Adherence to risk-assessment protocols to guide computed tomography pulmonary angiography in patients with suspected pulmonary embolism

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Aims	The use of computed tomography pulmonary angiography (CTPA) in the detection of pulmonary embolism (PE) has considerably increased due developing technology and better availability of imaging. The underuse of pre-test probability scores and overuse of CTPA has been previously reported. We sought to investigate the indications for CTPA at a University Hospital emergency clinic and seek for factors eliciting the potential overuse of CTPA.
Methods and results	Altogether 1001 patients were retrospectively collected and analysed from the medical records using a structured case report form. PE was diagnosed in 222/1001 (22.2%) of patients. Patients with PE had more often prior PE/ deep vein thrombosis, bleeding/thrombotic diathesis and less often asthma, chronic obstructive pulmonary disease, coronary artery disease, or decompensated heart failure. Patients were divided into three groups based on Wells PE risk-stratification score and two groups based on the revised Geneva score. A total of 9/382 (2.4%), 166/527 (31.5%), and 47/92 (52.2%) patients had PE in the CTPA in the low, intermediate, and high pre-test likelihood groups according to Wells score, and 200/955 (20.9%) and 22/46 (47.8%) patients had PE in the CTPA in the low-intermediate and the high pre-test likelihood groups according to the revised Geneva score, respectively. D-dimer was only measured from 568/909 (62.5%) and 597/955 (62.5%) patients who were either in the low or the intermediate-risk group according to Wells score and the revised Geneva score. Noteworthy, 105/1001 (10.5%) and 107/1001 (10.7%) of the CTPAs were inappropriately ordered according to the Wells score and the revised Geneva score. Altogether 168/1001 (16.8%) could theoretically be avoided.
Conclusions	This study highlights scant utilization of guideline-recommended risk-stratification tools in CTPA use at the emer- gency department.
Keywords	Pulmonary embolism • CTPA • D-dimer • Wells score • The Revised Geneva score

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Introduction

Technological advancements have lowered the threshold for diagnostic imaging by making imaging scans faster to execute and improved the availability of imaging in the recent decades. Yet, the increased use of imaging also raises costs and the radiation burden to patients.¹ Among US physicians, computed tomography pulmonary angiography (CTPA) was considered as the most useful imaging method for acute pulmonary embolism (PE) due to availability, lower rate of inconclusive results and the additional diagnostic capabilities.² However, these reasons are not sufficient to justify the vast amounts of CTPA used.

PE patients may be asymptomatic, or symptoms may vary from chest pain and dyspnoea to sudden death. Importantly, symptoms may mimic many other diseases. Therefore, clinical prediction rules have been established to evaluate patient's pre-test probability for PE. Wells score as well as the revised Geneva score are European Society of Cardiology (ESC) and Pulmonary Embolism Response Team (PERT) guideline-recommended PE prediction scores. The notable difference between the two scores is that Wells score include physician's subjective assessment whereas the revised Geneva score is based on objectively measurable criteria.

If the result of pre-test probability is low or intermediate, ESC and PERT guidelines recommend D-dimer testing. If pre-test probability and D-dimer suggest further testing, the primary imaging modality is CTPA.^{3–6} The use and interpretation of D-dimer may, however, be problematic, since D-dimer is often elevated in various other conditions such as advanced age, after surgery, pregnancy, or cancer.⁷

Although several studies have previously shown the underuse of PE pre-test probability scores,^{8,9} it has remained elusive which predisposing factors evoke the overuse of CTPA. The aim of this study was to investigate whether the use of CTPA is in line with the externally validated protocols and ESC and PERT guidelines, and to seek for factors eliciting the potential overuse of CTPA.

Methods

This study was set to investigate the indications for CTPA at Turku University Hospital emergency clinic. The data of 1001 patients were retrospectively collected from the medical records over the period of 1 January 2014 to 31 December 2016. The study included 1001 patients undergoing CTPA with any indication in the emergency clinic during the study period. If a patient had several CTPAs over the study period, only the first CTPA was included. There were no exclusion criteria. Because of the observational nature of the study, the Ethical Committee of the Hospital District of Southwest Finland waived written informed consent.

The data were gathered by trained research personnel using a structured case report form. The collected data included patients' medical history (previous diseases and medications), clinical examination findings, laboratory results, electrocardiogram (ECG), chest X-ray, and CTPA imaging reports. All the data collectors used pre-specified criteria, and in case of uncertainty, the case was discussed with a senior group member to reach the final decision. CTPA was done in accordance with the Turku University Hospital CTPA protocol. The CTPA was interpreted by radiologist of the emergency clinic.

The D-dimer values were analysed with particle enhanced immunoturbidimetric assay (D-DI2 [Tina-quant D-dimer Gen. 2 (2015-10, V5)], citrated plasma, Roche Diagnostics). The analytical range was 0.2–21.6 mg/L (limit of detection 0.15 mg/mL) (Analyzer: Cobas 8000 c702 Analyzer, Roche Diagnostics GmbH, Mannheim, Germany). The reference values <0.5 mg/L. The precision of the test is reported by the manufacturer (Supplementary material online, *Table S1*). The immunoturbidimetric assay has been noted to be as reliable as former enzyme-linked immunosorbent assay (ELISA) method.¹⁰

In this study, age-adjusted D-dimer cut-off levels were used as guidelines recommend.^{4,5} The D-dimer cut-off values were set to 0.5 (mg/L) for <59, 0.6 (mg/L) for 60–69, 0.7 (mg/L) for 70–79, 0.8 (mg/L) for 80–89, and 0.9 (mg/L) for over 90 years old patients.¹¹

Statistical analysis

The data of this study were analysed with SPSS (version 27.0.0, 64-bit edition). The continuous variables were reported as mean ± standard deviation, if normally distributed, and as median (25th–75th percentiles), if they were skewed. Kolmogorov–Smirnov and Shapiro–Wilk tests were used to test normal distribution of the data. Categorical variables were reported as counts and percentages. Pearson χ^2 and Fisher's exact tests were also used when appropriate. Receiver operating characteristic (ROC) analysis and area under the curve (AUC) values were used to illustrate the diagnostic ability of Wells score and the revised Geneva clinical prediction score. The presence of PE in the CTPA were stated as dichotomous variable in the ROC analysis. *P*-values <0.05 were considered as significant.

Results

Altogether 1001 patients were analysed. The patient baseline characteristics are presented in *Table 1*, the use of anticoagulant or antiplatelet drugs in *Table 2*, and the clinical symptoms at presentation in *Table 3*. PE was diagnosed in 222/1001 (22.2%) of patients. Patients with PE had more often prior PE/deep vein thrombosis (DVT), bleeding/thrombotic diathesis and less often asthma, chronic obstructive pulmonary disease (COPD), coronary artery disease, or decompensated heart failure. The pre-test likelihood and age-adjusted D-dimer of patients with prior asthma, COPD, coronary artery disease and decompensated heart failure are presented in the *Table 4*. Patients with PE experienced more often dyspnoea, unilateral lower extremity palpation pain and swelling.

Wells score

Patients were divided into three groups based on Wells Score: low (382 patients, 38.2%, <2 points), intermediate (527 patients, 52.6%, 2–6 points), and high pre-test likelihood groups (92, 9.2%, >6 points). Altogether 9/382 (2.4%), 166/527 (31.5%), and 47/92 (52.2%) patients had PE in the CTPA in the low, intermediate, and high pre-test likelihood groups, respectively.

The revised Geneva score

Patients were divided in two groups based on the revised Geneva score (*Table 5*): low-intermediate (955, patients, 95.4%, 0–10 points) and high (46 patients, 4.6%, >10 points). A total of 200/955 (20.9%) and 22/46 (47.8%) patients had PE in the CTPA in the low-intermediate and the high pre-test likelihood groups (*Table 5*).

D-dimer and low to intermediate pretest probability

D-dimer was measured from 568/909 (62.5%) and 597/955 (62.5%) patients, who were either in the low or the intermediate-risk group according to Wells score and the revised Geneva score.

Table I Baseline characteristics of the study population

Demographic	Finding in CTPA		P-value
	PE Count (%)	No PE Count (%)	
Female	126 (56.8)	463 (59.3)	0.474
Wells score			
Clinical signs and symptoms of DVT	73 (32.9)	123 (15.8)	<0.001
PE is #1 diagnosis OR equally likely	210 (94.6)	330 (42.4)	<0.001
Heart rate >100 ^a	59 (26.6)	134 (17.2)	0.002
Immobilization at least 3 days OR surgery in the previous 4 weeks	34 (15.3)	125 (16.0)	0.793
History of deep venous thrombosis or pulmonary embolism	54 (24.3)	83 (10.7)	< 0.001
Fracture or operation within 4 weeks	14 (6.3)	61 (7.8)	0.447
At least 3 days of immobilization within 4 weeks	23 (10.4)	93 (11.9)	0.517
Haemoptysis	2 (0.9)	16 (2.1)	0.391
Cancer with treatment within 6 months or palliative treatment	20 (9.0)	67 (8.6)	0.601
The revised Geneva score ^b			
Age >65 years	127 (57.2)	423 (54.3)	0.443
Surgery (under general anaesthesia) or lower limb fracture in past month	8 (3.6)	48 (6.2)	0.143
Cancer with treatment within 12 months or palliative treatment	21 (9.5)	73 (9.4)	0.968
Unilateral lower limb pain	48 (21.6)	71 (9.1)	<0.001
Pain on lower limb palpation and unilateral oedema	24 (10.8)	28 (3.6)	<0.001
Heart rate <75 b.p.m.ª	61 (27.5)	288 (37.0)	0.007
Heart rate 75–94 b.p.m.ª	81 (36.5)	260 (33.4)	0.418
Heart rate ≥95 b.p.m.ª	77 (34.7)	216 (27.7)	0.049
Other			
Flight within 4 weeks	12 (5.4)	33 (4.2)	0.458
Previous visit in the emergency clinic within 4 weeks	40 (18.1)	145 (18.6)	0.856
Asthma or chronic obstructive pulmonary disease	24 (10.9)	177 (22.8)	<0.001
Hypertension	105 (47.3)	387 (49.7)	0.520
History of heart failure	11 (5.0)	87 (11.2)	0.006
Atrial fibrillation	21 (9.5)	95 (12.2)	0.265
Diabetes	37 (16.7)	140 (18.0)	0.647
Previous stroke or transient ischaemic attack	16 (7.2)	71 (9.1)	0.368
Coronary artery disease	21 (9.5)	129 (16.6)	0.009
History of myocardial infarction	16 (7.2)	64 (8.2)	0.622
Arteriosclerosis obliterans	3 (1.4)	30 (3.9)	0.067
Pregnancy	0 (0.0)	10 (1.3)	0.91
Childbirth within 3 months	1 (0.5)	3 (0.4)	0.287
Bleeding or thrombotic diathesis	18 (8.1)	23 (3.0)	0.001

^aThe heart rate of 18 patients was not found in the medical records.

^bStatistics of patients with haemoptysis and previous DVT or PE are presented under Wells score.

From those patients, 461 (81.1%) and 488 (81.7) patients had positive age-adjusted D-dimer and 139 (30.2%) and 155 (31.8) patients had PE diagnosed using CTPA (*Table 4*).

In contrast, only 2/107 (1.9%) and 2/109 (1.8%) of patients with negative age-adjusted D-dimer and low to intermediate pre-test likelihood (Wells Score \leq 6 and the revised Geneva score \leq 10) had a PE. These two patients were designated in the intermediate-risk group according to Wells score and the revised Geneva score, but they presented clinical signs of PE that are not included in the score. Patient 1 had Wells score 4 and D-dimer 0.2 but enlarged right side of the heart in pre-CT echo. Patient 2 was an 83-year old patient, who had intermediate pre-test probability by Wells score (4.5) and Geneva clinical prediction rule (4) and age-adjusted D-dimer negative (0.7). Yet, CTPA showed PE unilaterally. Although it was controversial whether the finding in the CTPA was an acute or a chronic PE, the patient had other signs of acute PE, such as sudden onset of dyspnoea and new T-inversions in the precordial and limb leads in the ECG. The ECG showed heart rate of 61 but the patient used beta blockers. The patient also developed chronic thromboembolic pulmonary hypertension in the follow-up.

There were 341 (34.1%) and 358 (35.8%) patients, whose D-dimer status was not known in the low and the intermediate group

Table 2 The use of anticoagulant therapy or antiplatelet drugs in the study population

Medications	Finding	P-value	
	PE Count (%)	No PE Count (%)	
Aspirin	40 (18.0)	165 (21.3)	0.287
Clopidogrel or ticagrelol	7 (3.2)	32 (4.1)	0.506
Enoxaparin	6 (2.7)	37 (4.8)	0.179
Warfarin	3 (1.4)	42 (5.4)	0.009
Direct oral anticoagulants	2 (0.9)	18 (2.3)	0.277

Symptoms	Finding	P-value	
	PE Count (%)	No PE Count (%)	
Dyspnoea	190 (85.6)	576 (73.9)	<0.001
Fatigue	44 (19.9)	195 (25.1)	0.111
Chest pain	58 (26.1)	241 (30.9)	0.167
Syncope or presyncope	29 (13.1)	114 (14.6)	0.555
Altered level of consciousness	15 (6.8)	55 (7.1)	0.876

Manifostad symptoms in study populatio

according to Wells score and the revised Geneva score. PE was found in 34/341 (10.0%) and 43/358 (12.0) patients in those groups.

D-dimer and high pre-test probability

D-dimer was measured from 54/92 (58.7%) and 25/46 (54.3%) patients with Wells score >6 points and the revised Geneva score >10 points. In these high-risk groups, 27/54 (50.0%) and 11/25 (44%) patients with positive age-adjusted D-dimer had PE in CTPA, and only five and three patients had negative D-dimer in the high-risk group and none of them had PE. Furthermore, in the high-risk group patients without known D-dimer status, 20/38 (52.6%) and 11/21 (52.4%) had PE according to Wells score and the revised Geneva score.

The AUC was calculated to evaluate the performance of Wells score and the revised Geneva score in the prediction of PE in CTPA (*Figure 1*). The revised Geneva score was inferior (AUC 0.633) to Wells score (AUC 0.779).

Patients on anticoagulation treatment

The preceding use of anticoagulation or antiplatelet drugs is presented in *Table 2*. The international normalized ratio value was subtherapeutic in 9/46 (19.6%) patients on warfarin treatment, and one of those patients had PE. Enoxaparin, rivaroxaban, and dabigatran were used for thromboprophylaxis in 27/1001 (2.7%), 3/1001 (0.3%), and 1/1001 (0.1%) patients, respectively; of whom 4/27 (14.8%), 0/3 (0.0%), and 0/1 (0.0%) had PE. Furthermore, patients on enoxaparin, warfarin, apixaban, rivaroxaban, or dabigatran treatment with therapeutic dose had PE 2/16 (12.5%), 3/45 (6.7%), 0/2 (0.0%), 2/12 (16.7%), 0/2 (0.0%), respectively. Subgroup analyses were not calculated as the number of patients with these treatments were low.

Avoidable CTPAs

In an exploratory analysis, we assessed the underuse of guideline-recommended utilization of PE risk-stratification tools Wells score and D-dimer. D-dimer was measured from 568/909 (62.5%) and 597/955 (62.5%) patients, who were either in the low or the intermediate-risk group according to Wells score and the revised Geneva score. One hundred and five (18.5%) and 107 (17.9%) of them had negative ageadjusted D-dimer and CTPA was inappropriate (*Table 4*). Of those 105 patients 59 (56.2%) and 46 (43.8%) patients were in low- and intermediate-risk groups according to Wells score and only 2 PEs was found in the intermediate-risk group.

However, over one-third (341 by Wells score and 358 by the revised Geneva score) of the patients without D-dimer measurement before CTPA are not included in the above calculation. Theoretically, assuming a similar 17.9–18.5% rate of negative ageadjusted D-dimer we speculate that 63–64 more CTPAs could have been avoided.

Discussion

The main finding in this study was that CTPA was frequently used in the ED for ruling in/out PE also in patients with low to intermediate pre-test probability for PE. Secondly, D-dimer was sampled in less than two-thirds of patients with low- or intermediate-risk group. Guideline-recommended utilization of PE risk-stratification tools could have adequately ruled out PE without CTPA even in 168/568 (29.6%) patients who underwent the scan.

Thus, overutilization of CTPA can likely be explained by the challenge in diagnosing other diseases with overlapping symptoms. Although these diseases have distinct clinical work-up protocol, CTPA or D-dimer often aids in pointing out alternative diagnoses. Our findings underscore poor adherence to appropriateness criteria for CTPA in the ED setting. This is in line with previous studies that have reported increased use of diagnostic imaging, inappropriate use of CTPA to diagnose PE in the emergency department (ED)^{12,13,14–17} and that PE prevalence is 5.4-24.3% in the CTPA.^{12,14,17-20} Moreover, in the EDITED study 30% of patients with suspicion of DVT could be excluded with negative D-dimer and low pre-test probability.²¹ Our study represents a larger patient population than the many of the previous studies.^{12,14,18,19} In addition, populations of previous studies have been from different settings and many have taken account inpatients as well.^{14,18} Taken together, findings emphasize the importance of following the established guidelines.

Furthermore, the patients with PE were less likely to have decompensated heart failure, coronary artery disease, asthma, or COPD in this study. Since, the symptoms of these diseases resemble the symptoms of PE, they may cause an emergency room (ER) physician to proceed directly to CTPA over the PE protocol. For instance, such deviation from the protocol might occur if severe asthma is considered being a risk factor for PE.²² Yet, 2019 ESC guidelines on acute PE do not list COPD or asthma as predisposing factors for PE. The same guidelines list congestive heart failure and respiratory failure as a moderate risk factor for PE.⁴ Altogether, these risk factors alone

Table 2

Pre-test likelihood of patients with asthma or COPD		Finding in CTPA		
Wells score	D-dimer (age adjusted)	PE	No PE	
		Count (%)	Count (%	
.ow-intermediate	Negative	0 (0)	26 (100)	
-ow-intermediate	Positive	14 (15.7)	75 (84.3)	
_ow-intermediate	Unknown	5 (6.8)	68 (93.2)	
High	Negative	0	0	
High	Positive	5 (50)	5 (50)	
	Unknown	0 (0)	3 (100)	
High			. ,	
Pre-test likelihood of patients with as		Finding in C		
The revised Geneva score	D-dimer (age adjusted)	PE Count (%)	No PE Count (%	
_ow-intermediate	Negative	0 (0)	25 (100)	
_ow-intermediate	Positive	17 (18.3)	76 (81.7)	
_ow-intermediate	Unknown	4 (5.5)	69 (94.5)	
High	Negative	0 (0)	1 (100)	
High	Positive	2 (33.3)	4 (66.7)	
High	Unknown	2 (33.3) 1 (33.3)	2 (66.7)	
		. ,	in CTPA	
Pre-test likelihood of patients with decompensated heart failure Wells score D-dimer (age adjusted)		PE	No PE	
Wells Score	D-dimer (age adjusted)	Count (%)	Count (%	
.ow-intermediate	Negative	0 (0)	8 (100)	
ow-intermediate	Positive	3 (7.9)	35 (92.1)	
_ow-intermediate	Unknown	4 (9.3)	39 (90.7)	
		0	0	
High	Negative			
High High	Positive Unknown	2 (66.7) 2 (33.3)	1 (33.3) 4 (66.7)	
-		× ,	. ,	
Pre-test likelihood of patients with de	•	Finding in CTPA PE No		
The revised Geneva score	D-dimer (age adjusted)	Count (%)	No PE Count (%	
_ow-intermediate	Negative	0 (0)	7 (100)	
_ow-intermediate	Positive	4 (10.3)	35 (89.7)	
Low-intermediate				
	Unknown	5 (11.9)	41 (89.1)	
High	Negative	0 (0)	1 (100)	
High	Positive	1 (50)	1 (50)	
High	Unknown	1 (33.3)	2 (66.7)	
Pre-test likelihood of patients with co		Finding in CTPA		
Wells score	D-dimer (age adjusted)	PE Count (%)	No PE Count (%	
_ow-intermediate	Negative	2 (14.3)	12 (85.7)	
_ow-intermediate	Positive	11 (16.4)	56 (83.6)	
_ow-intermediate	Unknown	5 (8.5)	54 (91.5)	
High	Negative	0	0	
-	Positive	3 (42.9)	4 (57.1)	
High High	Positive Unknown	3 (42.9) 0 (0)	4 (57.1) 3 (100)	
Pre-test likelihood of patients with co			in CTPA	
The revised Geneva score		PE	No PE	
		Count (%)	Count (%	
Low-intermediate	Negative	2 (15.4)	11 (84.6)	
		- (13.1)	(00)	

Table 4Pre-test likelihood and age-adjusted D-dimer of patients with prior asthma, COPD, coronary artery diseaseand decompensated heart failure

Table 4 Continued

Pre-test likelihood of patients with asthma or COPD		Finding in CTPA	
Wells score	D-dimer (age adjusted)	PE	No PE
		Count (%)	Count (%)
Low-intermediate	Positive	11 (16.2)	57 (83.8)
Low-intermediate	Unknown	5 (8.5)	54 (91.5)
High	Negative	0 (0)	1 (100)
High	Positive	3 (50)	3 (50)
High	Unknown	0 (0)	3 (100)

Table 5 Age-adjusted D-dimer, different pre-test likelihoods of PE by Wells' score and the revised Geneva score

Pre-test likelihood		Finding	in CTPA	
Wells score	D-dimer (age adjusted)	PE	No PE	
		Count (%)	Count (%)	
Low-intermediate	Negative	2 (1.9)	105 (98.1)	
Low-intermediate	Positive	139 (30.2)	322 (69.8)	
Low-intermediate	Unknown	34 (10.0)	307 (90.0)	
High	Negative	0 (0)	5 (100)	
High	Positive	27 (55.1)	22 (44.9)	
High	Unknown	20 (52.6)	18 (47.4)	
Pre-test likelihood		Finding in CTPA		
The revised Geneva score	D-dimer (age adjusted)	PE	No PE	
		Count (%)	Count (%)	
Low-intermediate	Negative	2 (1.8)	107 (98.2)	
Low-intermediate	Positive	155 (31.8)	333 (68.2)	
Low-intermediate	Unknown	43 (12.0)	315 (88.0)	
High	Negative	0 (0)	3 (100)	
High	Positive	11 (50)	11 (50)	
High	Unknown	11 (52.4)	10 (47.6)	

are not sufficient to disregard the PE protocol. Moreover, the finding of less PE in patients with these diseases may reflect a pitfall of the subjectivity of the Well's criteria as the symptoms may cause a biased estimate of the likelihood of PE.

The revised Geneva score was inferior to Wells score when analysed with ROC curve. That may be due to distinct difference as Wells score uses subjective criteria unlike the Revised Geneva criteria. Specifically, the Wells score criterion 'PE is the number one diagnosis or equally likely' is debatable. The different assessment of the criterion by the ER physician can cause patient to shift from lowintermediate to high-risk group or vice versa, and yet lead to inappropriate D-dimer testing or CTPA.

Systematic analysis of patient history and clinical findings give a useful estimate to determine the pre-test probability of PE.^{22,23} However, clinical judgement lacks standardization as pointed out in the ESC guidelines.⁴ In this study, there were 359 (35.9%) patients, whose D-dimer was not known in low and intermediate group. Only 39/359 (10.9%) patients had PE in that group comparing the 134/454 (29.5%) and 2/96 (2.1%) patients with positive and negative age-adjusted D-dimer in the same risk group. Of note, as D-dimer levels decrease over time, the delay between symptom onset and D-dimer test should also be considered when assessing the probability of PE to avoid false negative D-dimer results.^{7,24} Both Wells score and the revised Geneva score together with D-dimer testing were reliable to exclude PE in the low and the intermediate-risk groups. Controversially, international guidelines do not recommend D-dimer testing for high-risk group patients,^{4,5} yet D-dimer was measured from 54/91 (59.3%) patients with Wells score >6 points. In this risk group, D-dimer testing is futile and can delay the diagnosis and treatment of PE.

Although technological progress has made imaging more accurate and faster to execute, its growing use has a slew of subsequent challenges. Inappropriate use of CTPA increased the annual costs of radiological imaging.¹ After the introduction of CTPA, the incidence

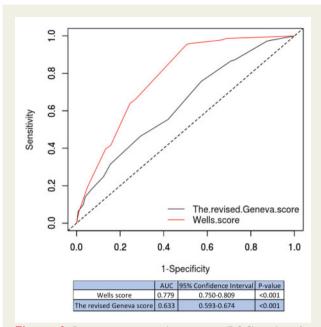


Figure I Receiver-operating characteristic (ROC) analysis for determining the accuracy of Wells score and the revised Geneva score to exclude pulmonary embolism.

of PE increased 81%, however, with minimal change of mortality (1998–2006).¹⁶ One of the controversial issues of high-resolution CTPA is the detection of small subsegmental emboli and incidental findings.^{15,16} There is still lack of evidence how to handle subsegmental emboli and whether these patients should be exposed to anticoagulants.

Some limitations should be noted. First, this is an observational, single-centre study and the data was collected from the available medical records and a possibility for residual confounding exists. Nevertheless, trained research personnel used a structured case report to collect data consistently. As only a few physicians reported Wells or the revised Geneva score in the patient data, the scores were calculated mostly retrospectively. It is also noteworthy that the pre-test probability scores do not take into account the bradycardic effect of beta blockers which may lead to misclassification in this patient group. Despite these potential limitations, this contemporary data represents well a relatively large volume centralized ED with half a million-inhabitant's catchment area where PE are treated exclusively.

The harms of over- and underdiagnoses are well-recognized. Our findings underscore the use of guideline-recommended risk-stratification tools to reduce unnecessary CTPA.

Supplementary material

Supplementary material is available at European Heart Journal – Quality of Care and Clinical Outcomes online.

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Data availability

Data is available from the corresponding author upon a reasonable request.

References

- Smith-Bindman R, Miglioretti DL, Larson EB. Rising use of diagnostic medical imaging in a large integrated health system. *Health Aff (Millwood)* 2008;27: 1491–1502.
- Weiss CR, Scatarige JC, Diette GB, Haponik EF, Merriman B, Fishman EK. CT pulmonary angiography is the first-line imaging test for acute pulmonary embolism: a survey of US clinicians. *Acad Radiol* 2006;**13**:434–446.
- Klok FA, Mos ICM, Nijkeuter M, Righini M, Perrier A, Le Gal G et al. Simplification of the revised Geneva score for assessing clinical probability of pulmonary embolism. Arch Intern Med 2008;168:2131–2136.
- 4. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP et al.; ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J 2020;41:543–603.
- Rivera-Lebron B, McDaniel M, Ahrar K, Alrifai A, Dudzinski DM, Fanola C et al.; PERT Consortium. Diagnosis, treatment and follow up of acute pulmonary embolism: consensus practice from the PERT Consortium. *Clin Appl Thromb Hemost* 2019;25:1076029619853037.
- Wells PS, Anderson DR, Rodger M, Stiell I, Dreyer JF, Barnes D et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and D-dimer. Ann Intern Med 2001;**135**: 98–107.
- Weitz JI, Fredenburgh JC, Eikelboom JW. A test in context: d-dimer. J Am Coll Cardiol 2017;70:2411–2420.
- Crichlow A, Cuker A, Mills AM. Overuse of computed tomography pulmonary angiography in the evaluation of patients with suspected pulmonary embolism in the emergency department. *Acad Emerg Med* 2012;19:1219–1226.
- Perera M, Aggarwal L, Scott IA, Cocks N. Underuse of risk assessment and overuse of computed tomography pulmonary angiography in patients with suspected pulmonary thromboembolisfile. *Intern Med J* 2017;47: 1154–1160.
- Knecht MF, Heinrich F. Clinical evaluation of an immunoturbidimetric D-dimer assay in the diagnostic procedure of deep vein thrombosis and pulmonary embolism. *Thromb Res* 1997;1:413–417.
- Righini M, Van Es J, Den Exter PL, Roy P-M, Verschuren F, Ghuysen A et al. Ageadjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study. JAMA 2014;311:1117.
- Anderson DR, Kovacs MJ, Kovacs G, Stiell I, Mitchell M, Khoury V et al. Combined use of clinical assessment and D-dimer to improve the management of patients presenting to the emergency department with suspected deep vein thrombosis (the EDITED Study). J Thromb Haemost 2003;1:645–651.
- Tan S, Haramati LB. Are we overdiagnosing pulmonary embolism? Yes! J Thorac Imaging 2018;33:346–347.
- Osman M, Subedi SK, Ahmed A, Khan J, Dawood T, Ríos-Bedoya CF et al. Computed tomography pulmonary angiography is overused to diagnose pulmonary embolism in the emergency department of academic community hospital. J Community Hosp Intern Med Perspect 2018;8:6–10.
- Costantino MM, Randall G, Gosselin M, Brandt M, Spinning K, Vegas CD. CT angiography in the evaluation of acute pulmonary embolus. *Am J Roentgenol* 2008; 191:471–474.
- Wiener RS, Schwartz LM, Woloshin S. Time trends in pulmonary embolism in the United States: evidence of overdiagnosis. *Arch Intern Med* 2011;**171**: 831–836.
- Wiener RS, Schwartz LM, Woloshin S. When a test is too good: how CT pulmonary angiograms find pulmonary emboli that do not need to be found. *BMJ* 2013;**347**:f3368.

- van Belle A, Büller HR, Huisman MV, Huisman PM, Kaasjager K, Kamphuisen PW et al.; Christopher Study Investigators. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. JAMA 2006;295:172–179.
- 19. van Strijen MJL, de Monyé W, Schiereck J, Kieft GJ, Prins MH, Huisman MV et al.; Advances in New Technologies Evaluating the Localisation of Pulmonary Embolism Study Group. Single-detector helical computed tomography as the primary diagnostic test in suspected pulmonary embolism: a multicenter clinical management study of 510 patients. Ann Intern Med 2003;**138**:307–314.
- Haap MM, Gatidis S, Horger M, Riessen R, Lehnert H, Haas CS. Computed tomography angiography in patients with suspected pulmonary embolism-too often considered? Am J Emerg Med 2012;30:325–330.
- Yadam S, Popuri A, Hattab Y, Cheema T. Controversies in venous thromboembolism. *Crit Care Nurs Q* 2017;40: 301–305.

- Majoor CJ, Kamphuisen PW, Zwinderman AH, ten Brinke A, Amelink M, Rijssenbeek-Nouwens L et al. Risk of deep vein thrombosis and pulmonary embolism in asthma. *Eur Respir J* 2013;42:655–661.
- Kabrhel C, Camargo CA, Goldharber SZ. Clinical gestalt and the diagnosis of pulmonary embolism: does experience matter? Ann Emerg Med 2004;44: S37–S38.
- 24. Penaloza A, Verschuren F, Meyer G, Quentin-Georget S, Soulie C, Thys F et al.. Comparison of the Unstructured Clinician Gestalt, the Wells Score, and the Revised Geneva Score to Estimate Pretest Probability for Suspected Pulmonary Embolism. Annals of Emergency Medicine 2013;**62**:117–124.
- 25. Goldin Y, Pasvolsky O, Rogowski O, Shapira I, Steinvil A, Halpern P et al. The diagnostic yield of D-dimer in relation to time from symptom onset in patients evaluated for venous thromboembolism in the emergency medicine department. *J Thromb Thrombolysis* 2011;**31**:1–5.