# Safety of the Combination of PERC and YEARS Rules in Patients With Low Clinical Probability of Pulmonary Embolism: A Retrospective Analysis of Two Large European Cohorts

Judith Gorlicki, MD, Andrea Penaloza, MD, PhD, Boris Germeau, MD, Thomas Moumneh, MD, Anne-Laure Philippon, MD, Jennifer Truchot, MD, Delphine Douillet, MD, Charlotte Steinier, MD, Caroline Soulié, MD, Ben Bloom, MD, Marine Cachanado, MsC, Pierre-Marie Roy, MD, PhD, and Yonathan Freund, MD, PhD

## ABSTRACT

**Background:** This study aimed to determine the failure rate of a combination of the PERC and the YEARS rules for the diagnosis of pulmonary embolism (PE) in the emergency department (ED).

**Methods:** We performed a retrospective analysis of two European cohorts of emergency patients with low gestalt clinical probability of PE (PROPER and PERCEPIC). All patients we included were managed using a conventional strategy (D-dimer test, followed, if positive, by computed tomographic pulmonary angiogram (CTPA). We tested a diagnostic strategy that combined PERC and YEARS to rule out PE. The primary endpoint was a thromboembolic event diagnosed in the ED or at 3-months follow-up. Secondary endpoints included a thromboembolic event at baseline in the ED and a CTPA in the ED. Ninety-five percent confidence intervals (CIs) of proportions were calculated with the use of Wilson's continuity correction.

**Results:** We analyzed 1,951 patients (mean ± SD age = 47 ± 18 years, 56% women) with an overall proportion of patients with PE of 3.5%. Both PERC and YEARS strategies were associated with 11 missed PE in the ED: failure rate 0.57 (95% CI = 0.32–1.02). At 3-month follow-up, the overall failure rate was 0.83% (95% CI = 0.51–1.35). Among the 503 patients who underwent a CTPA (26%), the use of the PERC–YEARS combination would have ruled out PE without CTPA in 249 patients (50% [95%CI = 45%–54%], absolute reduction 13% (95% CI = 11%–14%]).

**Conclusion:** The combination of PERC then YEARS was associated with a low risk of PE diagnostic failure and would have resulted in a relative reduction of almost half of CTPA.

From the Emergency Department, Hôpital Lariboisière (JG, JT), the Emergency Department, Hôpital Pitié-Salpêtrière (ALP, YF), and the Clinical Research Platform, Hôpital Saint Antoine (MC), Assistance Publique–Hôpitaux de Paris (APHP), Paris, France; the Emergency Department, Cliniques Universitaires St-Luc, Université Catholique de Louvain (AP, BG, CSt), Brussels, Belgium; the Emergency Department, Centre Hospitalier Universitaire Angers, Institut Mitovasc, Université d'Angers (TM, DD, CSo, PMR), Angers, France; the Emergency Department, Royal London Hospital, Barts Health NHS Trust (BB), London, UK; and the Sorbonne Université (YF), Paris, France.
Received May 22, 2018; revision received June 21, 2018; accepted June 23, 2018.
The authors have no relevant financial information or potential conflicts to disclose.
Author Contributions: YF, AP, and PMR conceived the study and wrote the protocol; JG carried the main statistical analysis and interpretation of the results; BG, DD, CSt, CSo, TM, ALP, and JT recruited patients; MC handled data management and statistical supervision; YF and JG drafted the manuscript; all authors made substantial contribution to the writing of the manuscript; and YF is responsible for the paper as a whole.
Supervising Editor: Shahriar Zehtabchi, MD.
Address for correspondence and reprints: Yonathan Freund, MD, PhD; e-mail: yonatman@gmail.com.
ACADEMIC EMERGENCY MEDICINE 2019;26:23–30.


doi: 10.1111/acem.13508
ISSN 1553-2712

The diagnosis of pulmonary embolism (PE) in the emergency department (ED) remains challenging. The nonspecific presentation of this potential lethal pathology and wide accessibility to computed tomographic pulmonary angiogram (CTPA) led to a significant rise in resource utilization and number of diagnosed PE, with no clear benefit in terms of outcomes.[1,2] The conventional diagnostic strategy in Europe first mandates the assessment of the clinical probability of PE, with unstructured gestalt, Wells rule, or Geneva rule, in either their original or their simplified scheme. In patients with a low or moderate clinical probability this strategy includes D-dimer testing, followed if positive by a CTPA, and is associated with a very low rate of failure (<0.2% in recent large trials).[3–5] This very low rate is in part due to the ever-decreasing prevalence of PE among this subset of patients, now below 5%.[3,4,6]

To safely limit ED resource use and especially reduce the number of CTPA examination, two rules were recently validated. The Pulmonary Embolism Rule-out Criteria (PERC) is an eight-item clinical decision rule that allows the emergency physician to obviate the need for D-dimer in patients with a low clinical probability of PE and a PERC score of zero (i.e., age < 50 years, heart rate < 100 beats/min, $SaO_2$ > 94%, no hemoptysis, no estrogen use, no surgery or trauma in the past 4 weeks, no unilateral leg swelling, and no previous venous thromboembolism).[7] The YEARS rule, that can be seen as a simplified Wells rules with three binary items (namely "hemoptysis," "clinical sign of deep vein thrombosis," and "PE the most likely diagnosis") also allowed a safe reduction in imaging studies by raising to 1000 μg/L (instead of 500 or age × 10) the threshold of D-dimer in patients without any YEARS item compared to the two-level Wells rule.[8] These two rules were recently prospectively validated.[3,4,9] The reported failure rate of PERC was < 1% in the PROPER and the PERCEPIC European cohorts, with a potential absolute reduction of more than 10% of CTPA.[3] Similarly, the reported failure rate of YEARS was < 1%, associated with a 14% absolute reduction of CTPA.[9] However, it is unclear whether these two rules could be safely combined and further reduce CTPA use in the ED.

The main objective of this study was to determine whether the combination of PERC and YEARS strategies are associated with a low diagnostic failure rate in ED patients with a low gestalt clinical probability. The secondary objective was to assess the reduction in CTPA use with this strategy combination.

## METHODS

### Study Design

This study is a post hoc analysis of two European prospective cohorts of ED patients with low clinical probability of PE with 3-month follow-up. The PROPER cohort includes 1,916 patients recruited from 14 EDs in France, in 2015–2016 in a cluster randomized clinical trial that compared a PERC-based strategy to the conventional diagnostic strategy for PE.[3] In the control arm, the workup for PE included D-dimer testing followed if positive by a CTPA. In the intervention arm, the PERC score was assessed. In patients with a PERC score of zero, PE was ruled out without any other testing. In patients with a positive PERC score, the workup for PE was similar as in the control arm. The PERCEPIC cohort includes 1,757 patients from an observational study on PERC performances recruited in 12 EDs France and Belgium in 2015 to 2016, including 1,052 low-risk patients.[4] In both studies, the clinical probability of PE was assessed by the emergency physicians with the use of implicit unstructured gestalt assessment. In the PROPER cohort, only patients with low gestalt probability were included, selected by the emergency physician as having a low clinical probability (<15%).[10] In the PERCEPIC cohort, the emergency physician completed their implicit clinical probability assessment by ticking one of the three categories low, moderate, or high. Only patients with a low gestalt clinical probability were included in this analysis (Figure 1).

Patients were followed-up at 3 months by phone interview, and the presence of a thromboembolic event during follow-up was confirmed by an independent adjudication committee, in both studies. In case of inability to perform the phone interview, the patient's general practitioner was contacted. For patients lost to follow-up, death records from the administrative records of the patient's hometown were sought. All deaths that occurred during follow-up were reviewed by the adjudication committee and a sudden unexplained death where a thromboembolic event could not be excluded was considered as a fatal PE.

The study protocols were approved by local ethic committees and institutional review boards, and as a post hoc analysis on anonymized data, patient's consent was waived for this study. We adhered to the Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) criteria for cohort studies.[11]

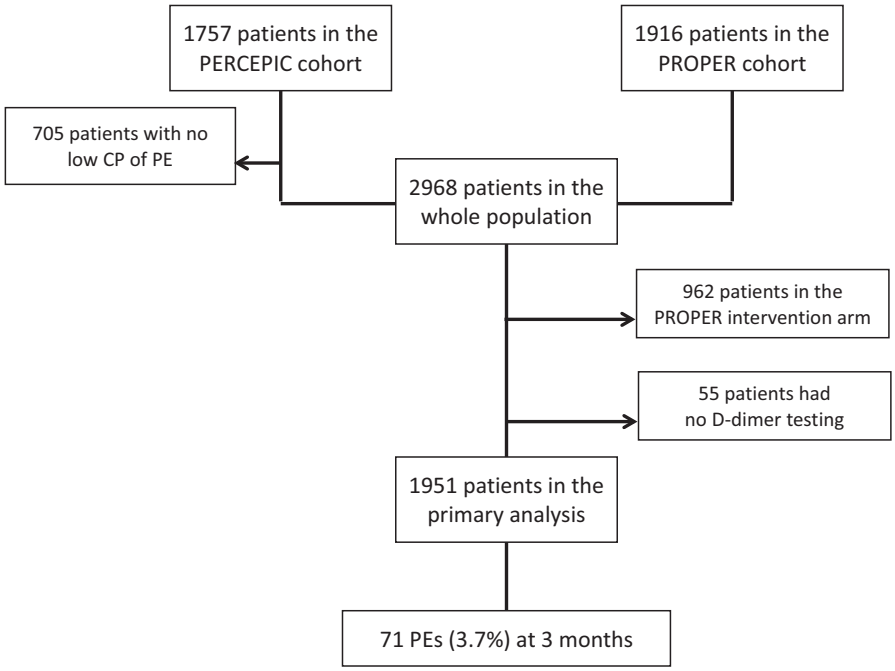


**Figure 1.** Flow diagram. CP = clinical probability; PE = pulmonary embolism.

## Selection of Participants

Patients were included in the two cohorts if they had a clinical suspicion of PE defined by a new-onset presence or worsening of shortness of breath or chest pain. Exclusion criteria composed other obvious causes for their acute presentation, or ongoing anticoagulant treatment, and pregnancy in the PROPER cohort.[4,12]

In this study, we included patients with a low gestalt clinical probability of PE and managed under the conventional strategy of D-dimer testing followed if positive (age-adjusted threshold) by a CTPA.[13,14] In the two studies, a low gestalt clinical probability corresponded to an unstructured impression of the treating physician as a less than 15% risk of PE. We selected patients with a low clinical probability so that PERC rule can be applied.[7] Furthermore, we excluded patients in the "intervention arm" of PROPER since some patients had their suspicion of PE ruled out with no D-dimer testing, and therefore we would be unable to apply the YEARS strategy to them. For the same reasons, we also excluded patients with no D-dimer testing in the other arm.

## Data Collection and Processing

We tested a diagnostic strategy that combined PERC and YEARS: a PE is ruled out with no CTPA for patients with:

1. PERC score of zero, or
2. PERC positive and YEARS score of 0 and D-dimer < 1000 μg/L, or
3. PERC positive and YEARS positive and D-dimer < the age-adjusted threshold (age × 10 μg/L).

PERC and Wells scores were prospectively collected in the both cohorts. The three items in the YEARS score are recorded in the Wells score, and hence both PERC and YEARS score were prospectively obtained. Since we did not include patients from the intervention group of PROPER and since YEARS score was not used in the ED, these two scores were retrospectively calculated on their prospectively collected components. Since the combination of PERC and YEARS could have been applied to the "intervention group" of PROPER, we performed a sensitivity analysis on the whole cohort of patients with low clinical probability.

## Outcome Measure

The primary objective was to assess the safety of a diagnostic strategy that combined PERC and YEARS. The secondary objective was to assess the reduction of CTPA. The primary endpoint was the diagnosis of a thromboembolic event in the ED or at 3-month follow-up. Secondary endpoints included a diagnosis of thromboembolic event during the index visit at baseline in the ED and CTPA performed in the ED. A thromboembolic event was diagnosed in the presence

of evidence of PE in the CTPA or at 3 months after confirmation by an independent adjudication committee in both studies. As the benefit of diagnosing an isolated subsegmental PE (i.e., without more proximal PE nor deep venous thrombosis) is unclear, we also performed a preplanned sensitivity analysis excluding isolated subsegmental PEs from the definition of the primary endpoint.[15]

### Primary Data Analysis

Baseline characteristics of the main analysis population were expressed as number (percentage) for qualitative variables, and mean (± standard deviation [SD]) or median (interquartile range [IQR]) for quantitative variables, depending on their distribution. The 95% confidence intervals (CIs) were calculated with Wilson continuity correction. To validate the safety of a decision rule in our population, we followed the recommendation of Dronkers et al.:[16] with an overall proportion of patients with PE of 3.5%, the upper bound of the 95% CI of our primary endpoint should be below 1.84%.

The analysis of the primary endpoint was performed on the main population that included all patients from both cohorts who were investigated as recommended by European guidelines, which mandates a D-dimer testing ($n$ = 1,951 of 2,006). However, we included patients with D-dimer testing who were not managed as recommended (namely, positive D-dimer and no CTPA or CTPA despite negative D-dimer) and performed a sensitivity analysis for the secondary endpoints with the theoretical population without guidelines violation.

A sensitivity analysis was performed on the whole population for the performance of the "PERC then YEARS" combination, but not for "YEARS" only as half of the PROPER cohort were already managed under PERC rules. We also performed a sensitivity analysis for the primary endpoint after the exclusion of isolated subsegmental PEs.

## RESULTS

Among the 2,968 patients with a low clinical probability included in the two cohorts, 962 were excluded was they were in the "intervention arm" of the PROPER cohort, and an additional 55 patients were excluded because they did not have D-dimer testing. Therefore, the main sample of this study comprised 1,951 patient (mean ± SD age = 47 ± 18 years, 56% women). The main baseline characteristics are presented in Table 1.

The overall proportion of patients with PE at 3 months was 3.7% in our analysis population. Among the 1,951 low-risk patients included in this study, 685 (35%) had a PERC score of zero and 1,427 (73%) a negative YEARS rule (i.e., YEARS score of zero and D-dimer < 1,000 μg/L). The use of either PERC or YEARS would have missed 11 PEs in the ED, which corresponds to a failure rate of 0.57% (95% CI = 0.32%–1.02%) for the diagnosis of PE at 3 months (Table 2). Overall, 1,526 patients (78%) had a negative PERC rule or a negative YEARS rule. The combination of PERC then YEARS would have missed 16 PEs—a failure rate of 0.83% (95% CI = 0.51%–1.35%). After the exclusion of isolated subsegmental PEs, the failure rate of the combination was 0.68% (95% CI = 0.40%–1.15%). A sensitivity analysis on the whole cohort showed a similar failure rate of 0.76% (95% CI = 0.50%–1.14%) and also a similar failure rate when counting overall PEs at 3-month follow-up (Table 2).

Overall, 503 patients (26%) underwent a CTPA. Among them, 117 had a PERC score of zero, and 208 had a YEARS score of zero and a D-dimer < 1,000 μg/L, which corresponds to 23 and 41% respective reductions of CTPA use. The combination of "PERC then YEARS" would have resulted in a total of 249 CTPA that could have been avoided, a relative reduction of 50% (95% CI = 45%–54%) and an absolute reduction of 13% (95% CI = 11%–14%; Table 3). Beside CTPA avoidance, the use of PERC would also have avoided an additional 685 (35%) patients with D-dimer testing. The incremental value of the "PERC then YEARS" combination compared to the different strategies is reported in Table 3. The diagnostic yield of CTPA was 13% with the conventional strategy and would have been of 22% with the use of "PERC then YEARS" combination.

The overall adherence to European guidelines was 93.5%. On 570 CTPA that should have been ordered, 266 studies would have been avoided (a relative reduction of 47% [95% CI = 43%–51%])

## DISCUSSION

In this retrospective analysis of two prospective cohort studies on low-risk patients assessed for PE in the ED, we report that the use of PERC, YEARS, and their combination "PERC then YEARS" resulted in a low

Table 1
Baseline Characteristics

| | PROPER (*n* = 1,916) | PERCEPIC (*n* = 1,052) | Total (*n* = 2,968) | Main analysis (*n* = 1,951) |
|---|---|---|---|---|
| Age (years) | 44 (±16.7) | 49.6 (±19.1) | 46 (±17.8) | 47 (±18) |
| Age > 50 years | 684 (35.7) | 507 (48.2) | 1191 (40.2) | 835 (42.8) |
| Sex | | | | |
| Male | 936 (48.8) | 448 (42.6) | 1,384 (46.6) | 854 (43.8) |
| Female | 980 (51.2) | 604 (57.4) | 1,584 (53.4) | 1,097 (56.2) |
| Heart rate | 84 (17.2) | 82 (17.8) | 83 (17.4) | 84 (18) |
| Heart rate > 100 | 313 (16.3) | 144 (13.7) | 457 (15.4) | 320 (16.4) |
| $SpO_2$ | 98.1 (±3.3) | 97 (±3) | 97.8 (±3) | 97.7 (±3.2) |
| Sat < 95% | 100 (5) | 117 (11.1) | 217 (7.3) | 156 (8) |
| Temperature (°C) | 36.7 (±0.5) | 36.9 (±3.2) | 36.8 (±1.8) | 36.8 (±2.3) |
| Risk factor for PE | | | | |
| Estrogen use | 160 (8.3) | 131 (12.5) | 291 (9.8) | 226 (11.6) |
| Clinical sign of DVT | 103 (5.4) | 32 (3) | 135 (4.6) | 94 (4.8) |
| prolonged immobilization | 48 (2.5) | 53 (5) | 101 (3.4) | 82 (4.2) |
| History of PE or DVT | 70 (3.7) | 76 (7.2) | 146 (4.9) | 112 (5.7) |
| Hemoptysis | 18 (0.9) | 20 (1.9) | 38 (1.3) | 30 1.52) |
| Active malignancy | 18 (0.9) | 33 (3.1) | 51 (1.6) | 38 (1.9) |
| PE is the most likely diagnosis | 201 (10.5) | 41 (3.9) | 242 (8.2) | 192 (9.8) |
| Simplified Geneva score | | | | |
| 0 | 476 (24.8) | 321 (30.5) | 797 (26.8) | 501 (25.7) |
| 1 | 1,123 (58.6) | 587 (55.8) | 1,710 (57.6) | 1,132 (58) |
| 2 | 259 (13.5) | 144 (13.7) | 403 (13.6) | 285 (14.6) |
| 3 | 50 (2.6) | 0 | 50 (1.7) | 27 (1.4) |
| 4 | 8 (0.4) | 0 | 8 (0.3) | 6 (0.3) |
| Wells score | | | | |
| <2 (low risk) | 1,621 (84.6) | 999 (95) | 2,620 (88.3) | 1,695 (86.9) |
| 2–6 (intermediate risk) | 281 (14.7) | 53 (5) | 334 (11.2) | 245 (12.5) |
| >6 (high risk) | 14 (0.7) | 0 | 14 (0.5) | 11 (0.6) |
| PERC score | | | | |
| 0 | 826 (43) | 337 (32) | 1,163 (39.2) | 685 (35) |
| ≥1 | 1,090 (57) | 715 (68) | 1,805 (60.8) | 1,266 (65) |
| YEARS score | | | | |
| 0 | 1,505 (78.5) | 964 (91.6) | 2,469 (83.2) | 1,591 (81.6) |
| 1 | 411 (21.5) | 88 (8.4) | 499 (16.8) | 360 (18.4) |
| Tested with D-dimer | 1,469 (76.7) | 1,008 (95.8) | 2,477 (83.5) | 1,951 (100) |
| Positive D-dimer test* | 366 (24.9) | 338 (33.5) | 704 (28.4) | 570 (29) |
| D-dimer value (μg/L) | | | | |
| 0–500 | 1,025 (79.8) | 623 (61.8) | 1,648 (66.5) | 1,290 (66.1) |
| 501–1,000 | 274 (18.7) | 189 (19.4) | 463 (18.7) | 356 (18.3) |
| >1,000 | 170 (11.5) | 196 (18.8) | 366 (14.8) | 305 (15.6) |
| CTPA in the ED | 349 (18.2) | 300 (28.5) | 649 (21.9) | 503 (26) |
| PE diagnosed in the ED | 40 (2.1) | 44 (4.2) | 84 (2.8) | 69 (3.5) |
| ISS PE | 4 (0.2) | 4 (0.4) | 8 (0.3) | 7 (0.4) |
| PE diagnosed at 3 months | 41 (2.2) | 46 (4.4) | 87 (3) | 71 (3.7) |
| ISS PE | 4 (0.2) | 4 (0.4) | 8 (0.3) | 7 (0.4) |
| All-cause death at 3 months | 5 (0.3) | 2 (0.2) | 7 (0.2) | 4 (0.2) |

Data are reported as mean (±SD) or *n* (%).
CTPA = computed tomography pulmonary angiogram; DVT = deep venous thrombosis; ISS = isolated subsegmental; PERC = Pulmonary Embolism Rule-out Criteria; PE = pulmonary embolism.
*Positive D-dimer if >500 μg/L in patients 50 years old and under and if > age × 10 μg/L in patients over 50 years old.

Table 2
Failure Rate of the Different Diagnostic Strategies

| Strategy | Missed PE (% [95% CI]) | |
|---|---|---|
| | At 3 Months ($n$ = 1,925) | In the ED ($n$ = 1,951) |
| Main analysis population | | |
| Usual | 0.10 (0.00–0.27) ($n$ = 2) | 0 ($n$ = 0) |
| PERC | 0.57 (0.32–1.02) ($n$ = 11) | 0.46 (0.24–0.87) ($n$ = 9) |
| YEARS | 0.57 (0.32–1.02) ($n$ = 11) | 0.46 (0.24–0.87) ($n$ = 9) |
| PERC then YEARS | 0.83 (0.51–1.35) ($n$ = 16) | 0.72 (0.43–1.20) ($n$ = 14) |
| Without isolated subsegmental PEs | | |
| Usual | 0.10 (0.00–0.27) ($n$ = 2) | 0 ($n$ = 0) |
| PERC | 0.47 (0.25–0.89) ($n$ = 9) | 0.36 (0.17–0.74) ($n$ = 7) |
| YEARS | 0.42 (0.21–0.82) ($n$ = 8) | 0.31 (0.14–0.67) ($n$ = 6) |
| PERC then YEARS | 0.68 (0.40–1.15) ($n$ = 13) | 0.56 (0.32–1.00) ($n$ = 11) |
| Whole population | ($n$ = 2908) | ($n$ = 2968) |
| PERC | 0.52 (0.31–0.85) ($n$ = 15) | 0.40 (0.23–0.71) ($n$ = 12) |
| PERC then YEARS | 0.76 (0.50–1.14) ($n$ = 22) | 0.64 (0.41–1.00) ($n$ = 19) |

PE = pulmonary embolism; PERC = Pulmonary Embolism Rule-out Criteria.

Table 3
CTPA Use With the "PERC Then YEARS" Strategy Compared With Different Diagnostic Strategies

| Strategy Compared to PERC Then YEARS | No. CTPA avoided | Absolute Reduction, % (95% CI) | Relative Reduction, % (95% CI) |
|---|---|---|---|
| Usual | 249 | 12.8 (11.3–14.3) | 49.5 (45.0–54.0) |
| PERC | 132 | 6.8 (5.7–8.0) | 26.2 (22.4–30.3) |
| YEARS | 45 | 2.3 (1.6–3.1) | 8.9 (6.6–11.8) |

CTPA = computed tomography pulmonary angiography; PERC = Pulmonary Embolism Rule-out Criteria.

failure rate and therefore appeared safe, with a substantial reduction of CTPA use in the ED.

The increasingly availability of CTPA and fear of missing a PE led to a rise in CTPA use and a decreased prevalence of PE among patients tested in the ED.[2,6] The challenge now is more to safely reduce exposure to irradiative and time-consuming investigations than to further reduce the failure rate of our diagnostic strategies. In this context, several strategies were tested and validated such as limiting the indication for D-dimer testing or raising the D-dimer threshold with an age adjustment or a clinical decision rule.[4,5,9,12]

After a meta-analysis of 11 studies, PERC was considered a safe strategy for the early exclusion of PE.[17] Two recent European prospective cohort studies confirmed this safety and the use of PERC should now be widely accepted among patients with low clinical probability. YEARS, on the other hand, has only been prospectively tested in one cohort in Netherlands and showed that, compared to a two-level Wells rule, the YEARS rule safely allows a significant reduction of CTPA by raising the D-dimer threshold to 1,000 μg/L. Our study supports the safe use of YEARS as this rule would have allowed a 41% relative reduction in the use of CTPA with only 11 missed PE (failure rate of 0.57% [95% CI = 0.32%–1.02%]). Historically, the diagnostic safety threshold was set at 2.7%–3%, which corresponded to the upper bound of the false-negative rate of pulmonary angiogram.[5,18,19] However, recent recommendations suggested that this threshold should be adjusted to the prevalence of PE in the studied population.

A recent retrospective analysis of a part of the YEARS cohort suggested that this combination may not be safe for the exclusion of PE with a 1.4% failure rate and a wide 95% CI that did not lead to the conclusions that there is a sufficiently low failure rate. However, patients included in this study were not only those with a low clinical probability of PE, and PERC was intended to be used only in this specific population. The low rate of PERC-negative patients (19%) in this study contrasts with the usual rate found in other studies aimed at low-risk patients (30%–50%).[12,20,21]

Moreover, the overall 14% PE prevalence of their study confirms that their population did not comprise only low-risk patients.[22]

In this analysis, we report that combining PERC then YEARS resulted in a very low failure rate, with the upper bound of its 95% CI below the recommended threshold of 1.84%. Of note this upper bound is also below 1.4%, which is considered as the testing threshold for PE, below what testing for PE would be inappropriate because of the potential harm of unneeded diagnostic tests.[23] This suggests that combining these two rules is safe for the exclusion of PE in low-risk patients in the ED and that this would be associated with a 50% relative reduction in the rate of CTPA use compared to the conventional strategy. The reduction in CTPA achieved with the use of the combination of PERC then YEARS may seem close to the one achieved with YEARS only (8.9% relative reduction) with a slightly increased failure rate (0.72% vs. 0.46% for YEARS alone) and therefore can be seen of limited added value. However, this strategy would be also associated with a significant reduction in the rate of D-dimer testing (35%). The use of this combination could have resulted in some more benefit, such as shorter ED length of stay or reduced number of patients exposed to undue anticoagulant therapy. A prospective trial should evaluate the effect of this combination in terms of ED resource use and economic benefit.

## LIMITATIONS

Our study presents some limitations. First the YEARS items were not prospectively calculated. However, in the two cohort studies, all items from the Wells score were prospectively recorded; therefore, we believe that our calculation of YEARS is accurate. Second, all patients were tested for PE with D-dimer, which could have led to some false-positive findings or isolated subsegmental PEs that did not need to be diagnosed. The PE failure rate could be actually lower than the one we report here. A prospective study that would implement this combination rule may actually find a lower rate of missed PE, as was the case with the PROPER trial. We performed a sensitivity analysis with the exclusion of isolated subsegmental PEs; however, the presence of deep venous thrombosis were not systematically sought, and therefore we cannot ascertain that they were true "isolated" subsegmental PEs in whom equipoise remains on the benefit of anticoagulation. Third, the overall adherence was 93.5% and therefore the proportion of CTPA avoided following different strategies would have been different. However, we found this difference to be moderate as the relative reduction of CTPA from the use of "PERC then YEARS" would have been 47% instead of 50%. Finally, although we followed Dronkers et al.[16] recommendation, we believe that the overall failure rate of a strategy may not be the optimal mean to assess the safety: the real false-negative rate (i.e., number of PE missed divided by number of PE diagnosed or "1 – sensitivity") could be an important marker for this, although it is rarely reported conversely to the overall failure rate being "1 – negative predictive value," highly dependent on the prevalence.

## CONCLUSION

The combination of PERC and YEARS was associated with a low risk of diagnostic failure, with an upper bound of the 95% confidence interval below the recommended maximal failure rate of 1.84%. This combination would have resulted in a relative reduction of almost half of computed tomographic pulmonary angiogram.

## References

1. 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.
2. Wiener RS, Schwartz LM, Woloshin S. Time trends in pulmonary embolism in the united states: evidence of overdiagnosis. Arch Intern Med 2011;171:831–7.
3. Freund Y, Cachanado M, Aubry A, et al. Effect of the Pulmonary Embolism Rule-Out Criteria on subsequent thromboembolic events among low-risk emergency department patients: the PROPER randomized clinical trial. JAMA 2018;319:559–66.
4. Penaloza A, Soulié C, Moumneh T, et al. Pulmonary embolism rule-out criteria (PERC) rule in European patients with low implicit clinical probability (PERCEPIC): a multicentre, prospective, observational study. Lancet Haematol 2017;4:e615–21.
5. Righini M, Van Es J, Den Exter PL, et al. Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study. JAMA 2014;311:1117–24.
6. Pernod G, Caterino J, Maignan M, et al. D-dimer use and pulmonary embolism diagnosis in emergency units: why is there such a difference in pulmonary embolism prevalence

between the United States of America and countries outside USA? PLoS One 2017;12:e0169268.
7. Kline JA, Mitchell AM, Kabrhel C, Richman PB, Courtney DM. Clinical criteria to prevent unnecessary diagnostic testing in emergency department patients with suspected pulmonary embolism. J Thromb Haemost 2004;2:1247–55.
8. van Es J, Beenen LF, Douma RA, et al. A simple decision rule including D-dimer to reduce the need for computed tomography scanning in patients with suspected pulmonary embolism. J Thromb Haemost 2015;13:1428–35.
9. 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 Lond Engl 2017;390:289–97.
10. Runyon MS, Webb WB, Jones AE, Kline JA. Comparison of the unstructured clinician estimate of pretest probability for pulmonary embolism to the Canadian score and the Charlotte rule: a prospective observational study. Acad Emerg Med 2005;12:587–93.
11. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet 2007;370:1453–7.
12. Freund Y, Rousseau A, Guyot-Rousseau F, et al. PERC rule to exclude the diagnosis of pulmonary embolism in emergency low-risk patients: study protocol for the PROPER randomized controlled study. Trials 2015;16:537.
13. Konstantinides SV, Torbicki A, Agnelli G, et al. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J 2014;35:3033–69, 3069a–k.
14. Lapner ST, Kearon C. Diagnosis and management of pulmonary embolism. BMJ 2013;346:f757.
15. Long B, Koyfman A. Best clinical practice: current controversies in pulmonary embolism imaging and treatment of subsegmental thromboembolic disease. J Emerg Med 2017;52:184–93.
16. Dronkers CE, van der Hulle T, Le Gal G, et al. Towards a tailored diagnostic standard for future diagnostic studies in pulmonary embolism: communication from the SSC of the ISTH. J Thromb Haemost 2017;15:1040–3.
17. Singh B, Mommer SK, Erwin PJ, Mascarenhas SS, Parsaik AK. Pulmonary embolism rule-out criteria (PERC) in pulmonary embolism–revisited: a systematic review and meta-analysis. Emerg Med J 2013;30:701–6.
18. Roy PM, Durieux P, Gillaizeau F, et al. A computerized handheld decision-support system to improve pulmonary embolism diagnosis: a randomized trial. Ann Intern Med 2009;151:677–86.
19. Perrier A, Roy PM, Sanchez O, et al. Multidetector-row computed tomography in suspected pulmonary embolism. N Engl J Med 2005;352:1760–8.
20. Penaloza A, Verschuren F, Dambrine S, Zech F, Thys F, Roy PM. Performance of the Pulmonary Embolism Rule-out Criteria (the PERC rule) combined with low clinical probability in high prevalence population. Thromb Res 2012;129:e189–93.
21. Bokobza J, Aubry A, Nakle N, et al. Pulmonary Embolism Rule-out Criteria vs D-dimer testing in low-risk patients for pulmonary embolism: a retrospective study. Am J Emerg Med 2014;32:609–13.
22. van der Pol LM, van der Hulle T, Mairuhu AT, Huisman MV, Klok FA. Combination of Pulmonary Embolism Rule-out Criteria and YEARS algorithm in a European cohort of patients with suspected pulmonary embolism. Thromb Haemost 2018;118:547–52.
23. Lessler AL, Isserman JA, Agarwal R, Palevsky HI, Pines JM. Testing low-risk patients for suspected pulmonary embolism: a decision analysis. Ann Emerg Med 2010;55:316–326.e1.