Bibliographic Cite	PMID Link	Literature Type	Level of Evidence	Purpose	Population	Intervention and Outcome Measures	Results / Recommendations	Study Limitiations
Banerjee I, Sofela M, Yang J, et al. Development and performance of the pulmonary embolism result forecast model (PERFORM) for computed tomography clinical decision support. JAMA Netw Open. 2019; 2(8):e198719.	31390040	Retrospective Multicenter Study	Low	To develop a machine learning model to generate a patient-specific risk score for PE by analyzing longitudinal clinical data as clinical decision support for patients referred for CT imaging for PE.	A total of 137,834 contrast-enhanced CT chest examinations performed between January 1, 1998, and January 1, 2016, including inpatient, emergency department, and outpatient scans. An external data set was also collected, comprised of 227,809 contrast-enhanced CT examinations of the chest from Duke performed between January 1, 2013, and August 31, 2017, including inpatient, emergency department, and outpatient scans. After exclusion of all patients with chronic PE, 3397 annotated PE-CT examinations from 3214 unique patients were curated as an internal annotated data set, and 244 annotated PE-CT examinations from 240 unique patients from Dukewere curated as an external data set. Of the 3214 patients included in the study, 1704 (53.0%) were women from Stanford University hospitals and clinics; mean (SD) age was 60.53 (19.43) years. The 240 patients from Duke University Medical Center used for validation included 132women (55.0%); mean (SD) agewas 70.2 (14.2) years.	Proposed workflow for the machine learning model, the Pulmonary Embolism Result Forecast Model (PERFORM), transforms raw electronic medical record (EMR) data into temporal feature vectors and develops a decision analytical model targeted toward adult patients referred for CT imaging for PE. The modelwas tested on holdout patient EMR data from 2 large, academic medical practices. Prediction performance of diagnosing acute PE was evaluated using artificial neural networks, and other machine learning approaches on holdout data sets from both institutions, and performance of models was measured by area under the receiver operating characteristic curve (AUROC).	The best-performing model achieved an AUROC performance of predicting a positive PE study of 0.90 (95%CI, 0.87-0.91) on intrainstitutional holdout data with an AUROC of 0.71 (95%CI, 0.69-0.72) on an external data set from Duke University Medical Center; superior AUROC performance and cross institutional generalization of the model of 0.81 (95%CI, 0.77-0.87) and 0.81 (95%CI, 0.73-0.82), respectively,were noted on holdout outpatient populations from both intrainstitutional and extrainstitutional data. The authors conclude that the machine learning model, PERFORM, may consider multitudes of applicable patient-specific risk factors and dependencies to arrive at a PE risk prediction that generalizes to new population distributions. This approach might be used as an automated clinical decision-support tool for patients referred for CT PE imaging to improve CT use.	This was a retrospective analysis. All patients included in the study underwent CT imaging, even those for whom an age-adjusted D-dimer level would have precluded imaging in most scoring systems. In addition, patients not referred for imaging were excluded because the design of the study was not to displace existing rule-out criteria, but instead to reduce unneeded PE imaging for patients referred for CT imaging for PE.
Bates SM, Takach Lapner S, Douketis JD, et al. Rapid quantitative D-dimer to exclude pulmonary embolism: a prospective cohort management study. J Thromb Haemost. 2016;14(3):504-9.	26707364	Multicenter Study	High	To determine if PE can be safely excluded in patients with a negative D-dimer without incorporating clinical probability assessment.	808 consecutive patients with suspected PE who were at least 18 years old and from outpatient clinics, emergency departments or inpatient wards of four tertiary care centers in Canada (St Joseph's Healthcare Hamilton, Hamilton General Hospital, McMaster University Medical Centre and Juravinski Hospital and Cancer Centre) were assessed for eligibility. Patients were excluded if they: had received therapeutic-dose anticoagulants for more than 24 h; had undergone another test for PE (e.g. other D-dimer test); had another indication for anticoagulation; had evidence of cardiorespiratory instability; had a contraindication for intravenous contrast; had an expected survival of less than 3 months; had no symptoms of PE in the last 7 days; were pregnant; had a central venous catheter; or were unable to return for follow-up. The mean age of the patients was 56 years. Of the 808 patients, 691 (85%) were outpatients at the time of enrollment. After completion of the study, clinical pretest probability was categorized as low in 578 patients (72%), moderate in 172 patients (21%) and high in 58 patients (7%). Ninety-nine (12%) patients were diagnosed with VTE at initial presentation. No patients were lost to follow-up.	Patients had a history taken and physical examination before any diagnostic testing. Although information was gathered to enable calculation of the Wells clinical prediction rule for PE [5], this was not used for patient management. All patients had D-dimer testing, which was reported as either negative (less than 750 lg FEU/L) or positive (750 lg FEU/L or higher); caregivers and study personnel were blinded to the quantitative D-dimer test result. If the D-dimer result was negative, anticoagulants were withheld and no further testing for PE was performed. If the D-dimer result was positive, patients underwent CTPA or V/Q lung scanning, according to local availability. Patients with a normal CTPA, a non-diagnostic CTPA or a CTPA with defects confined to the subsegmental vessels and patients with a non-diagnostic V/Q lung scan underwent bilateral proximal vein compression ultrasonography with repeat testing on days 6–8 and 13– 15 if the initial ultrasound was normal. Patients were categorized as PE positive at initial evaluation if: V/Q lung scanning was interpreted as high probability; CTPA revealed an intraluminal filling defect in the main, lobar or segmental level vessels; or proximal vein compression ultrasound showed a non-compressible venous segment. Radiologists and technologists who interpreted the diagnostic imaging were blinded to D-dimer results. Anticoagulation was withheld in patients who were not diagnosed with PE, whereas patients with confirmed PE or deep vein thrombosis (DVT) on imaging were treated with anticoagulants. The primary outcome was the proportion of patients with a negative MDA D-dimer at initial evaluation who had objectively confirmed symptomatic PE or DVT during 3 months of follow-up.	Four hundred and twenty (52%) patients had a negative D-dimer level at presentation and were not treated with anticoagulants; of these, one had VTE during follow-up. In conclusion, the authors' findings suggest that PE can be safely ruled out in patients with an MDA D-dimer level less than 750 lg FEU/L. Although additional studies are needed to ensure that the results with this assay apply to other D-dimer tests and to patients with high clinical pretest probability, D-dimer testing alone may be a reasonable option for clinicians who wish to exclude PE without clinical probability assessment or diagnostic imaging.	This is a prospective, multicenter study on MDA D-dimer negative predictive values in patients with concern for PE. Strengths of the study include large sample size, standardized protocol, and no patients lost to followup. The assay used has since been discontinued, though post-hoc analysis verified findings with a similar assay.
Begic A, Opankovic E, Cukic V, et al. Impact of ventilation/perfusion single-photon emission computed tomography on treatment duration of pulmonary embolism. Nucl Med Commun. 2015;36(2):162-7.	25321156	Prospective Study	Low	To establish whether the duration of anticoagulant (AC) therapy can be tailored, on an objective basis, by using ventilation / perfusion singlephoton emission computed tomography (V/P SPECT) and to assess the extent of residual perfusion defects over time. In particular, the authors addressed the following: (a) is the extent of perfusion recovery at 3 months of initial pulmonary embolism (PE) diagnosis a satisfactory criterion for deciding the duration of oral AC? (b) Is it safe to withdraw AC at 3 months if perfusion recovery is complete?	Total of 269 consecutive patients with suspected PE were examined from September 2011 to September 2012 at the Department of Nuclear Medicine University Hospital in Sarajevo using V/P SPECT. The referring physicians suspected PE on the basis of relevant clinical symptoms and signs, predisposing risk factors and elevated D-dimer levels (cutoff 0.55 mg/l). Exclusion: patients with history of PE or those "who could not be followed up"	V/P SPECT is performed as a 1-day protocol starting with inhalation of aerosolized 99mTc-Technegas (Cyclomedica Ltd, Lucas Heights, New South Wales, Australia) while in a supine position, until about 30MBq has reached the lung. Immediately thereafter, and without patient movement, 120MBq 99mTc-MAA (TechneScan LyoMAA; Mallinckrodt Medical BV, Petten, the Netherlands) is given intravenously for the perfusion study. Patients carefully maintain their supine position during V/P acquisition. Immobilization lasting 20 min is usually well tolerated even by critically ill patients. The methodology has been described in full elsewhere [8,13]. Quantification of PE was made by counting segments or subsegments showing a complete or relative mismatch, and expressing this figure as a percentage of total lung parenchyma [5,14–17]. A segmental reduction or a subsegmental total deficiency of function was attributed one point, and segmental total deficiency was attributed two points. Each lung comprises nine segments, representing 18 points. Mismatch defects were expressed as mismatch points, which after division by 36 give the percentage of the lung that is embolized. All regions with V/P defects were calculated to estimate the reduction in total lung function. Recurrent PE was defined if a new perfusion defect was objectively visualized by V/P SPECT in a patient at one of the control stages.Follow-up with V/P SPECT at 6 months? (no real reference test of any kind)	100/269 pts with PE on index test; 67/100 with 3 month followup - of these, 48 had normal scan and 19 still had perfusion defects. 3/19 with defects lost to follow-up. 64 patients at 6 months, 35 who did not have AC therapy from 3-6 months and 29 who remained on therapy. of these 64, 53 had normal V/P Spect, 10 had perfusion defects remaining, and 1 had a new PE despite ongoing AC treatment.Normalization of perfusion at 3 months of PE diagnosis was a reliable indicator that AC could be safely withdrawn Fig. 4 Initial 3 months 6 months V P qV/P Sagittal V/P SPECT images of a patient with PE (arrow) and pleural fluid (intercepted arrow) at initial examination. Perfusion returns to normal at 3 months and remains normal at 6 months' control. P, perfusion; PE, pulmonary embolism; qV/P, V/P quotient; V, ventilation; V/P SPECT, ventilation/perfusion single-photon emission computed tomography. 166 Nuclear Medicine Communications 2015, Vol 36 No 2 in the case of patients who were without hypercoagulability risk. Tailoring AC treatment is feasible by incorporating V/P SPECT in the clinical decision tree. The short-term regimen appears safe whenever pulmonary perfusion is normal after 3 months of the embolic event in the absence of persistent risk factors for PE recurrence. The first results indicate that V/P SPECT can be successfully used for follow-up and for tailoring AC therapy after acute PE. The results merit further study.	large number (more than 25%) patients excluded or dropped out single reader or no inter-reader reliability was calculated
den Exter PL, van Es J, Kroft LJ, et al. Thromboembolic resolution assessed by CT pulmonary angiography after treatment for acute pulmonary embolism. Thromb Haemost. 2015;114(1):26-34.	26017397	Multicenter Study	Moderate	To assess the rate of PE resolution and its implications for clinical outcome	Prospective, multi-center cohort study; 157 patients with acute PE diagnosed by CT pulmonary angiography (CTPA) underwent follow-up CTPA-imaging after six months of anticoagulant treatment. Two expert thoracic radiologists independently assessed the presence of residual thromboembolic obstruction.	The degree of obstruction at baseline and follow-up was calculated using the Qanadli obstruction index. All patients were followed-up for 2.5 years. At baseline, the median obstruction index was 27.5%. After six months of treatment, complete PE resolution had occurred in 84.1% of the patients (95% confidence interval (CI): 77.4-89.4%). The median obstruction index of the 25 patients with residual thrombotic obstruction was 5.0%.	During follow-up, 16 (10.2%) patients experienced recurrent VTE. The presence of residual thromboembolic obstruction was not associated with recurrent VTE (adjusted hazard ratio: 0.92; 95% CI: 0.2-4.1).This study indicates that the incidence of residual thrombotic obstruction following treatment for PE is considerably lower than currently anticipated. These findings, combined with the absence of a correlation between residual thrombotic obstruction and recurrent VTE, do not support the routine use of follow-up CTPA-imaging in patients treated for acute PE.	Given the low number of recurrent events during follow-up and the small proportion of residual PE, it cannot be excluded that the authors study was underpowered to detect this association. Still, the fact that residual PE was present in a minority of patients and that only two of these patients developed recurrent VTE, does not indicate that implementing follow-up CTPA
Glober N, Tainter CR, Brennan J, et al. The DAGMAR Score: D-dimer assay-guided moderation of adjusted risk. Improving specificity of the D-dimer for pulmonary embolism. Am J Emerg Med. 2019; 37(5):895-901.	30104092	Retrospective Study	Low	To generate a novel scoring system to iprove the test characteristics of D-dimer in patients with suspected PE.	Cases were included if they visited the ED, age 18 years old or greater, and had a D-dimer and imaging (CT pulmonary angiography or VQ scan) completed.	Electronic Medical Record datawere retrospectively reviewed on Emergency Department (ED) patients 18 years or older for whom a D-dimer and imaging were ordered between June 4, 2012 and March 30, 2016. Symptoms (dyspnea, unilateral leg swelling, hemoptysis), age, vital signs, medical history (cancer, recent surgery, medications, history of deep vein thrombosis or PE, COPD, smoking), laboratory values (quantitative D-dimer, platelets, and mean platelet volume (MPV)), and imaging results (CT, VQ) were collected. Points were designated to factors that were significant in two multiple regression analyses, for PE or positive D-dimer. Points predictive of PE were designated positive values and points predictive of positive D-dimer, irrespective of presence of PE, were designated negative values. The DAGMAR (D-dimer Assay-Guided Moderation of Adjusted Risk) score was developed using age and platelet adjustment and points for factors associated with PE and elevated D-dimer.	D-dimer was ordered on 8486 patients who visited the ED in the designated time period. Of those, 170 (2%) results were excluded as theywere duplicate D-dimer assays ordered on the same patient during the same ED visit. An additional 4793 were excluded as they were D-dimers (positive or negative) without associated imaging. Of the remaining 3523 patients, 2253 (64.0%) had a positive D-dimer and 1270 (36.0%) had a negative D-dimer. Of the positive D-dimers, 198 PE were detected by imaging (8.8%). Of the negative D-dimers, 9 PE were detected by imaging. A DAGMAR Score < 2 equated to overall PE risk b 1.2%. Specificity improved (38% to 59%) without compromising sensitivity (94% to 96%). Use of the DAGMAR Score would have reduced CT scans from 2253 to 1556 and lead to fewer false negative results. The authors conclude that, by considering factors that affect D-dimer and also PE, they were able to improve specificity without compromising sensitivity.	This study was limited by its retrospective nature, and the inherent limitations of using a single hospital system with the same physicians. The most significant limitation is the exclusion of patients without imaging and lack of follow up on the patients with imaging. Also due to the retrospective nature, many factors were not documented.

Kaya F, Ufuk F, Karabulut N. Diagnostic performance of contrast-enhanced and unenhanced combined pulmonary artery MRI and magnetic resonance venography techniques in the diagnosis of venous thromboembolism. Br J Radiol. 2019; 92(1095):20180695.	30629460	Prospective Study	Low	To determine the diagnostic performance of the contrast-enhanced and unenhanced combined pulmonary arterial MRI and magnetic resonance venography techniques in the diagnosis of venous thromboembolism (VTE).	Patients with contraindications for MRI, those who were uncooperative or who had MRI incompatible implants, those with claustrophobia or history of gadolinium based contrast medium allergy, those with an estimated glomerular filtration rate (eGFR) of <60 ml min−1 1.73 m2, and those with a duration of >72 h between CTPA and MRI were not included. The final study group consisted of 44 patients (33 male, 11 female; mean age, 52.1 ± 15.3 years; range, 23–83 years)	Patients underwent combined pulmonary and lower extremity MRI, and Doppler ultrasonography within 72 h after CTPA. Combined MRI included two sequences: unenhanced steady-state free precession (SSFP) and contrast-enhanced three-dimensional (3D) gradient echo (GRE). The presence of emboli in pulmonary arteries and thrombi in lower extremity veins on 3D-GRE and SSFP sequences was recorded.	CTPA showed a total of 244 emboli in 33 (75%) patients whereas contrast-enhanced 3D-GRE MRI showed deep vein thrombosis (DVT) in 34 (77%) subjects. Sensitivities for SSFP vs 3D-GRE MRI respectively in PE detection were 87.9 vs 100% on a per-patient basis, and 53.7 vs 73% on a per-embolus basis. Of 34 patients with established DVT, 31 (91%) were detected by Doppler ultrasound and 29 (85%) were detected by SSFP technique respectively. The authors conclude that both contrast-enhanced and unenhanced combined MRI of acute PE and DVT are feasible one-stop-shopping techniques in patients with suspected thromboembolism.	Study population is small and the number of patients with PE was higher than those without PE. This disproportion may be due to patients with severe clinical symptoms are more likely to participate in the study. Second, since the images were evaluated by single radiologist, authors did not assess interobserver variability. Third, authors did not use the respiratory or cardiac gating that would have minimized the motion artifact and potentially improved diagnostic performance. Fourth, authors used thicker slices in SSFP compared to contrast-enhanced 3D-GRE technique.
Kearson C, de Wit K, Parpia S, et al. Diagnosis of pulmonary embolism with D-dimer adjusted to clinical probability. N Engl J Med. 2019; 381(22):2125-2134.	31774957	Prospective Study	Moderate	To test a strategy of ruling out pulmonary embolism in outpatients with a low C-PTP and a D-dimer level of less than 1000 ng per milliliter (i.e., twice the usual threshold used to rule out pulmonary embolism) and in those with a moderate C-PTP and a D-dimer level of less than 500 ng per milliliter.	Outpatients with symptoms or signs suggestive of pulmonary embolism were potentially eligible to be included. Patients were excluded if they were younger than 18 years of age, had received full-dose anticoagulant therapy for 24 hours, had undergone major surgery in the past 21 days, had a d-dimer level that was known before the C-PTP was assessed, had undergone chest imaging contrary to the protocol, had undergone contrast-enhanced CT of the chest for another reason, had an ongoing need for anticoagulant therapy, had a life expectancy of less than 3 months, or were pregnant or geographically inaccessible for follow-up. A total of 3133 patients were assessed by the clinical centers as meeting the inclusion criteria; of those, 941 met one or more exclusion criteria and 136 did not provide consent, which resulted in the registration of 2056 patients. The mean age of the patients was 52 years, and 66.2% were female.	Pulmonary embolism was considered to be ruled out without further testing in outpatients with a low C-PTP and a D-dimer level of less than 1000 ng per milliliter or with a moderate C-PTP and a D-dimer level of less than 500 ng per milliliter. All other patients underwent chest imaging (usually computed tomographic pulmonary angiography). If pulmonary embolism was not diagnosed, patients did not receive anticoagulant therapy. All patients were followed for 3 months to detect venous thromboembolism.	A total of 2017 patients were enrolled and evaluated, of whom 7.4% had pulmonary embolism on initial diagnostic testing. Of the 1325 patients who had a low C-PTP (1285 patients) or moderate C-PTP (40 patients) and a negative d-dimer test (i.e., <1000 or <500 ng per milliliter, respectively), none had venous thromboembolism during follow-up (95% CI, 0.00 to 0.29%). These included 315 patients who had a low C-PTP and a D-dimer level of 500 to 999 ng per milliliter (95% CI, 0.00 to 1.20%). Of all 1863 patients who did not receive a diagnosis of pulmonary embolism initially and did not receive anticoagulant therapy, 1 patient (0.05%; 95% CI, 0.01 to 0.30) had venous thromboembolism. Our diagnostic strategy resulted in the use of chest imaging in 34.3% of patients, whereas a strategy in which pulmonary embolism is considered to be ruled out with a low C-PTP and a D-dimer level of less than 500 ng per milliliter would result in the use of chest imaging in 51.9% (difference, −17.6 percentage points; 95% CI, −19.2 to −15.9). The authors conclude that a combination of a low C-PTP and a d-dimer level of less than 1000 ng per milliliter identified a group of patients at low risk for pulmonary embolism during follow-up.	Limitations of the study include that almost all patients who were enrolled were outpatients (only 1 inpatient), so the findings may not apply to inpatients; too few patients had a moderate C-PTP and a D-dimer level of less than 500 ng per milliliter to precisely identify the negative predictive value in this subgroup; and it is possible that physician discretion influenced which patients were enrolled.
Kornblum J, Daugherty RJ, Bounds R, et al. Diagnostic yield of computed tomographic pulmonary angiography for suspected pulmonary embolism varies across settings within a community-based health system. Emerg Radiol. 2021; 28(2):291-296.	33000363	Retrospective Multicenter Study	Low	To evaluate the yield of CTPA for PE in a community-based tertiary healthcare system across a variety of patient settings in order to help establish relevant bechmarks which may then be used for future quality improvement initiatives in nonacademic centers.	A total of 7850 CTPA studies met criteria for inclusion with a mean patient age of 58.1 ± 17.6 years. Female patients accounted for 4734 (60.3%) of the studies. Included studies were performed in patients 18 years or older and were obtained in the emergency department (including observation status of < 24 h), in the inpatient setting (> 24 h admission), and on an outpatient basis. Studies ordered for indications other than PE were manually excluded (464 studies).	Study included data collected from three sites within a single healthcare system, including a tertiary care level 1 trauma center, an urban community hospital, and a surburban free-standing emergency department. The encounter diagnoses were then searched for the presence of pulmonary embolism ICD-9 codes (415.1, 415.11–415.13, 415.19) in order to establish whether the CTPA was positive or negative for PE. Additional assessment was made for particular venous thromboembolism risk factors, which were identified in discharge diagnoses by ICD-9 codes.	Pulmonary embolism was found in 884 (11.3%) of the studies performed. Outpatients had a lower yield of pulmonary embolism (3.8%, p < 0.001) compared with inpatients (14.1%) and emergency department patients (10.7%, p < 0.001). Patients with diagnoses of deep vein thrombosis or neoplasm had increased incidence of pulmonary embolism when compared with patients without these diagnoses (p < 0.001 for both). The authors conclude that the overall yield of CTPA for pulmonary embolism in this community-based system was similar to that at academic centers. The yield was significantly lower in the outpatient setting compared with studies originating in the emergency department or inpatient setting.	Data were gathered retrospectively from a single community-based tertiary care health system, thus, generalizability of the findings to other community-based systems may vary based on regional and organizational characteristics. While the data was validated in approximately 10% of the cohort, the CTPA positivity for PE was determined based on diagnosis codes, leading to the possibility of both false-positive and false-negative results. Although differences were found between patients presenting from different healthcare settings, no further inquiry was made into potential reasons for these differences due to the large cohort size and the retrospective nature of the study.
Lindner G, Funk GC, Pfortmueller CA, et al. D-dimer to rule out pulmonary embolism in renal insufficiency. Am J Med. 2014;127(4):343-7.	24355353	Retrospective Study	Low	D-dimer levels are often elevated in renal insufficiency. The diagnostic accuracy of D-dimer to rule out pulmonary embolism in patients with renal insufficiency is unclear. In the present study the authors wanted to investigate the diagnostic accuracy of D-dimer determination in a large collective of patients receiving computed tomography angiography (CTA) to rule out pulmonary embolism.	All patients presenting to an academic Department of Emergency Medicine who received a D-dimer and a CTA scan in order to rule out PE from 12/1/2005 - 6/30/2012 were included in the analysis. In total, 1305 patients were included in the analysis, with a median age of 62 years (IQR: 47 to 73), 678 (52 %) were male, 627 (48 %) were male	D-Dimer and eGFRCTPA (Overall objective was to determine the clinical utility of D-dimer for diagnosis of acute PE in patients with kidney disease)	D-Dimer was significantly higher in patients with a CKD-EPI eGFR < 30 mL/min (2.903 [IQR 1539 to 3953]), then in those with 30-60 mL/min (1277 [912 to 2077]), and > 60 mL/min (1065 [IQR 664 to 1763]), p < 0.0001. 2. The AUC of the receiver operating characteristic for D-dimer to rule out PE was 0.725 for all patients, 0.734 for patients with a CKD-EPI eGFR of > 60 mL/min, 0.673 for patients with 30-60 mL/min eGFR, and 0.713 for patients with <30 mL/min eGFR. 3. In patients with a eGFR of 30-60 mL/min, a cutoff for D-Dimer of < 594 uq/L resulted in a sensitivity of 0.97, specificity of 0.1, PPV of 0.17, and NPV of 0.95. 4. A decrease in eGFR consistent with kidney disease resulted in a three-fold increase in cutoff for D-dimer to achieve a high NPV: based on a cutoff for D-dimer of < 1738 ug/L in patients with an eGFR , 30 mL/min, sensitivity was 0.8, specificity 0.38, PPV 0.21, and NPV 0.9. In conclusion, the authors study showed that the specificity of D-dimer to rule out pulmonary embolism dramatically decreases with declining renal function. D-dimer levels significantly correlated inversely with eGFR, and "normal" D-dimer levels were hardly seen in patients with moderate to severe renal insufficiency.	Retrospective design
Liu J, Lacros G. Radionuclide lung scans for suspected acute pulmonary embolism: Single photon emission computed tomography (SPECT) or hybrid SPECT/CT? J Med Imaging Radiat Oncol. 2019; 63(6):731-736.	31515905	Prospective Study	Low	To evaluate whether the use of attenuation correction and/or the depiction of lung pathology with hybrid SPECT/CT could significantly reduce potentially false-positive ventilation–perfusion (VQ) SPECT studies or obviate the need for a ventilation study.	165 patients total referred for assessment of suspected PE from 2009 to 2014. There were 77 women and 88 men, with mean age of 64 years (yrs) (range: 19– 91 yrs).Exclusion criteria from participation in the study included pregnancy, age < 16 years old and severe co morbidities (such as orthopnoea from cardiorespiratory disease, excess weight exceeding the scanning bed limit and claustrophobia) preventing tomography being undertaken.	Two specialists (S1 and S2) reviewed prospectively acquired VQ SPECT/CT. Studies were reported using standard criteria and compared to VQ SPECT and Q SPECT/CT. Cohen's kappa (k) statistic was used to characterise the intra- and inter-observer agreement of the four data sets; a one-tailed t-test was used to compare VQ SPECT with the other three data sets for each of S1 and S2; and McNemar's test was used to compare the proportions of positive and negative studies between S1 and S2 Probability (P) values of <0.05 were considered significant.	S1 and S2 recorded positive VQ SPECT in 54 (32.7%) and 42 (25.6%) cases, respectively. Hybrid SPECT/CT showed non-embolic pathology in 41 (S1) and 46 (S2) patients, but compared to VQ SPECT, neither hybrid SPECT/ CT nor attenuation correction SPECT/CT had significantly fewer positive studies. Intra-observer agreement with VQ SPECT/CT was almost perfect (k = 0.91 for S1 and k = 0.95 for S2; P < 0.001), but not with Q SPECT/CT (k = 0.4 for S1 and k = 0.62 for S2; P < 0.001). Inter-observer agreement was moderate for VQ SPECT (k = 0.65) and VQ SPECT/CT (k = 0.63). The authors conclude that hybrid VQ SPECT/CT did not reduce the number of potentially false-positive VQ SPECT, nor did the CT obviate the need for a ventilation study. Thus, the routine use of hybrid SPECT/CT for suspected pulmonary embolism is not justified.	First, the final diagnosis was not determined with reference to clinical outcome and/or other tests. Second, this was a single institutional study and it is possible that findings may not apply elsewhere; for example, the institution uses a Siemens Symbia T6 and physicians have experience in cross-sectional anatomy. Third, the proportion of positive VQ SPECT studies was somewhat higher than anticipated, but nevertheless consistent with previous research. Finally, not all patients undergoing VQ scans at during the study period were included in this research and there may have been selection bias.

Masy M, Giordano J, Petyt G, et al. Dual-energy CT (DECT) lung perfusion in pulmonary hypertension: Concordance rate with V/Q scintigraphy in diagnosing chronic thromboembolic pulmonary hypertension (CTEPH). Eur Radiol. 2018; 28(12):5100-5110.	29846802	Retrospective Study	Low	To evaluate the concordance between DECT perfusion and ventilation/perfusion (V/Q) scintigraphy in diagnosing chronic thromboembolic pulmonary hypertension (CTEPH).	204 consecutive patients fulfilling the following criteria: (a) PH of any cause, except group 3 patients in whom extensive lung infiltration or destruction could have hampered analysis of perfusion changes; (b) chest CT examination obtained with injection of iodinated contrast material (i.e. chest CTA) and using a dual-energy CT (DECT) scanning mode; and (c) V/Q scintigraphy obtained within an interval of time of less than 6 months. On the basis of these criteria, 83 consecutive patients were selected; three of them were excluded because of poor DECT perfusion image quality, leading to a final study group of 80 patients. The final study group included 36 patients with CTEPH (36/80; 45%; group A) and 44 patients with non-CTEPH (44/80; 55%; group B).	For each patient, the final diagnosis had been established by expert clinicians according to the recommended guidelines. The diagnostic workup included standard CT angiographic information but not CT perfusion imaging. Patients underwent V/Q scintigraphy and DECT perfusion on a 2nd- and 3rd-generation dual-source CT system. The imaging criteria for diagnosing CTEPH relied on at least one segmental triangular perfusion defect on DECT perfusion studies and V/Q mismatch on scintigraphy examinations.	Based on multidisciplinary expert decisions that did not include DECT perfusion, 36 patients were diagnosed with CTEPH and 44 patients with other aetiologies of PH. On DECT perfusion studies, there were 35 true positives, 6 false positives and 1 false negative (sensitivity 0.97, specificity 0.86, PPV 0.85, NPV 0.97). On V/Q scans, there were 35 true positives and 1 false negative (sensitivity 0.97, specificity 1, PPV 1, NPV 0.98). There was excellent agreement between CT perfusion and scintigraphy in diagnosing CTEPH (kappa value 0.80). Combined information from DECT perfusion and CT angiographic images enabled correct reclassification of the 6 false positives and the unique false negative case of DECT perfusion. The authors conclude there is excellent agreement between DECT perfusion and V/Q scintigraphy in diagnosing CTEPH. The diagnostic accuracy of DECT perfusion is reinforced by the morpho-functional analysis of data sets.	Sample size was limited to 80 patients, with only 36 patients with CTEPH. Authors excluded group 3 PH patients with extensive infiltrative or destructive lung changes for whom the diagnostic approach of PH does not primarily rely on perfusion alterations. Authors analyzed perfusion abnormalities on DECT perfusion examinations with a diagnostic image quality, suggesting a highly selected study group and thus an artificially favourable situation for DECT. Authors could not exclude an incorporation bias as there is no strict independence between the gold standard for CTEPH diagnosis and the perfusion methods that were evaluated.
McLenachan CJ, Chua O, Chan BS, et al. Comparison of Wells and YEARS clinical decision rules with D-dimer for low-risk pulmonary embolus patients. Intern Med J. 2019; 49(6):739-744.	30324677	Retrospective Study	Low	To compare the sensitivity and specificity of varying D-dimer cut-offs in the diagnosis of PE for Wells low-risk patients.	Patients presenting to a tertiary emergency department over 42 months who had a D-dimer performed for PE risk stratification. Patients were excluded if their D-dimer tests were not ordered for suspected PE, such as for suspected deep venous thrombosis. Patients were also excluded if the medical records could not be located or they had a non-viable D-dimer result, for example, clotted, mislabelled or unsuitable specimens. 2125 patients were assessed as low risk for PE as per the two-tier Wells criteria. The median age was 48 years (IQR: 34–64) and 1290 (61%) were females. The most common presenting symptom was chest pain in 1757 (83%), followed by shortness of breath in 1019 (48%).	Wells scores were calculated for each patient, those with Wells score of ≤4 ('PE unlikely') were analysed. Four D-dimer thresholds were compared, including traditional threshold (0.5 µg/mL), age-adjusted (age in years × 0.01 µg/mL), doubled-traditional threshold and YEARS criteria.	A total of 46 low-risk patients (2.2%) were found to have a PE. The sensitivity and specificity for each D-dimer threshold were traditional threshold (95.6% and 65.6%), age-adjusted (93.5% and 71.7%), doubled traditional (69.6% and 85.5%) and YEARS criteria (80.4% and 84.0%). Utilising an age-adjusted threshold, YEARS criteria or doubled-traditional threshold would have resulted in 70, 217 and 245 fewer imaging investigations. The authors conclude that the prevalence of PE in this low-risk cohort was very low. Utilizing an age-adjusted D-dimer would have reduced imaging tests performed while maintaining good sensitivity. Although The YEARS criteria and doubled-traditional threshold would have reduced scanning considerably both had sensitivities of less than 90%.	There was no uniform guideline followed to investigate for PE. The population selected was identified according to which patients had a D-dimer performed which excludes patients who either correctly or incorrectly had PE excluded without a D-dimer. This would include patients who met PERC or who proceeded directly to imaging at a clinician's discretion. In follow up the authors assumed that every patient who did not undergo further imaging, and/or who did not represent after discharge did not have PE. Lastly, when calculating each patient's risk, if a clinical symptom was not documented then authors presumed it was not present and it may have been. It should also be noted this study was taken in a single center and thus would benefit from findings from multiple healthcare institutions.
Moores L, Kline J, Portillo AK, et al. Multidetector computed tomographic pulmonary angiography in patients with a high clinical probability of pulmonary embolism. J Thromb Haemost. 2016;14(1):114-20.	26559176	Research Support, Non-U.S. Gov't	Moderate	Investigate the sensitivity of computed tomography (CT) in patients with a high probability of pulmonary embolism (PE)	A prospective investigation of 498 patients with a priori clinical assessment of a high probability of PE and a completed CTPA study to study the sensitivity of multidetector CTPA among patients with a priori clinical assessment of a high probability of PE according to the Wells criteria.	Among patients with a negative CTPA result, the diagnosis of PE required at least one of the following conditions: ventilation/perfusion lung scan showing a high probability of PE in a patient with no history of PE, abnormal findings on venous ultrasonography in a patient without previous deep vein thrombosis at that site, or the occurrence of venous thromboembolism (VTE) in a 3-month follow-up period after anticoagulation was withheld because of a negative multidetector CTPA result.	CTPA excluded PE in 134 patients; in these patients, the pooled incidence of VTE was 5.2% (seven of 134 patients; 95% confidence interval [CI] 1.5-9.0). Five patients had VTEs that were confirmed by an additional imaging test despite a negative CTPA result (five of 48 patients; 10.4%; 95% CI 1.8-19.1), and two patients had objectively confirmed VTEs that occurred during clinical follow-up of at least 3 months (two of 86 patients; 2.3%; 95% CI 0-5.5). None of the patients had a fatal PE during follow-up.; CONCLUSIONS: A normal multidetector CTPA result alone may not safely exclude PE in patients with a high clinical pretest probability.	Large number (more than 25%) of patients excluded or dropped out
Pasin L, Zanon M, Moreira J, et al. Magnetic Resonance Imaging of Pulmonary Embolism: Diagnostic Accuracy of Unenhanced MR and Influence in Mortality Rates. Lung. 2017;195(2):193-9.	28116500	Prospective observational study	Low	To evaluate the diagnostic value for pulmonary embolism (PE) of the True fast imaging with steady-state precession (TrueFISP) MRI, a method that allows the visualization of pulmonary vasculature without breath holding or intravenous contrast.	Prospective investigation - ninety-three consecutive patients referred to the Radiology Department with clinical suspicion of acute PE were included in the study [59 women and 34 men; mean age of 63 years (SD ± 13; range 22–89)]. Exclusion criteria were any contraindications to MRI examinations, such as claustrophobia or to iodinated contrast media. Two patients could not undergo the real-time MRIand were excluded from the study.	Patients initially underwent multidetector CT imaging to confirm the diagnosis and afterwards, without postponing medical treatment, underwent real-time MR imaging. One year after the CTPA and MR imaging, patients were reassessed through hospital records and mortality was registered.	During the 1-year follow-up period, eight patients died, whereas PE was responsible for 12.5% of cases. Betweenpatients who developed PE, only 5% died due to this condition. There were no differences between MR and CTembolism detection in these subjects. MR sequences had a sensitivity of 85%, specificity was 98.6% and accuracy was95.6%. Agreement between readers was high (κ= 0.87). Conclusions Compared with contrast-enhanced CT, unenhanced MR sequences demonstrate good accuracy and no differences in the mortality rates in 1 year were detected.	One of the limitations of this study was the lack of additional examinations to confirm the initial suspicion of PE, such as D-dimer tests, echocardiography and duplex phlebosonography, which could lead to an underestimated PE prevalence. However, the prevalence found in this study (22%) is comparable to previous CTPA series. Another limitation is that this is a single-centre study, which could limit the accuracy of the results, however, this also increases the homogeneity of the technical parameters.
Pressaco J, Papas K, Lambert J, et al. Magnetic resonance angiography imaging of pulmonary embolism using agents with blood pool properties as an alternative to computed tomography to avoid radiation exposure. Eur J Radiol. 2019; 113:165-173.	30927943	Prospective Study	Low	To evaluate the feasibility and accuracy of a combined magnetic resonance angiography (MRA) - magnetic resonance venography (MRV) protocol using contrast agents with blood pool properties, gadofosveset trisodium and gadobenate dimeglumine, in the evaluation of pulmonary embolus (PE) and deep venous thrombosis (DVT) as compared to the standard clinical reference imaging modalities; computed tomography pulmonary angiography (CTPA) and color-coded Duplex ultrasound (DUS).	40 patients presenting to the emergency department with clinical suspicion for PE and scheduled for a clinically indicated CTPA. Inclusion criteria included patients with a minimum age of 18 years presenting to the ED with clinically suspected PE and undergoing evaluation by clinically indicated CTPA. Exclusion criteria were contraindication to MRI, claustrophobia, pregnancy, an estimated glomerular filtration rate (GFR) of less than 30 mL/min/1.73m2, and unwillingness to participate in the study.	Authors performed both MRA of the chest for the evaluation of PE as well as MRV of the pelvis and thighs to evaluate for DVT using a single contrast injection. MRA-MRV data was compared to the clinical reference standard CTPA and DUS, respectively. Coronal source images and axial and multi-planar reformatted images were used for interpretation. Image interpretation was performed by two experienced radiologists, both unaware of patients' clinical data and clinical CTPA and DUS results.	The results on a per-patient basis comparing MRA to CTPA for pulmonary embolus yielded 100% sensitivity and 97% specificity. There was a small subset of patients that underwent clinical DUS to evaluate for DVT, which demonstrated a sensitivity and specificity of 100% for MRV. The authors conclude that this single-center, preliminary study using contrast agents with blood pool properties to perform a relatively rapid combined MRA-MRV exam to image for PE and above knee DVT shows potential as an alternative imaging choice to CTPA. Further large-scale, multicenter studies are warranted.	Single institution study and a relatively small number of patients recruited for each contrast agent.

Sharif S, Eventov M, Kearon C, et al. Comparison of the age-adjusted and clinical probability-adjusted D-dimer to exclude pulmonary embolism in the ED. Am J Emerg Med. 2019; 37(5):845-850.	30077494	Retrospective Study	Low	To compare the efficacy and safety of using age-adjusted D-dimer interpretation, clinical probability adjusted D-dimer interpretation and standard D-dimer approach to exclude PE in ED patients.	All ED patients who had a D-dimer ordered, a CT pulmonary angiogram, or VQ scan ordered by an ED physician to investigate for PE; these patients were considered to have had suspected PE. The current analysis was restricted to patients who had a low or moderate clinical probability (i.e., PE Wells Score 6.0 or less) and who also had a D-dimer level measured. Authors did not include patients who had a high clinical suspicion because D-dimer is generally not used to evaluate PE in these patients. The average age of the 1075 included patients was 48, 69.6% were female, and 6.8% had an active malignancy.	The authors performed a health records review at two emergency departments over a two-year period. They reviewed all cases where patients had a D-dimer ordered to test for PE or underwent CT or VQ scanning for PE. PE was considered to be present during the emergency department visit if PE was diagnosed on CT or VQ (subsegmental level or above), or if the patient was subsequently found to have PE or deep vein thrombosis during the next 30 days. They applied the three D-dimer approaches to the low and moderate probability patients. The primary outcome was exclusion of PE with each rule. Secondary objective was to estimate the negative predictive value (NPV) for each rule.	1163 emergency patientswere tested for PE and 1075 patientswere eligible for inclusion in the analysis. PE was excluded in 70.4% (95% CI 67.6–73.0%), 80.3% (95% CI 77.9–82.6%) and 68.9%; (95% CI 65.7–71.3%) with the age-adjusted, clinical probability-adjusted and standard D-dimer approach. The NPVs were 99.7% (95% CI 99.0–99.9%), 99.1% (95% CI 98.3–99.5%) and 100% (95% CI 99.4–100.0%) respectively. The authors conclude that the clinical probability-adjusted rule appears to exclude PE in a greater proportion of patients, with a very small reduction in the negative predictive value.	There are a number of limitations with this study relating to its retrospective nature. First, although the authors standardized data abstraction for the Wells score components, retrospective data collection may not accurately reflect the clinical findings. Second, by relying on health records at two hospitals to identify VTE recurrence as opposed to direct patient contact, authors may have missed some episodes of recurrent VTE during follow-up, which would lead to an over estimation of NPV. Third,authors took no specific steps to ensure independence of clinical data abstraction, D-dimer levels and imaging study results; this could have led to a biased assessment of agreement between these findings.
Stubbs M, Chan K, McMeekin H, et al. Incidence of a single subsegmental mismatched perfusion defect in single-photon emission computed tomography and planar ventilation/perfusion scans. Nuclear medicine communications. 2017;38(2):135-40.	27977536	Retrospective Study	Moderate	This study aims to compare the incidence of ventilation / perfusion (V/Q) scans interpreted as indeterminate for the diagnosis of pulmonary embolism (PE) using single-photon emission computed tomography (SPECT) versus planar scintigraphy and to consider the effect of variable interpretation of single sub-segmental V/Q mismatch (SSM).	V/Q scans from a total of 1300 consecutive scans (408 men and 829 women, mean (SD) age 52 (+/- 20) years) referred to the Royal Free Hospital, London for scintigraphic evaluation of clinically suspected PE were retrospectively collected for analysis. V/Q scans were excluded from analysis if the indication was to characterize or assess for the resolution of previously diagnosed PE or to assess for suspected chronic PE. Any scans from a patient in whom a previous V/Q scan had been performed and the images were available to observers for comparison were also excluded, as were scans from any patient who had undergone CTPA in the 7 days preceding scintigraphy, for whom the images or results were available. The authors hoped that these exclusions would make the groups more comparable for analysis, and reduce reporting bias because of the availability of previous radiographic or scintigraphic information in these cases, which could potentially reduce the rate of indeterminate studies.	The index test in this study was single-photon emission computed tomography (SPECT). All SPECT scans were analyzed by a single observer and categorized as positive, negative, or indeterminate for diagnosis of acute PE on the basis of a set of predefined criteria. SPECT scans were also analyzed for the presence of single sub-segmental mismatch. The reference test was planar V/Q scans. The authors sought to compare the performance of SPECT vs. planar V/Q scan in terms of incidence of indeterminate PE diagnosis and to consider the effect of variable interpretation of single sub-segmental V/Q mismatch among these two studies.	There was a small but significant increase in the number of scans reported as positive for PE in the SPECT group compared with the planar group (15.0 vs. 10.9%, P<0.05). The total number of scans reported as indeterminate were 42/542 (7.7%) in the SPECT group and 72/589 (12.2%) in the planar group (P < 0.05). 2. SSM in the absence of other abnormalities was uncommonly identified in both planar (1/589; 0.17%) and SPECT (20/542; 3.70%) scans. There was a significant difference between the reported presence of SSM in planar and SPECT scans (P < 0.0001). If all SSMs in the absence of other abnormalities are recategorized as indeterminate, the total numbers of indeterminate scans were 72/589 (12.2%) in the planar group and 45/542 (8.3%) in the SPECT group (P<0.05). 3. Of the 21 patients who had SSM, 19 underwent CTPA within 48 h of V/Q scans (one from the planar group, 18 from the SPECT group). Two cases had identifiable PE on CTPA (both from the SPECT group) and in only one case was this considered clinically significant and treated with anticoagulation. None of the patients died at 3 months. From the observations of this head-to-head comparison of SPECT and planar V/Q scintigraphy in modern practice, the authors can conclude that: 1. Rates of non-diagnostic scans are lower using SPECT than planar acquisition, irrespective of the reporter's interpretation of SSM., 2. SSM is more commonly identified in SPECT than planar V/Q studies., 3. SSM is unlikely to represent clinically significant PE in more than 95% of patients.	Retrospective design
Wang M, Wu D, Ma R, et al. Comparison of V/Q SPECT and CT angiography for the diagnosis of chronic thromboembolic pulmonary hypertension. Radiology. 2020; 296(2):420-429.	32427559	Prospective Study	Moderate	To compare the performance of ventilation-perfusion (V/Q) scanning, V/Q SPECT, and CT pulmonary angiography (PA) in CTEPH by using digital subtraction PA as the reference standard.	A total of 150 participants (mean age, 42 years 6.15 [standard deviation]; 99 women) were enrolled. Participants who did not undergo V/Q scanning, CT PA, and digital subtraction PA procedures within a week or whose mean pulmonary artery pressure was less than 25 mm Hg were excluded from the study.	Participants were evaluated by using the diagnostic algorithm for CTEPH as published in the 2015 ESC/ERS Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension, and those in whom a diagnosis of CTEPH was suspected were consecutively enrolled in the study. V/Q scanning, CT PA, and digital subtraction PA procedures were all conducted within a 1-week period for each participant. Differences in the diagnostic performance of V/Q SPECT, V/Q planar scintigraphy, and CT PA were evaluated with areas under the curve receiver operator curve, the McNemar test, and generalized estimating equations analysis.	Digital subtraction PA assessments confirmed CTEPH in 51 participants and indicated that 602 of 1020 lung segments (20 segments per participant) were obstructed. The three imaging methods showed high sensitivity (V/Q SPECT, 98%; V/Q planar scintigraphy, 98%; CT PA, 94%) and specificity (V/Q SPECT, 89%; V/Q planar scintigraphy, 91%; CT PA, 96%) (all P . .05). However, both V/Q scanning techniques were more sensitive (V/Q SPECT: 85%, P , .001 vs CT PA: 67%; V/Q planar scintigraphy: 83%, P , .001 vs CT PA: 67%), and less specific (V/Q planar scintigraphy: 51%, P = .03 vs CT PA: 60%; V/Q SPECT: 42%, P , .01 vs CT PA: 60%) than was CT PA for segmental analysis. Areas under the curve for CT PA, V/Q planar scintigraphy, and V/Q SPECT were 0.95, 0.95, and 0.94, respectively (all P . .05), for individual analysis, and 0.64, 0.67, and 0.64, respectively, by segment (V/Q planar scintigraphy vs V/Q SPECT, P = .02; V/Q planar scintigraphy vs CT PA, P = .08; V/Q SPECT vs CT PA, P = .94). The authors conclude that ventilation-perfusion was more sensitive and less specific than was CT pulmonary angiography for detecting vascular obstructions at the segmental pulmonary arterial level.	All procedures and protocols were conducted at a single center. The participant number is not large enough to exclude differences in the performance of diagnostic modalities. Furthermore, digital subtraction PA is considered the reference standard for diagnosis of CTEPH and operability assessments because of its exquisite resolution and ability to demonstrate the extent of proximal disease and a vascular roadmap for planning the surgical procedure.