells' rule and revised Geneva score for diagnosis of PE were 24.6% and 68.1% and 91.4% and 42.7%, respectively. When combined with age-adjusted D-dimer, sensitivities of Wells' rule and revised Geneva score were 100%. Specificities were 63.2% for Wells' rule and D-dimer and 16.4% for revised Geneva score and D-dimer

were 91.4% and 42.7%, respectively. When combined with age-adjusted D-dimer, sensitivities of Wells' rule and revised Geneva score were 100%. Specificities were 63.2% for Wells' rule and D-dimer and 16.4% for the revised Geneva score and D-dimer. Diagnostic accuracies of Wells' rule and revised Geneva score as determined by the area under the ROC curves (AUC) were significant [0.69 (95% CI, 0.56–0.71, $p=0.06$) and 0.64 (95% CI, 0.55–0.70, $p=0.07$), respectively] [Fig. 2].

CI-AKI was detected in 99 (20.7%) of 479 patients in whom pre- and posttest creatinine levels are known. The median increase of serum creatinine level from the basal value was (IQR) 42.5% (32–65), $p<0.001$. Comparison of potential risk factors in patients with CI-AKI and without CI-AKI are listed in Table 3. History of MI within 3 months is the only predictor of CI-AKI [OR (95% CI)] [6.30 (1.46–27.90)].

Discussion

Findings of a retrospective cohort of patients who underwent CTPA over a period of 12 months for PE were used to assess the role of Wells' rule and Geneva scores in

predicting PE. The incidence of CI-AKI in patients who underwent CTPA was also calculated. In this study, we found the frequency of PE as 10.3%. Our result (1.3%–31%) was consistent with previous studies.^[11,15–22] The low rate PE obtained is likely to reflect the high number of CTPAs requested unnecessarily on suspicion of PE. Possible reasons for the overuse of CTPA could be its high availability and rapid results for a valid diagnosis of PE. In the study group, the CTPA exam was requested more in ED, while the detection of PE was relatively low.

The data on signs or symptoms at presentation did not discriminate the patients with and without PE in this study similar to the report of EMPEROR study.^[23] Dyspnea, hypocapnia, and tachycardia were the most common signs and symptoms in this study. The frequency of tachycardia and hemoptysis, which are components of PPSs, did not differ between patients with and without PE. Syncope, which is associated with a higher prevalence of hemodynamic instability and RV dysfunction, is common in PE patients and may be valuable in diagnosing but is not included in PPSs.^[24,25]

In this study, malignancy, surgery, immobility, and fracture, which are components of PPS, have been demonstrated to provoke PE. The prevalence of concurrent DVT on CTPA was 35% in this study; however, it was reported as a substantial proportion of symptomatic PE (30%–78%) in recent studies.^[26–30] This discordance may be due to some CTPAs lacking a CTV sequence, which could have underestimated the true prevalence of DVT in our participants.

Appropriate use of pretest clinical tools, including scoring systems and D-dimer, is likely to avoid CTPA overuse in ED, in particular. Since clinical assessment for PE is based on the clinician's own evaluation, PPS should be used for standardizing the PE prediction. Wells' rule and revised Geneva score are the most commonly used PPSs for PE and are sufficiently validated.^[13,31,32] In recent publications, the prevalence of PE among patients considered "PE likely" and "PE unlikely" was similar for both PPSs (around 30% and 15%, respectively).^[33,34] Our results for Wells' PE likely group were consistent with the reported data while for the revised Geneva score, they were not. Possible causes of the inconsistency with the revised Geneva group can be explained as that compared with Wells' rule, the threshold value for tachycardia is lower than in Wells' rule, as well as a

Table 3: Comparison of possible risk factors between patients with AKI and without CI-AKI

Variables	All patients evaluated for AKI (n=479)	Patients with AKI (n=99) (20.7)	Patients without AKI (n=380) (79.3)	p
Age, median (min-max)	66 (18-96)	68 (23-91)	65 (18-96)	0.313
Gender, male	227 (47.4)	49 (49.5)	178 (46.8)	0.638
Malignancy	202 (42.2)	47 (47.5)	155 (40.8)	0.230
DM	109 (22.8)	19 (17.4)	90 (23.6)	0.419
CHF	81 (16.9)	23 (23.2)	58 (15.3)	0.060
MI within 3 months	9 (1.9)	5 (5.1)	4 (1.1)	0.009
Hypotension*	7 (2)	2 (2.7)	5 (1.8)	0.635
Pre-CTPA creatinine	0.73±0.29	0.74±0.41	0.73±0.26	0.306
Post-CTPA creatinine	0.83±0.50	1.19±0.81	0.73±0.23	<0.001
Troponin >0.04 ng/mL	143 (38.8)	29 (38.2)	114 (38.9)	0.905
BNP, n=322				0.031
0–100 pg/mL	133 (41.3)	22 (30.1)	111 (44.6)	
>100 pg/mL	189 (58.7)	51 (69.9)	138 (55.4)	
Use of nephrotoxic drugs	139 (42.2)	30 (49.2)	109 (40.7)	0.225
Place of admission				0.002
Emergency	320 (66.8)	75 (23.4)	245 (76.6)	
Inpatient wards	159 (33.2)	16 (16.8)	112 (29.5)	
ICU	31 (6.5)	8 (8.1)	23 (6.1)	

Statistically significant p values are represented in bold. *Mean arterial pressure <65 mmHg, CI-AKI: Contrast-induced acute kidney injury, DM: Diabetes mellitus; CHF: Chronic heart failure; MI: Myocardial infarction; CTPA: Computed tomographic pulmonary angiogram; BNP: Brain natriuretic peptide, ICU: Intensive care unit

higher contribution to the total score. Unlike Wells' rule, the age factor also has a score. Combining these two parameters, all patients over the age of 65 years with a pulse greater than 95 min⁻¹ are considered PE likely. Due to these two items which facilitate getting a high score, the number of patients matched "PE likely" in the revised Geneva group might be higher than in Wells' rule. Likewise, as in our study, the cumulative number of "PE likely" patients in the revised Geneva group, which is fivefold higher than in Wells' group, might have diluted this ratio. However, in a meta-analysis, rates very close to our results have been reported.^[35]

In a large meta-analysis including 3613 patients, the sensitivity of the PPSs changed from 55% to 79%, and the specificity changed from 49% to 90%.^[32,33] In predicting PE, the revised Geneva score had higher sensitivity (68% vs 24.6%), while Wells' rule had higher specificity (91.4% vs 42.7%). The disproportionate results between these two PPSs may be due to the uneven distribution of the number of "PE likely" patients between the PPS groups [Fig. 1]. Nevertheless, the overall diagnostic performances of both PPSs assessed with ROC analysis were found to be close to each other (0.69 vs 0.64), which was in the range reported by the meta-analysis.^[32] D-dimer test has a high negative predictive value and thereby normal D-dimer level helps to rule out

acute PE.^[4,36] D-dimer testing should be restricted to patients with low probability scores or considered PE unlikely.^[37] However, in this study, it was ordered in 27%–38% of the patients who were considered to have PE unlikely, which shows poor adherence to the diagnostic algorithm. The specificity of D-dimer in suspected PE has been shown to decrease with age.^[35,36,38] Therefore, age-adjusted D-dimer cutoff may be used instead of conventional cutoff in elderly patients. In this study, using age-adjusted D-dimer increased the PE exclusion rate from 7% to 10%. Also, we demonstrated that using age-adjusted D-dimer either alone or in combination with PPS matched "PE unlikely" excluded PE diagnosis with 100% accuracy.

Troponin and BNP are markers of cardiac involvement in PE and are used to stratify the severity of PE.^[4,37] These biomarkers can help diagnosis with a combination of clinical assessment and CT findings. Although they are helpful in determining the prognosis of PE rather than diagnosing or excluding PE, they were ordered more than D-dimer testing. Since these markers are also used in conditions other than PE, the proportion of patients with an alternative diagnosis to PE among the patients referred to CTPA is probably high. In this study, troponin levels were higher in PE patients, but in multivariate analysis, the result was not significant.

There are mixed data on the risk of CI-AKI following CTPA performed for suspicion of PE. Some retrospective observational studies have reported from 12% to 13% incidence of CI-AKI as well as up to 41% in critical patients who underwent CTPA.^[9,39,40] However, lower rates of CI-AKI from 4% to 6.4% have been reported in all patients who underwent any enhanced CT. This difference suggests that the patients suspected of PE are more likely to be at high risk for CI-AKI than the overall patient population.^[41] In this study, CI-AKI prevalence was found to be 20.7%, which was more in emergency room patients (23.4%) than in ward patients (15.1%). It is probably associated with the fact that detailed evaluation and preventive measures could not be taken adequately in urgent conditions. Also, unnecessary CTPA orders might contribute to a higher CI-AKI rate.

In this study, we could not observe the impact of conventional risk factors such as diabetes, hypertension, CHF, advanced age, use of concurrent nephrotoxic medications on the development of CI-AKI.^[42] Apart from the usual risk factors, we analyzed whether the history of MI within 3 months is a risk factor for CI-AKI. History of recent MI was associated with increased risk of CI-AKI in our study despite conflicting data in previous studies.^[42,43] Repeated contrast exposure due to prior percutaneous coronary intervention (PCI) could at least partially explain the increase in risk in these patients. We could not evaluate volume depletion or hemodynamic instability of patients and use of large volume or high osmolality of the contrast agent, which were risk factors for CI-AKI^[42] in our patients. A recent meta-analysis investigating CI-AKI after PCI revealed that high BNP levels were a predictor for CI-AKI.^[43,44] In this study, BNP levels were high in patients with CI-AKI but this result was not significant in multivariate analysis. In contrast to previous studies,^[42-45] concurrent use of nephrotoxic drugs was not found to be related to CI-AKI. We do not know whether these drugs were withheld before the contrast exposure.

The major limitation of this study is its single-center retrospective nature. Due to many missing data, PPS could not be estimated in a substantial number of patients. However, this study is valuable in pointing out inappropriate use of CTPA, less use of PPS, and increased frequency of CI-AKI.

Conclusion

Using age-adjusted D-dimer in combination with PPSs matching "PE unlikely" can exclude PE safely up to

100% sensitivity. Although the number of patients who had undergone CTPA on suspicion of PE in the emergency department was higher than that in the wards, the number of patients with PE was proportionately lower and CI-AKI prevalence was higher. Requesting D-dimer test and usage of PPS for every patient considered PE may reduce overuse of CTPA.

Conflicts of interest

There are no conflicts of interest.

Ethics Committee Approval

The study was approved by the Hacettepe University Non-interventional Clinical Research Ethics Committee (No: GO 16/399-22, Date: 14/06/2016).

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Authorship Contributions

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