Additive evidence of the competence of pregnancy-adapted YEARS algorithm in reducing the need for CTPA, Q and/or V/Q scintiscan

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Abstract

Objective: To determine whether a pregnancy-adapted clinical and D-dimer-based algorithm, termed the "YEARS algorithm," can reduce the need for radiological imaging, including lung scintigraphy in pregnant women with suspected pulmonary embolism (PE). **Patients and Methods:** This retrospective study included all pregnant women with suspected PE between January 2014 and September 2019 who have undergone D-dimer testing and radiological imaging (computed tomography pulmonary angiography or lung perfusion scans) at presentation. Three criteria from the YEARS algorithm were assessed: clinical signs of deep vein thrombosis, haemoptysis, and whether PE was clinically considered as the most likely diagnosis. Patients who did not have to undergo imaging per the YEARS algorithm were defined as those with no YEARS criteria and a D-dimer of <1μg/mL (group 1) and those with 1-3 YEARS criteria and a D-dimer of <0.5μg/mL (group 2). Patients who had to undergo imaging were those with no YEARS criteria and a D-dimer ≥1μg/mL (group 3) and those with 1-3 YEARS criteria and a D-dimer ≥0.5μg/mL (group 4). Women with symptoms of deep-vein thrombosis had to undergo Doppler ultrasound: If positive, they were anticoagulated and excluded from this analysis, and if negative, they were evaluated further for the need of imaging based on other YEARS criteria and D-dimer level. **Results:** Of 117 pregnant women with suspected PE analyzed according to the YEARS algorithm five had confirmed deep-vein thrombosis by Doppler ultrasound, were anticoagulated and excluded from the analysis. Of the remaining 112 women (mean age; 30.4±5.7 years), 50 underwent computed tomography pulmonary angiography (CTPA), 54 lung perfusion or ventilation-perfusion (V/Q) scan and eight both; PE was diagnosed in 7 (6.25%), two by CTPA, two by lung perfusion or V/Q scan and three by both. Thirty-three of the 112 women (29.5%) were in groups 1+2 and could, therefore, have avoided CTPA or lung perfusion scans per the YEARS algorithm. None of those 33 women had PE by CTPA or lung perfusion scans vs. 7/79 patients (8.9%) who required CTPA or lung perfusion scans per the YEARS algorithm. **Conclusions:** The pregnancy-adapted YEARS algorithm can safely rule out PE in about one-third of pregnant women with suspected PE without the need for radiological imaging.

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Introduction

Pulmonary embolism (PE) remains a diagnostic dilemma in pregnancy due to significant overlapping with pregnancy symptoms. While only a small fraction of pregnant women with clinical suspicion of PE are ultimately proven to have PE, missing a PE in pregnancy can have catastrophic consequences, including death [1].

One difficulty in managing PE in pregnancy pertains to the variable recommendations in clinical practice guidelines [2-4]. Wells and Geneva's scores are validated clinical probability scoring systems used to assess the likelihood of PE in males and nonpregnant females. However, they could not be validated in pregnancy [5]. Biomarkers such as D-dimer, B-type natriuretic peptide, C-reactive protein, fibrinogen, and serum troponin also failed to predict or rule out PE in pregnant women [6].

Because it is critical to diagnose or rule out PE, imaging tests, such as computed tomography pulmonary angiography (CTPA) and ventilation-perfusion (V/Q) scan, are frequently performed even if the clinical suspicion is low or intermediate resulting in a very high rate of negative imaging. However, CTPA and V/Q scans involve the use of ionizing radiation with potential harm to the mother and fetus [7]. The meagre yield of these imaging tests in pregnant women with low/intermediate clinical and laboratory (D-dimer) suspicion of PE has prompted the development of algorithms combining clinical and laboratory parameters to minimize unnecessary radiological tests while safely ruling out PE. One of these algorithms that has received attention lately is the pregnancy-

adapted YEARS algorithm based on the combination of clinical symptoms or impressions (YEARS criteria), the use of D-dimer, and selective use of lower limb compression ultrasonography (CUSP) [8]. This algorithm assesses the presence or absence of each of the YEARS criteria (i.e., symptomatic deep vein thrombosis, hemoptysis, and whether PE is the most likely diagnosis) scored as yes or no with a pretest probability-dependent threshold of the D-dimer level. Briefly, PE is excluded without imaging (CTPA and/or V/Q scan) in patients with no YEARS criteria and a D-dimer concentration of <1μg/mL or with one or more YEARS criteria and a D-dimer concentration of <0.5μg/mL. In contrast, patients with no YEARS criteria and a D-dimer concentration of ≥1μg/mL or with one or more YEARS criteria and a D-dimer concentration of ≥0.5μg/mL require further imaging to diagnose or rule out PE. Based on this algorithm, in a large study involving 510 patients with suspected PE, PE was safely ruled out without performing unnecessary CTPA in 32% of pregnant women who began the study in the third trimester and 65% who began the study in the first trimester [8].

The primary goal of the current investigation is to retrospectively determine whether the pregnancy-adapted YEARS algorithm can reduce the need for radiological imaging, including lung scintigraphy in pregnant women seen at our emergency room for suspected acute PE. To our knowledge, this study is the first of its kind in nuclear medicine literature.

Patients and Methods

Study setting and population

This retrospective study was approved by the Ethics Committee at Jordan University Hospital. Information about the study was posted in the hospital. We reviewed the clinical charts (both electronic and paper-based) of all pregnant women seen at our emergency department (ED) for suspected PE between January 1, 2014, and September 1, 2019. Pregnancy and gestational age were diagnosed and confirmed by the last menstrual period (LMP) and ultrasound (U/S) scan. All women had viable pregnancies as confirmed by the U/S scan, which was performed on the day of presentation by a trained obstetrician. The first, second and third trimesters were considered as follows; 1-12 weeks, 13-26 and 27 weeks or more, respectively. Of this cohort, only women who had D-dimer testing at the time of assessment in the ED with subsequent imaging studies (CTPA or lung perfusion scans) were included. Exclusion criteria were age less than 18 years, charts with missing data needed to determine YEARS criteria, anticoagulation treatment before doing D-dimer, and diagnosis of deep vein thrombosis with Doppler ultrasound. Our requirement that all included patients in this study underwent CTPA and/or lung perfusion scan is based on the premise that imaging is the most reliable approach to confirm whether the patients had PE or not, in a retrospective setting.

Determination of YEARS criteria

Three criteria from the YEARS algorithm were assessed in all the patients, according to van der Pol et al. (2019) [8]: Whether clinical signs of deep vein thrombosis were present, whether hemoptysis (defined as the coughing up of small amounts of blood or a streak of blood) was reported and whether PE was considered by the treating physician to be the most likely diagnosis. The third criterion (PE as the most likely diagnosis, above any alternative diagnosis) was evaluated based on the patient's history and results of physical examination.

Procedures

The D-dimer level was measured with the use of an automated, well-validated, high-sensitivity, quantitative d-dimer assays (ROCHE cardiac D-dimer to be used on Cobas h 232 instruments). Measurement range was 0.1-4μg/mL, the normal range includes values less than 0.5 μg/mL. Values ≥0.5μg/mL are deemed pathologically elevated. Computed tomography pulmonary angiography was performed using special protocol for pregnant lady including a high flow rate of administration of contrast medium, a high concentration of contrast medium, shallow breath holds, and a reduced dose of radiation [9]. Pulmonary embolism was present if CTPA showed a new filling defect in a subsegmental or more proximal pulmonary artery [10]. A board-certified radiologist read all CTPA's.

Lung perfusion scintigraphy (Q scan) was used as an alternative to CTPA based on treating physician's preferences, resources available, and, whenever CTPA was contraindicated. This last scenario includes impaired renal function (n=2), contrasts allergy (n=1), inconclusive CTPA due to breathing artifacts, poor signal-to-noise ratio, or insufficient opacification of pulmonary arteries (n=2).

A Q scan was performed by administering a low activity of only 37MBq of technetium-99m-macroaggregated albumin (^{99m}Tc-MAA) to minimize the radiation dose to the mother and fetus. The 37MBq activity is within the range of acceptable ^{99m}Tc-MAA administered activities according to the 2019 European Association of Nuclear Medicine guidelines for ventilation/perfusion (V/Q) imaging [11]. The number of MAA particles associated with this activity level was approximately 150,000. To further minimize the radiation dose, no ventilation scan was performed if the Q scan was normal or unequivocally positive. Pulmonary embolism was present if the Q scan showed at least one segment or two subsegments that conform to pulmonary vascular anatomy. A Q scan was deemed inconclusive if there were multiple perfusion abnormalities that are not typical of a specific disease (i.e., not conforming to the pulmonary vascular anatomy) [11]. In the few patients with inconclusive Q scan (n=5), a ventilation scan was performed the following day using only 18-37MBq of ^{99m}Tc-diethylenetriamine-penta-acetic acid (^{99m}Tc-DTPA) aerosol, in which case a PE was present if there was a V/Q mismatch of at least one segment or two subsegments that conform to the pulmonary vascular anatomy [11]. A board-certified nuclear medicine physician interpreted all Q or V/Q scans.

Outcome analysis

Based on the algorithms provided by the pregnancy-adapted YEARS study, we determined the number of patients and their outcome (PE or venous thromboembolism (VTE) vs. none). The following groups, as well as the diagnostic tests they underwent to diagnose or rule out PE are as follow:

Group 1: Patients with no YEARS criteria and a D-dimer concentration of <1μg/mL (based on the YEARS algorithm, PE can be excluded in these patients without further testing). Group 2: Patients with one or more YEARS criteria and a D-dimer concentration of <0.5μg/mL (PE was can also be excluded in these patients without further testing). Group 3: Patients with no YEARS criteria and a D-dimer concentration of ≥ 1μg/mL (based on the YEARS algorithm, imaging, such as CTPA, Q, or V/Q scans should be performed to diagnose or rule out PE). Group 4: Patients with one or more YEARS criteria and a D-dimer concentration of ≥0.5μg/mL (based on the YEARS algorithm, CTPA, Q, or V/Q scans should also be performed to diagnose or rule out PE). The outcome of all patients (i.e., whether they had PE or VTE or not) was based on the findings of the CTPA, Q, and/or V/Q scans at the time of assessment. In addition to the D-dimer and clinical criteria above, women with symptoms of deep-vein thrombosis had to undergo Doppler ultrasound: If positive, they were anticoagulated and excluded from this analysis, and if negative they were evaluated further for the need of imaging based on other YEARS criteria and D-dimer level.

The percentage of patients with PE or VTE in groups 1 and 2 combined was determined. If the incidence of PE/VTE in these patients was very low (i.e., ≤3%), this provided validation for the pregnancy-adapted YEARS algorithm in our population. The 3% threshold represents the upper 95% confidence limit (CL) of the rate of confirmed episodes of venous thromboembolism deemed acceptable used for a safe diagnostic strategy [12]. The percentage of patients with PE or VTE in groups 3 and 4 combined was also determined, allowing us to compare the incidence of PE/VTE in these patients with that reported in the literature.

Statistical analysis

We used SPSS version 21.0 (Chicago, USA) in our analysis. We used the mean ± standard deviation (SD) to describe continuous variables (e.g., age) and count (frequency) to describe other nominal variables (e.g., patients meeting YEARS criteria). We performed an independent sample t-test to analyze the relation between age and each of Doppler, V/Q scan, and spiral CT, where age was found to be normally distributed with no outliers. We used the chi-square test to analyze the difference between YEARS in the three trimesters. We adopted a P-value of 0.05 as a statistically significant threshold.

Results

During the study period, 147 pregnant women with suspected PE were referred to our emergency department. Of those, 30 patients were excluded from this study either because they did not undergo D-dimer testing (n=16), any imaging (n=5), or because of incomplete data to enable the assessment of YEARS criteria (n=9).

Of 117 pregnant women with suspected PE analyzed according to the YEARS algorithm, five had confirmed deep-vein thrombosis by Doppler ultrasound, were anticoagulated, and excluded from the analysis, leaving 112 patients who were analyzed according to the pregnancy-adapted YEARS algorithm shown in Figure 1. The patients' mean age was 30.4±5.7 years. Most (80.4%) were in the third trimester, and the majority (65.2%) had only one YEARS criterion, namely "pulmonary embolism is the most likely diagnosis, above any alternative diagnosis". Only 4.5 % had clinical signs of deep-vein thrombosis, and none had hemoptysis (Table 1).

Table 1. *Characteristics of included patients.*

		Count	Column N %
Trimester	1.00	5	4.5%
	2.00	17	15.2%
	3.00	90	80.4%
D-Dimer	<0.5	15	13.4%
	0.5-<1	81	72.3%
	≥1	16	14.3%
Spiral CT	Not done	54	48.2%
	Negative	53	47.3%
	Positive	5	4.5%
Q(V/Q) scan	Not done	50	44.6%
	Negative	57	50.9%
	Positive	5	4.5%
YEAR's	<0>	34	30.4%
	<1>	73	65.2%
	<2>	5	4.5%
	<3>	0	0

No significant association was found between age and Doppler scanning (P=0.710), V/Q scanning (P=0.088), or spiral CT imaging (P=0.130) in the 112 patients studied. Table 2 shows the number of YEARS criteria (0 to 3) in the three trimesters. No significant difference in the number of YEARS criteria was found between the three trimesters (P=0.286). The median D-dimer level was 0.3μg/mL (interquartile range from 0.29-0.31) during the first trimester, 0.4μg/mL (interquartile range from 0.36-0.68) during the second trimester and 1.32μg/mL (interquartile range from 0.69-2.8) during the third trimester.

The distribution of D-dimer levels categorized as <0.5, ≥ 0.5- <1.0, and ≥1.0μg/mL is shown in Table 3. As expected, the vast majority of patients in the 1st trimester had D-dimer of <0.5μg/mL (in our small sample size it is 4 of 5 patients or 80%) while 35.3% and 5.6% of patients in the 2nd and 3rd trimester, respectively had D-dimer of <0.5μg/mL. However, D-dimer levels of <1.0μg/mL were noted in 100%, 100% and 82.2% of patients in the 1st, 2nd, and 3rd trimester, respectively.

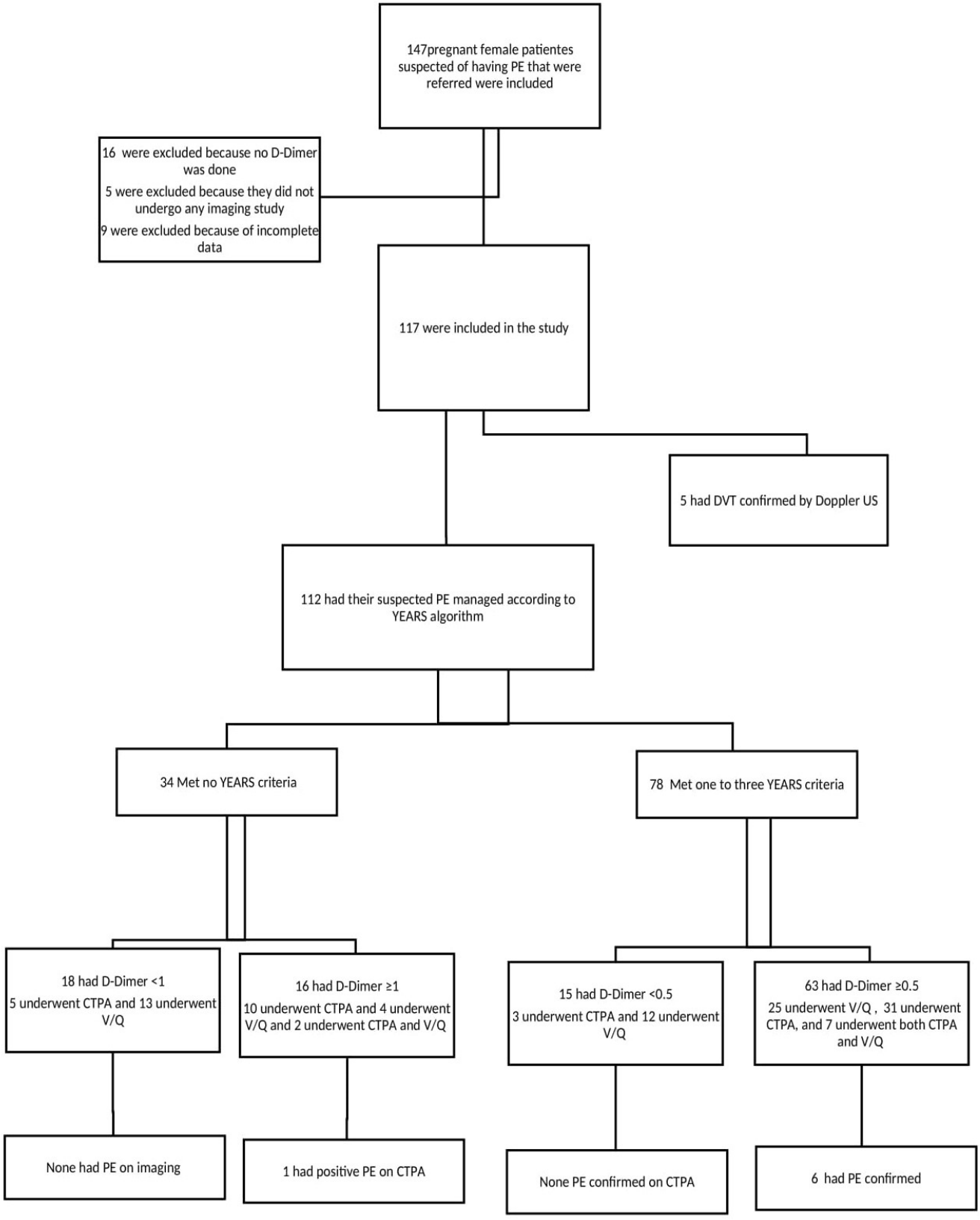

Figure 1. Flow chart of study patients.

Table 2. *YEARS criteria (0 to 3) per trimesters.*

			Years			Total
			0	1	2	
Trimester	First	Count	1	4	0	5
		% within trimester	20.0%	80.0%	0.0%	100.0%
	Second	Count	7	8	2	17
		% within trimester	41.2%	47.1%	11.8%	100.0%
	Third	Count	26	61	3	90
		% within trimester	28.9%	67.8%	3.3%	100.0%
Total		Count	34	73	5	112
		% within total	30,4%	65.2%	4.5%	100%

Table 3. *Distribution of D-dimer levels.*

			D-dimer (μg/mL)			Total
			<0.5	≥0.5 <1	≥1	
Trimester	First	Count	4	1	0	5
		% within trimester	80.0%	20.0%	0.0%	100.0%
	Second	Count	6	11	0	17
		% within trimester	35.3%	64.7%	0.0%	100.0%
	Third	Count	5	69	16	90
		% within trimester	5.6%	76.7%	17.8%	100.0%
Total		Count	15	81	16	112
		% within total	13.4%	72,4%	14,3%	100%

Seventy-eight patients (69.6 %) met one to three YEARS criteria, while 34 (30.4%) did not meet any YEARS criteria. The latter patients were referred for imaging primarily due to elevated D-dimer of ≥0.5μg/mL or others symptoms/risk factors not included in YEARS criteria, such as history of old VTE. Fifty patients underwent CTPA, 54 Q or V/Q scan, and eight both; PE was diagnosed in 7 (6.25%) patients; two by CTPA, two by Q or V/Q scan, and three by both. All patients with PE were in the third trimester. From the 34 patients who did not meet any YEARS criteria, 16 (47%) had a D-dimer ≥1μg/mL, which would mandate radiological imaging per pregnancy-adapted YEARS algorithm and, of those one patient (6.25%) had PE by imaging. The other 18 patients who did not meet any YEARS criteria had D-dimer <1μg/mL, thereby not requiring imaging per YEARS algorithm. When imaged, none of these patients did show any PE. From those 78 patients who met 1-3 YEARS criteria, 63 (80.8%) had a D-dimer ≥0.5μg/mL, which would mandate radiological imaging and, of those 6 (7.7%) had PE by imaging. The remaining 15 patients who met 1-3 criteria had a D-dimer <0.5μg/mL, thereby not requiring imaging per YEARS algorithm. None of those patients had PE upon imaging. Thus, none of the 33 patients in groups 1 and 2 (no YEARS criteria and a D-dimer <1μg/mL or 1-3 YEARS criteria and a D-dimer of <0.5μg/mL) who would not have required imaging per YEARS algorithm had PE. In contrast, 7 of the 78 patients (~9%) in groups 3 and 4 (no YEARS criteria and a D-dimer of ≥1μg/mL or 1-3 YEARS criteria and a D-dimer ≥0.5μg/mL, respectively) had PE.

Overall, 5/5 (100%), 13/17 (76.5%) and 15/90 (16.7%) patients in the 1st, 2nd and 3rd trimester, respectively were in groups 1 and 2 (no YEARS criteria and a D-dimer <1μg/mL or 1-3 YEARS criteria and a D-dimer <0.5μg/mL, respectively), thereby not requiring imaging per the pregnancy-adapted YEARS algorithm. We found a significant relationship (P<0.001) between trimester and YEARS criteria group, where patients in the 3rd trimester were more likely to be in Group 4 (1-3 YEARS criteria and a D-dimer ≥0.5μg/mL) compared to patients in the 1st or 2nd trimester (Table 4).

Finally, Doppler U/S was done in 31 (27.2%) patients, all of whom did not show evidence of DVT. All these patients did not have clinical signs of DVT and should not have undergone Doppler U/S according to the YEARS algorithm. These patients were first referred for Doppler U/S before performing CTPA, Q and/or V/Q scintiscan despite absence of

Table 4. *Analysis of the groups per trimester.*

			Group				
			Group 1*	Group 2*	Group 3*	Group 4*	Total
Trimester	1.00	Count	1	4	0	0	5
		% within trimester	20.0%	80.0%	0.0%	0.0%	100.0%
	2.00	Count	7	6	0	4	17
		% within trimester	41.2%	35.3%	0.0%	23.5%	100.0%
	3.00	Count	10	5	16	59	90
		% within trimester	11.1%	5.6%	17.8%	65.6%	100.0%
Total		Count	18	15	16	63	112
		% within total	16.1%	13.4%	14.3%	56.3%	100%

**patients with no YEARS criteria and a D-dimer concentration of <1μg/mL; ** patients with 1-3 YEARS criteria and a D-dimer concentration of <0.5μg/mL; & patients with no YEARS criteria and a D-dimer concentration of ≥ 1μg/mL; # patients with 1-3 YEARS criteria and a D-dimer concentration of ≥ 0.5μg/mL.*

clinical signs of DVT due to referring physicians' preference to avoid conventional radiological or nuclear medicine imaging if Doppler turned out to be positive. This preference was also shared by some patients.

Discussion

Although YEARS algorithm emerged only recently [13], it was rapidly adopted in clinical guidelines, as shown by the 2019 European Society of Cardiology guidelines for the diagnosis and management of acute pulmonary embolism [14], so it is essential to validate its accuracy in different clinical settings. Since very few studies validated the YEARS algorithm so far, especially in pregnancy, more studies were needed to confirm its validity. The results of our study validated the algorithm in a developing country. Our retrospective study showed that a pregnancy-adapted YEARS algorithm, which has the advantage of avoiding radiation exposure to the fetus and mother, would have resulted in safely ruling out PE in about one-third of patients (33/112 or 29.4%) without performing conventional and/or nuclear medicine imaging. These findings, albeit in a relatively small number of patients, are generally consistent with those of a recent prospective study, where PE was safely ruled out without conventional radiological imaging in 32%-65% of pregnant women with suspected PE [8].

A previous study used available data from CT-PE pregnancy study to validate the YEARS algorithm showed that radiation exposure would have been avoided in 21% of women by using the YEARS algorithm and found the algorithm to be 100% accurate, meaning that all pregnant women who were spared imaging based on algorithm did not have or develop PE [15]. An ongoing prospective study to assess the impact of adopting the YEARS algorithm in various clinical settings has already started [16].

As a study inclusion criterion in our analysis, every pregnant woman with suspected PE had conventional and/or nuclear medicine imaging. This inclusion criterion provided a reliable approach for confirming and ruling out PE in a retrospective setting. The fact that none of the 33 patients who would not have required imaging per YEARS algorithm had PE is reassuring and provides retrospective validation of the YEARS criteria in routine clinical practice.

We found only a few patients (n=5) in the first trimester who met the study criteria (D-dimer testing and radiological imaging). The majority of 1st-trimester patients were assessed clinically without D-dimer testing because of the treating physician's hesitance to order radiological imaging in this sensitive period for the fetus based on a potentially non-specific D-dimer elevation. Furthermore, the risk of venous thromboembolism is higher in the third trimester of pregnancy [17]. Consistent with expectations from the pregnancy-adapted YEARS algorithm, all four 1st trimester patients with 1-3 YEARS criteria who underwent imaging despite a D-dimer of <0.5μg/mL did not have PE as well as the one patient with no YEARS criteria who underwent imaging with a D-dimer of <1μg/mL.

A more meaningful evaluation was possible in the 2nd and 3rd trimesters with a relatively more significant number of patients. Based on our data, the most apparent impact of the YEARS algorithm is likely to be seen in the 2nd trimester. Over three-fourths of pregnant women with suspected PE in this trimester could have been spared imaging based on the YEARS algorithm, and we confirmed that none of those had PE. The primary reason for this favourable scenario is the relatively preserved specificity of D-dimer in this trimester as 35% of pregnant women had a D-dimer of <0.5, excluding PE regardless of the number of YEARS criteria while the other 65% had a D-dimer <1, which would exclude PE if there are no YEARS criteria. Both constellations combined resulted in a high fraction (76.5%) of 2nd-trimester patients that can be spared imaging with no incidence of PE.

The curtailed specificity of the D-dimer in the 3rd trimester substantially reduced the utility of the YEARS algorithm. Only 5.6% of our patients had a D-dimer of <0.5, hence this "safe" level was not available to exclude PE in the vast majority of

pregnant women with 1-3 YEARS criteria. The low percentage of healthy third-trimester women (i.e., those without suspected PE) with a normal D-dimer level of <0.5 is well-documented in the literature [18, 19].

About 76% of 3rd-trimester patients had a D-dimer <1 that could exclude PE if there were no YEARS criteria. There was an insufficient number of patients in this category (~ 11% of 3rd-trimester patients), this may be due to the 3rd-trimester patients more commonly having nonspecific symptoms mimicking PE, resulting in the assignment of the one YEARS criterion "pulmonary embolism is the most likely diagnosis, above any alternative diagnosis" to most of these patients. Nevertheless, imaging could have been avoided and PE safely excluded in one-sixth of patients in the 3rd trimester representing ~45% of all patients in whom imaging could have been avoided in the current study.

There is conflicting data on the use of D-dimer in pregnancy. Most studies used a D-dimer cut-off value in pregnant women that are identical to that used in males and nonpregnant females, which proved to be invalid because of the pregnancy-induced increase in D-dimer [18, 19]. The pregnancy-adapted YEARS algorithm uses a higher cut-off D-dimer level combined with clinical criteria, thereby increasing the specificity of D-dimer and reducing the need for imaging studies in pregnant women with a very low likelihood of PE. In our study, the use of the higher cut-off D-dimer level of <1 rather than the traditional <0.5 could have reduced the need for imaging in 18 of 112 patients (1, 7 and 10 in the 1st, 2nd, and 3rd trimester, respectively), with highest impact noted in the 3rd trimester.

In addition to CTPA and Q (V/Q) scans that could have been avoided in 33 of the 112 patients examined, Doppler U/S could also have been avoided in 31/112 (27.7%) of patients who have undergone this test despite not having any clinical suspicion of deep vein thrombosis. Such patients not supposed to undergo the Doppler U/S per YEARS algorithm, and the lack of any DVT in these patients lends support to this notion. The use of Doppler US is not cost-effective unless clinically indicated, although it is still advised in some of the guidelines to avoid radiological imaging, as shown by Righini et al. (2018) [20].

Interestingly, Q (V/Q) scan was the preferred imaging modality in pregnant ladies with suspected PE, especially in the first and second trimesters, when all patients who underwent imaging had a Q (V/Q) scan while CTPA was exclusively performed in the third trimester. Performing a Q (V/Q) scan rather than CTPA during early pregnancy may be explained by published data demonstrating that both imaging methods have similar diagnostic accuracy but that Q (V/Q) scan results in lower radiation dose to the mother [21-23]. Finally, it should be noted that performing a lung perfusion scan (Q scan) alone, with a ventilation scan (V scan) only performed if the Q scan is inconclusive is an acceptable approach. This approach is both effective and potentially safer for both the mother and fetus as it substantially reduces the radiation dose in the vast majority of pregnant women undergoing nuclear imaging and has been successfully used in the vast majority of our patients [11].

Limitations of our study include its retrospective nature resulting in a significant fraction of patients not having their D-dimer measured (16 patients) being excluded (a requirement of the YEARS algorithm) and a small fraction having incomplete data to determine the YEARS criteria. Also, our study was single-center and included a relatively small number of patients, particularly in the 1st trimester.

In conclusion, radiological imaging, including lung scintigraphy, is frequently performed but is undesired in pregnant women with suspected PE unless necessary, resulting in efforts aimed at reducing the need for radiological imaging in these patients. Our study has shown that the pregnancy-adapted YEARS diagnostic algorithm could have resulted in safely ruling out acute PE in about one-third of pregnant women with suspected PE without performing radiological imaging. Adoption of the pregnancy-adapted YEARS algorithm has significant implications in the clinical practice of conventional radiology and nuclear medicine by sparing patients CTPA, lung perfusion and/or perfusion/ventilation scintigraphy when it is unlikely to impact on patient diagnosis, thereby avoiding potential harm to the mother and fetus.

Bibliography

1. Say L, Chou D, Gemmill A et al. Global causes of maternal death: a WHO systematic analysis. *Lancet Glob Health* 2014; 2(6): e323-33.
2. Wan T, Skeith L, Karovitch A et al. Guidance for the diagnosis of pulmonary embolism during pregnancy: consensus and controversies. *Thromb Res* 2017; 157: 23-8.
3. Konstantinides SV, Torbicki A, Agnelli G et al. Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J* 2014; 35: 3033-69.
4. Leung AN, Bull TM, Jaeschke R et al. ATS/STR Committee on Pulmonary Embolism in Pregnancy. American Thoracic Society documents: an official American Thoracic Society/Society of Thoracic Radiology clinical practice guideline-evaluation of suspected pulmonary embolism in pregnancy. *Radiology* 2012; 262: 635-46.
5. Touhami O, Marzouk SB, Bennasr L et al. Are the Wells Score and the Revised Geneva Score valuable for the diagnosis of pulmonary embolism in pregnancy? *Eur J Obstet Gynecol Reprod Biol* 2018; 221: 166-71.
6. Hunt BJ, Parmar K, Horspool K et al. The DiPEP (Diagnosis of PE in Pregnancy) biomarker study: An observational cohort study augmented with additional cases to determine the diagnostic utility of biomarkers for suspected venous thromboembolism during pregnancy and puerperium. *Br J Haematol* 2018; 180(5): 694-704.
7. Revel MP, Cohen S, Sanchez O et al. Pulmonary embolism during pregnancy: diagnosis with lung scintigraphy or CT angiography? *Radiology* 2011; 258(2): 590-8.
8. van der Pol LM, Tromeur C, Bistervels IM et al. Pregnancy-Adapted YEARS Algorithm for Diagnosis of Suspected Pulmonary Embolism. *N Engl J Med* 2019; 380: 1139-49.
9. Tromeur C, van der Pol LM, Le Roux PY et al. Computed tomography pulmonary angiography versus ventilation-perfusion lung scanning for diagnosing pulmonary embolism during pregnancy: a systematic review and meta-analysis. *Haematologica* 2019; 104: 176-88.
10. Huisman MV, Klok FA. Diagnostic management of acute deep vein thrombosis and pulmonary embolism. *J Thromb Haemost* 2013; 11: 412-22.
11. Bajc M, Schümichen C, Grüning Tt al. EANM guideline for ventilation/perfusion single-photon emission computed tomography (SPECT) for diagnosis of pulmonary embolism and beyond. *Eur J Nucl Med Mol Imaging* 2019; 46(12): 2429-51.
12. Kruip MJ, Leclercq MG, van der Heul C et al. Diagnostic strategies for excluding pulmonary embolism in clinical outcome studies. A systematic review. *Ann Intern Med* 2003; 138: 941-51.

13. Van der Hulle T, Cheung WY, Kooij S et al. Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study. *Lancet* 2017; 390: 289-97.
14. Konstantinides SV, Meyer G, Becattini C et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS) The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). *Eur Heart J* 2020; 41(4): 543-603.
15. Langlois E, Cusson-Dufour C, Moumneh T et al. Could the YEARS algorithm be used to exclude pulmonary embolism during pregnancy? Data from the CT-PE-pregnancy study. *J Thromb Haemost* 2019; 17(8): 1329-34.
16. Van Maanen R, Rutten FH, Klok FA et al. validation and impact of a simplified clinical decision rule for diagnosing pulmonary embolism in primary care: design of the PECAN prospective diagnostic cohort management study. *BMJ Open* 2019; 9(10): e031639.
17. Pomp E, Lenselink A, Rosendaal F, Doggen C. Pregnancy, the postpartum period, and prothrombotic defects: Risk of venous thrombosis in the MEGA study. *J Thromb Haemost* 2008; 6: 632-7.
18. Hedengran KK, Andersen MR, Stender S, Szecsi PB. Large D-Dimer fluctuation in normal pregnancy: a longitudinal cohort study of 4,117 Samples from 714 Healthy Danish Women. *Obstet Gynecol Int* 2016; 2016: 3561675.
19. Goodacre S, Horspool K, Nelson-Piercy C et al. On behalf of the DiPEP research group. The DiPEP study: an observational study of the diagnostic accuracy of clinical assessment, D-dimer, and chest x-ray for suspected pulmonary embolism in pregnancy and postpartum. *BJOG* 2019; 126: 383-92.
20. Righini M, Robert-Ebadi H, Antoine Elias A et al. For the CT-PE-Pregnancy Group Diagnosis of Pulmonary Embolism During Pregnancy: A Multicenter Prospective Management Outcome Study. *Ann Intern Med* 2018; 169(11): 766-73.
21. Grüning T, Mingo RE, Gosling MG et al. Diagnosing venous thromboembolism in pregnancy. *Br J Radiol* 2016; 89: 20160021.
22. Bokan A, Matijasevic J, Vucicevic Trobok J. Pregnancy adapted YEARS algorithm: can YEARS do more for pregnant women? *Breathe* 2020; 16:190307.
23. Van Mens TE, Scheres LJJ, de Jong PG et al. Imaging for the exclusion of pulmonary embolism in pregnancy. *Cochrane Database Syst Rev* 2017; 1(1): CD011053.