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Ventilation/perfusion (V/Q) scanning in contemporary patients with pulmonary embolism: utilization rates and predictors of use in a multinational study

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Abstract

Ventilation/perfusion (V/Q) imaging and computed tomography pulmonary angiography (CTPA) are common tools for acute pulmonary embolism (PE) diagnosis. Limited contemporary data exist about the utilization of each modality, including the predictors of using V/Q versus CTPA. We used the data from patients diagnosed with PE using V/Q or CTPA from 2007 to 2019 in Registro Informatizado Enfermedad ThromboEmbolica, an international prospective registry of patients with venous thromboembolism. Outcomes was to determine the trends in utilization of V/Q vs. CTPA and, in a contemporary subgroup fitting with current practices, to evaluate predictors of V/Q use with multivariable logistic regression. Among 26,540 patients with PE, 89.2% were diagnosed with CTPA, 7.1% with V/Q and 3.7% with > 1 thoracic imaging modality. Over time, the proportional use of V/Q scanning declined (13.9 to 3.3%, P < 0.001). In multivariable analysis, heart failure history (odds ratio [OR]:1.5; 95% confidence interval [CI] 1.14–1.98), diabetes ([OR 1.71; 95% CI 1.39–2.10]), moderate and severe renal failure (respectively [OR 1.87; 95% CI 1.47–2.38] and [OR 9.36; 95% CI 6.98–12.55]) were the patient-level predictors of V/Q utilization. We also observed an influence of geographical and institutional factors, partly explained by time-limited V/Q availability (less use over weekends) and regional practices. Use of V/Q for the diagnosis of PE decreased over time, but it still has an important role in specific situations with an influence of patient-related, institution-related and logistical factors. Local and regional resources should be evaluated to improve V/Q accessibility than could benefit for this population.

Keywords Pulmonary embolism · Computed tomography angiography · V/Q scan · Radionuclide imaging

Abbreviations

CI	Confidence interval
CRI	Chronic renal insufficiency
CrCl	Creatinine clearance
CTPA	Computed tomography pulmonary angiography
CT	Computed tomography
ESC	European society of cardiology
pDVT	Proximal deep venous thrombosis
OR	Odds ratio
PE	Pulmonary embolism
PIOPED	Prospective investigation of pulmonary embolism diagnosis
Sat O2	Oxygen saturation
SBP	Systolic blood pressure
SPECT	Single photon emission computed tomography
VTE	Venous thrombo-embolism
V/Q	Ventilation/perfusion

A full list of the RIETE investigators is given in the online appendix.

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Hightlights

- Despite the widespread use of CTPA, V/Q scan remains an important modality for specific patient subgroups.
- History of heart failure, renal failure or diabetes were clinical predictors of use of V/Q scanning over CT-scan.
- Regional variations in practice and resource availability deserve further attention to improve V/Q scan availability for patients who may benefit from the technology.

Introduction

Pulmonary embolism (PE) is a common and severe disease, with an increasing incidence in the recent years [1, 2]. Over the past two decades, clinical decision rules encompassing signs and symptoms and D-dimer values have facilitated the pathways for diagnosis of PE with use of additional imaging testing [3, 4].

Two common imaging techniques are currently validated for PE diagnosis [5]. Ventilation/perfusion lung scan (V/Q scan) is a scintigraphy technique based on direct assessment of both perfusion and ventilation [6–8] with the advantage of low radiation burden [9]. Limitations with V/Q scanning include availability only in selected centers and selected times of the week (especially diurnal and working days practices due to production of radiopharmaceuticals). Computed tomography pulmonary angiography (CTPA) is the other available modality [10, 11], aimed to visualize directly the clot in pulmonary arteries with the use of iodine contrast media. The widespread availability of CTPA with low rates of inconclusive results [12] and the ability to offer alternative diagnoses other than PE, has led to its quick adoption [13] despite the relatively higher radiation dose.

The last ten years have seen a deep change in PE diagnosis. The incidence of PE has been progressively increasing, in part due to advances in diagnostic algorithms and tests leading to identification of more patients, including less severe previously undetected cases [14, 15]. The choice of imaging modalities for diagnosis of PE may be influenced by patient factors (i.e., preference of V/Q scan for patients with severe renal insufficiency) but also by institutional or technical factors (such as the availability of the imaging modality), among others [16]. The optimal choice of imaging modalities remains an area of active debate, as reflected by the recent changes in recommendations (for further consideration of V/Q scanning) in some clinical guidelines [5, 17].

The aim of this study was to describe the trends in use of V/Q scanning vs. CTPA in a large prospective cohort of patients with objectively confirmed PE. Further, we explored the use of V/Q vs. CTPA depending on patient-level, institutional and regional factors. Finally, we identified the predictors of use of V/Q in multivariable analysis in contemporary patients with PE.

Materials and methods

Data source

Data were obtained from the Registro Informatizado Enfermedad ThromboEmbolica (RIETE) registry, an ongoing, international, multicenter, prospective registry of consecutive patients presenting with acute and symptomatic venous thromboembolism (deep-vein thrombosis, PE, or both) confirmed by objective tests (CTPA, V/Q scan or pulmonary angiography). For patients included in the current study, acute symptomatic PE was confirmed by high probability V/Q scanning and/or positive CTPA. All patients provided informed consent according to the requirements of the ethics committees at participating hospitals. More details about the methodology of the RIETE registry have been described previously [18–20].

Inclusion and exclusion criteria

We included consecutive patients with acute symptomatic PE enrolled in RIETE between January 2007 and December 2019 and diagnosed by V/Q scanning and/or CTPA. In this study, we excluded patients with incidental (asymptomatic) PE, or patients with PE diagnosed with modalities other than V/Q scan or CTPA. Patients were not included in the RIETE registry if they were currently participating in a therapeutic clinical trial with blinded assigned treatments.

Groups constitution, study variables and definitions

For the main outcome defined as the description of the trends in use of V/Q scanning vs. CTPA, we considered patients whose final diagnosis of PE was established by V/Q scan or by CTPA from January 2007 to December 2019. We also identified subgroups of patients in whom both of these imaging modalities were performed. For this outcome, we compared the demographics and clinical characteristics of patients who were diagnosed by CTPA versus those diagnosed by V/Q scanning.

For the secondary outcome, defined as the identification of predictors of V/Q scanning use in contemporary patients with PE, we chose to refine the pool of patient to fit with current practice and guidelines [5, 17, 21]. Also, we evaluate in this analysis patient diagnosed for PE in RIETE between 2015 and 2019. Demographics and clinical characteristics of patients was compared to evaluate predictors of V/Q use with multivariable logistic regression.

The choice between CTPA vs. V/Q may be driven by patient-related factors, but also resource availability, or institutional or regional practice patterns. As such, we decided to

review the utilization of CTPA vs. V/Q across the countries and also according to hospital size. Thus, generating groups of variables depending on patient-level, institutional and regional factors as explained below.

Statistical analysis

We reported the categorical variables as percentages and the continuous variables as mean with standard error (or median with interquartile range, where the data were not normally distributed). Categorical variables were compared using the chi-squared test (two-sided) and Fisher's exact test (two-sided). Continuous variables were compared using Student's *t* test. We presented the proportions with respective 99% CI. We used linear regression analysis to test for linear trends. A two-sided $P < 0.01$ was considered as significant.

Several considerations were made for assessment of the predictors of the use of CTPA vs. V/Q for multivariable analysis. First, to reflect the determinants of use of CTPA vs. V/Q in current contemporary practice, we restricted the cohort to years 2015 to 2019 for this analysis. Further, since resource availability is a key determinant of use of diagnostic tests, for this analysis we restricted the patient cohort only to those enrolled from centers that had availability both for V/Q scanning and CTPA (either in the hospital, or in a nearby facility). With respect to the choice of variables for multivariable modeling, it was decided a priori to choose the covariates based on clinical reasoning, without removing the variables from the multivariable model. The selected variables included hospital-level and regional characteristics such as enrollment from Western Europe, Eastern Europe, Americas, or rest of the world (assessed for countries with at least 25 valid patients), hospital size (< 100 beds, 100–300 beds, > 300 beds) and diagnosis made on Saturday and Sunday versus the rest of the weekdays (dichotomous variable). Patient-level variables included age (< 25, 26–40, 41–55, 56–70 and > 71 years old), sex, body weight (Kg), Geneva score < 4, diabetes mellitus, history of heart failure, history of prior venous thrombo-embolism (VTE), history of chronic lung disease, active cancer, and renal insufficiency (3-category categorical variable, with creatinine clearance levels ≤ 30, 31–59, and ≥ 60 mL/min based on the Cockcroft and Gault method [22]). Results were presented as odds ratio (OR) with 95% confidence interval (CI).

Statistical analyses were performed with SPSS for Windows (version 22.0, SPSS Inc.), except for analysis of trends, which was performed by STATA 1C (v.12.0, StataCorp, College Station, Texas).

Results

Patient population

Between January 2007 and December 2019, 66,290 patients were included in the RIETE registry. Of these, 32,985 had acute symptomatic PE confirmed with positive chest imaging (V/Q scan and/or CTPA) and were included in the current study (Fig. 1). Clinical characteristics of patients are presented in Supplementary information 1–2. Mean age was 66.8 years, and 47% of the patients were male. Most patients (21,095, 64%) presented with intermediate pre-test probability of PE (Revised Geneva score: 4–10) and few criteria of severity (only 3106 patients, 9.5% had sPESI ≥ 3). Of all the study participants, 4794 (15%) had chronic lung disease, 2888 (8.8%) history of heart failure, 11,287 (34%) had chronic renal failure and 4711 (16%) had diabetes mellitus. The majority of patients were included in centers located in Western Europe (30,483 patients; 92%) and from hospitals with capacity > 300 beds (28,088 patients; 78%).

Evolution of thoracic imaging modality utilization and patient characteristics according to the test used for diagnosis of PE

Over the period between 2007 and2019, on average 89.2% of enrolled patients were diagnosed by CTPA and 7.1% by V/Q scanning. The proportional use of CTPA progressively increased whereas the use of V/Q scan decreased (79.1 to 96.1% for CTPA and 13.9 to 3.3% for V/Q scan, $P < 0.001$ for linear trend for both; Fig. 2). CTPA and V/Q scan were both widely available in most RIETE centers and 32,176 patients (97.5%) were diagnosed in centers with access to both CTPA and V/Q scan.

The clinical characteristics of patients diagnosed with V/Q scan or CTPA were similar with equivalent distribution on clinical probabilities and severity signs between the two groups (Table 1). We observed a lower utilization of V/Q scan in patients aged between 26 and 70 years and higher utilization in patients aged > 80 years. Patients diagnosed with V/Q scan had more comorbidities, such as chronic heart failure (13% for V/Q scan vs. 8.4% for CTPA), moderate or severe renal failure (respectively 34% and 17% for V/Q scan and 29% and 4% for CTPA), atrial fibrillation (23% for V/Q scan vs. 13% for CTPA) and diabetes mellitus (21% for V/Q scan vs. 16% for CTPA). Patients with prior VTE were more likely to be diagnosed with V/Q scan (17% for V/Q scan vs. 14% for CTPA) but patients with associated proximal deep venous thrombosis (pDVT) were more likely diagnosed with CTPA (31% for CTPA vs. 27% for V/Q scan). Most patients were recruited in large centers (> 300

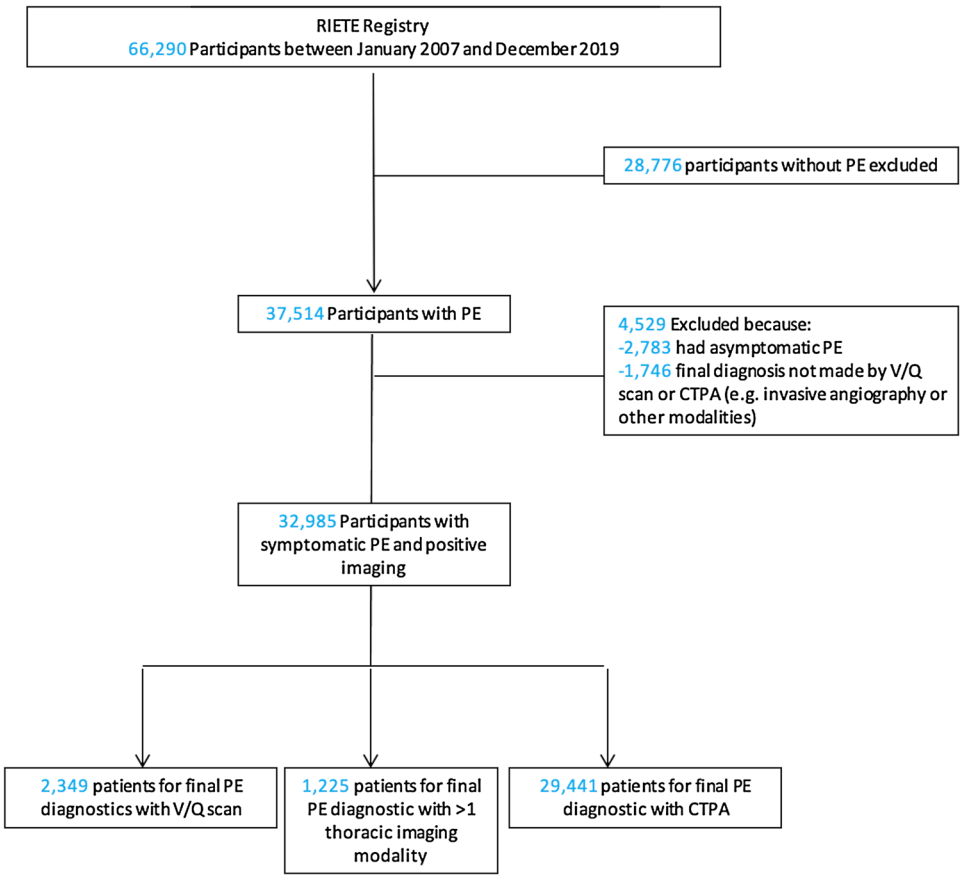

Fig. 1 Flow diagram of study participants

beds) localized in Western Europe both for V/Q scan and CTPA. The use of V/Q scan was lower in hospitals ≤ 100 beds (1.3% vs. 2.1% for CTPA). Moreover, a smaller proportion of patients were diagnosed with V/Q scanning on weekend compared to CTPA (16% vs. 20% for CTPA).

The use of > 1 chest imaging modality to diagnose PE in the same patients was low with progressive decline from 6.9% in 2007 to only 0.6% in 2019. Clinical characteristics of patient diagnosed with > 1 thoracic imaging modality was quite similar to the population evaluated with CTPA (Supplementary information 3).

Institutional and regional variation in contemporary patients diagnosed with thoracic imaging

Institutional and regional variations in use of CTPA and V/Q scan were observed in a contemporary subgroup (2015–2019) of this cohort (Fig. 3). CTPA was the predominant modality of diagnosis in Western Europe, Eastern Europe, Americas and in the rest of the world. The use of V/Q scan was low but even lower in Eastern Europe and Americas (respectively 1% and 2%) compared to Western Europe and Rest of the world (respectively 5% and 8%). CTPA was the predominant modality of diagnosis both in large, medium and small hospitals. V/Q scan was used in 5% both in large and medium hospitals but only in 2% in small hospitals.

Predictors for V/Q scan used identified with multivariable analysis

The predictors for V/Q scan utilization were established in a population diagnosed between 2015 and 2019 to in multivariable analysis. For this analysis, patients were selected from centers with > 25 patients included to reflect the decisions from experienced centers. Finally, we restricted the patient cohort only to those patients enrolled from centers that had availability both for V/Q scanning and CTPA. The clinical characteristics of patients included in this analysis are summarized in Supplementary information 4. Results of the multivariable model (Table 2) are as follows:

Among the patient-related factors, heart failure history ([OR 1.5; 95% CI 1.14–1.98], P < 0.01), moderate renal failure ([OR 1.87; 95% CI 1.47–2.38], P < 0.001), severe renal failure ([OR 9.36; 95% CI 6.98–12.55], P < 0.001) or diabetes ([OR 1.71; 95% CI 1.39–2.10], P < 0.001) were among the significant predictors of V/Q scan utilization.

Institutional factors are also predictors for thoracic imaging preference: The need to diagnosis on weekend days

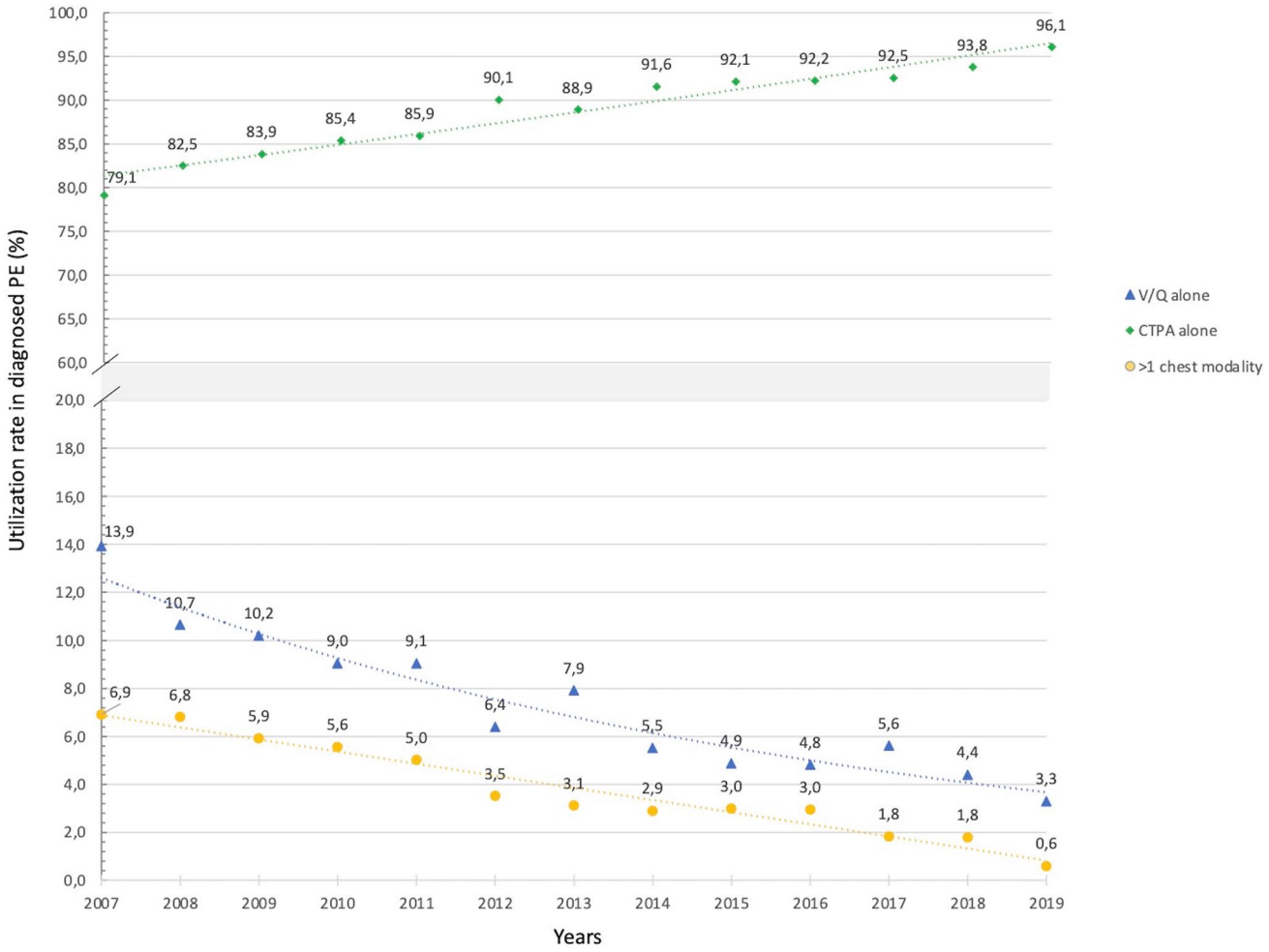

Fig. 2 Evolution in utilization of thoracic imaging modalities from 2007 to 2019 as the diagnostic modality for PE

correlated with to a lower utilization of V/Q scan ([OR 0.63; 95% CI 0.49–0.81]; P < 0.001). Hospital size was not a significant predictor in multivariable analysis.

Regional factors also had an influence: Compared to Western Europe (the reference category), V/Q scan was less likely to be used in Eastern Europe ([OR 0.17; 95% CI 0.06–0.45]; P < 0.001), not significantly different in the Americas ([OR 0.5; 95% CI 0.22–1.14], P = 0.1) and more likely to be performed in the rest of the world ([OR 2.04; 95% CI 1.29–3.22], P < 0.01).

Discussion

The current study specifically aimed to evaluate the trends in use of V/Q scanning vs. CTPA especially in contemporaneous patients to fit with current practices and guidelines. We observed that a significant minority of patients with PE still underwent V/Q scan despite a progressive decline in utilization. In bivariate analyses from this multinational large cohort of patients with PE, we noted important differences in patient characteristics, institutional, and regional factors associated with the likelihood of using CTPA or V/Q scanning for confirmation of PE diagnosis. Multivariable models revealed the influence of some well-known clinical factors (such as diabetes or renal failure) but also highlighted additional comorbidities (as history of heart failure or prior VTE) to be among predictors of use of V/Q scanning. Our study also points out the influence of time-selected availability of the technique (lower utilization of V/Q in weekend vs. weekday). In turn, we also observed variations in use of both modalities in different regions of the world.

The important role of CTPA in diagnosed PE is a fact well established. With improvement of CT technology, the amount of radiation exposure has decreased, and the diagnostic accuracy has increased. CTPA has many advantages over a V/Q scan including establishing the diagnosis in a timely manner in severely ill patients, diagnosis of right ventricle enlargement, and the assessment of several other potential diagnoses, such as pulmonary infiltrates,

Table 1 Patient characteristics according to thoracic imaging modality used for PE confirmation in RIETE

	V/Q scan only		CTPA only	
	n(%)	%99 CI (%)	n(%)	%99 CI (%)
Patients, n	*2349*		*29,411*	
Male sex	980 (42%)	39.1–44.4	14,061 (48%)	47.1–48.6
Age, years (mean ± SD)	69.9 ± 17		66.6 ± 17	
< 25 years	34 (1.4%)	0.8–2.1	516 (1.8%)	1.6–2.0
26–40 years	143 (6.1%)	4.8–7.4	2358 (8.0%)	7.6–8.4
41–55 years	269 (11%)	9.8–13.2	4261 (14%)	14.0–15.0
55–70 years	515 (22%)	19.7–24.1	7660 (26%)	25.4–26.7
71–80 years	662 (28%)	25.8–30.6	7914 (27%)	26.2–27.6
> 80 years	726 (31%)	28.5–33.4	6702 (23%)	22.2–23.4
Weight, kg (mean ± SD)	75.4 ± 17.9		77.3 ± 16.8	
BMI	28.4 ± 6.3	28.0–28.8	28.4 ± 6	28.3–28.5
Comorbidities				
Chronic heart failure	314 (13%)	11.6–15.2	2476 (8.4%)	8.0–8.8
Chronic lung disease	348 (15%)	12.9–16.7	4271 (15%)	14.0–15.0
CrCl levels > 60 mL/min	1158 (49%)	46.6–52.0	19,710 (67%)	66.3–67.7
CrCl levels 31–59 mL/min	803 (34%)	31.7–36.7	8422 (29%)	28.0–29.3
CrCl levels < 30 mL/min	388 (17%)	14.5–18.5	1279 (4.3%)	4.0–4.7
Atrial fibrillation	227 (23%)	19.9–26.9	2230 (13%)	12.2–13.5
Diabetes mellitus	415 (21%)	19.0–23.8	4130 (16%)	15.2–16.3
Active cancer	427 (18%)	16.1–20.2	4975 (17%)	16.4–17.5
Prior VTE	392 (17%)	14.7–18.7	4093 (14%)	13.4–14.4
Characteristics of PE at presentation				
Revised geneva score, median 0–3	469 (20%)		5521 (19%)	
Revised geneva score, median 4–10	1508 (64%)		18,821 (64%)	
Revised geneva score, median 11–22	372 (16%)		5069 (17%)	
Dyspnea	1905 (82%)	80.0–84.0	23,504 (81%)	80.8–82.0
Heart rate > 95 bpm	810 (36%)	33.5–38.8	11,691 (41%)	40.4–41.9
Sat O2 < 95%	825 (66%)	63.0–70.0	10,430 (66%)	64.6–66.6
Sat O2 < 90%	378 (30%)	27.1–33.8	4575 (29%)	27.9–29.7
SBP levels < 90 mmHg	64 (2.7%)	1.9–3.6	976 (3.3%)	3.0–3.6
sPESI, median (IQR)	1.2 ± 1.1		1 ± 1	
Associated pDVT	641 (27%)	24.9–29.7	9076 (31%)	30.2–31.6
Diagnosed on a Saturday–Sunday	366 (16%)	13.7–17.5	5902 (20%)	19.5–20.7
Hospital capacity				
< 100 beds	30 (1.3%)	0.7–1.9	626 (2.1%)	1.9–2.4
100–300 beds	331 (14%)	12.2–15.9	3767 (13%)	12.3–13.3
> 300 beds	1988 (85%)	82.7–86.6	25,018 (85%)	84.5–85.6
Regional variables				
Western Europe	2063 (88%)	86.1–89.6	27,285 (93%)	92.4–93.2
Eastern Europe	37 (1.6%)	0.9–2.2	759 (2.6%)	2.3–2.8
Americas	152 (6.5%)	5.2–7.8	715 (2.4%)	2.2–2.7
Rest of the world	97 (4.1%)	3.1–5.2	652 (2.2%)	2.0–2.4

V/Q scan ventilation/perfusion lung scan, *CTPA* computed tomography pulmonary angiography, *CrCl* creatinine clearance, *Sat O2* oxygen saturation, *SBP* systolic blood pressure, *pDVT* proximal deep venous thrombosis, *SD* standar deviation, *IQR* interquartile range, *sPESI* simplified pulmonary embolism severity index, *BMI* body mass index, *bpm* beats per minute

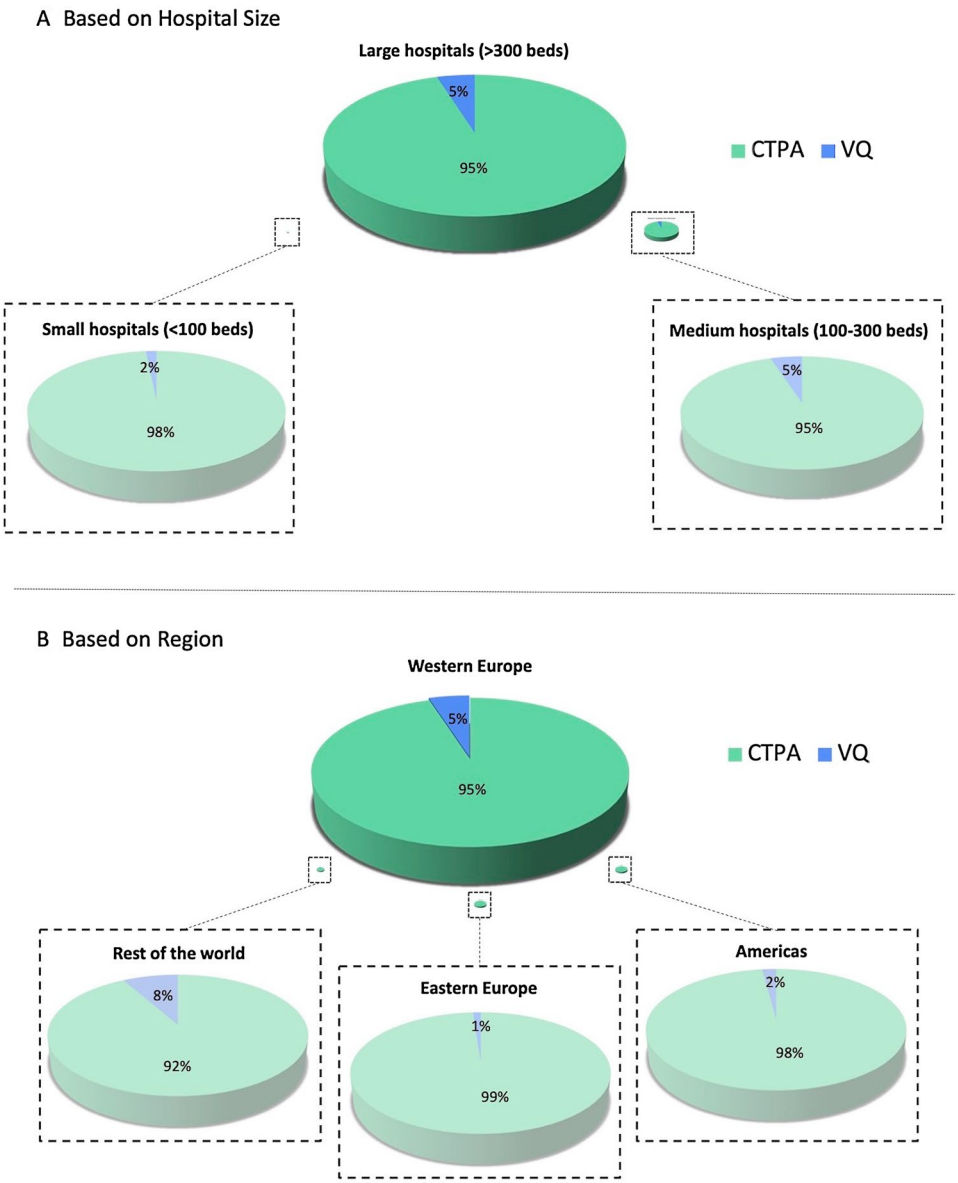

Fig. 3 Institutional (Panel A) and regional variation (Panel B) of CTPA and V/Q scan use in contemporising Period (2015–2019). *The size of the original circles is proportional to the number of patients enrolled in each category. The framed figures correspond to an enlargement of the actual-size panels that were small

aortopathy, pleural disease, and others. In turn, V/Q scan may be most helpful in stable patients, in patients for whom there is major concern for contrast-induced nephropathy, and in patients with history of life-threatening anaphylaxis to iodinated contrast agents. Because of the contraindication of iodine contrast or side effects in patients with severe renal failure or diabetes [23], the important proportion of patients with these comorbidities in the V/Q scan arm could have been expected. It is generally agreed that there is some risk of contrast-induced acute kidney injury in patients with advanced kidney disease who undergo iodinated contrast studies such as CTPA [24]. The extent of the risk remains uncertain and controversial in some studies, which has been attributed to residual confounding and lack of head-to-head randomized comparisons [25]. Other comorbidities such as heart failure or atrial fibrillation were also more common in patients diagnosed by V/Q scan. Although some of such associations may be related to coexisting conditions, such as diabetes and kidney disease, the association between heart failure and use of V/Q persisted in multivariable analysis. In patients with congestive heart failure, the delayed transit time of the contrast agent may bring limitation and reduce the diagnostic yield of CTPA [26], thereby explaining the use of V/Q scan. In a previous study, we demonstrated the high utilization of CTPA in PE diagnosis compared to other strategies, even in patients in whom it is recommended to avoid irradiation or the use of contrast agents [16]. This finding is concerning because it reflects on a dominant diagnostic practice pattern even in subgroups likely to suffer more adverse effects from the technique. This issue deserves

Table 2 Predictors of use of V/Q Scanning vs CTPA in multivariable analysis in contemporary patients

	Odds ratio	95% Confidence interval	P value
Patient level variable			
Male sex	1.04	(0.86–1.26)	0.678
Age			
≤25	0.85	(0.31–2.34)	0.752
26–40 years	1.25	(0.82–1.92)	0.303
41–55 years	0.91	(0.65–1.28)	0.589
55–70 years	0.96	(0.75–1.24)	0.760
71 years and above (reference category)	Ref		
Weight (per each 1 kg increase)	1.00	(1.00–1.01)	0.092
Geneva score < 4 (dichotomous variable)	1.30	(1.04–1.62)	0.019
History of heart failure	1.50	(1.14–1.98)	0.004
History of lung disease	1.16	(0.91–1.47)	0.232
Creatinine Clearance			
CrCl levels > 60 mL/min (reference category)	Ref		
CrCl levels 31–59 mL/min	1.87	(1.47–2.38)	0.000
CrCl levels < 30 mL/min	9.36	6.98–12.55)	0.000
Prior history of VTE	1.39	(1.09–1.77)	0.008
Diabetes mellitus	1.71	(1.39–2.10)	0.000
Active cancer	1.16	(0.91–1.47)	0.226
Patient diagnosed on a Saturday or Sunday (Yes/No)	0.63	(0.49–0.81)	0.000
Hospital level variable			
Admission to hospitals with size < 100 beds	0.30	(0.07–1.23)	0.095
Admission to hospitals with size 100–300 beds	0.95	(0.68–1.33)	0.770
Admission to hospitals with size > 300 beds (reference category)	Ref		
Regional level variable			
Enrollment from Western Europe (reference category)	Ref		
Enrollment from Eastern Europe	0.17	(0.06–0.45)	0.000
Enrollment from Americas	0.50	(0.22–1.14)	0.101
Enrollment from the rest of the world	2.04	(1.29–3.22)	0.002

This analysis was performed in patients from 2015 to 2019 from hospitals with at least 25 patients in the study period, where both CTPA and V/Q scanning were available to be offered

additional attention via educational and quality-improvement programs.

Not only patient factors but also hospital factors as well as technical availability influence the medical decision process. The availability of the tests is an obvious factor influencing the choice between the two imaging techniques. For that reason, for the analysis of predictive factors of V/Q scan use in multivariable analysis, we chose to exclude centers that could not perform one of these tests in order to avoid availability bias. It should be noted, however, that the majority of physicians working through the RIETE network had the option of using both tests for the diagnosis of their patients, indicating a good overall availability of both techniques. Despite good availability, use of V/Q trended to be lower in small hospitals, possibly due to a limited knowledge of this availability. Moreover, the V/Q scan is a test that is known to be less accessible during certain periods, particularly at weekends, a fact confirmed by our multivariate analysis. There was a time when many nuclear medicine departments performed V/Q scans on weekend (especially for emergency on Saturday morning), however, limited use and excess costs have led to the disappearance of this availability in most centers. We strongly recommend health systems to locally evaluate the accessibility to this technique within individual hospitals or nearby health systems and, with the help of local or regional nuclear medicine units, to implement ways to perform V/Q scan in a timely manner.

Contemporary data from RIETE showed similar practices in Western Europe and the American continent whereas Eastern Europe have a lower utilization rate of V/Q scan. We also noticed the unexpected finding that V/Q scan was proportionally more commonly used in centers located in the rest of the world. This fact is all the more surprising given the global distribution of

nuclear medicine. There are over 25,000 SPECT cameras in the world distributed in 134 out of 195 countries [27] but global distribution is heterogenous and range 17.9 cameras/million in high-income countries against < 1.7 in other countries. Currently, the discipline of diagnostic nuclear medicine has the smallest share of the global medical imaging market at 6.5% but it is observed a global nuclear medicine growth through the world.

Another interesting fact revealed in this analysis was the situations where more than 1 thoracic imaging modality was requested for PE diagnosis. Unfortunately, the RIETE registry was not built to explore prioritization between these tests or circumstances leading to their utilization. However, it appears that this is an infrequent observation and with significant decrease over time. This decrease could be explained by technological innovation with lead to decrease inconclusive results both with CTPA [28] and V/Q scan [29, 30] with a better confidence on tests results. The clinical characteristics of patients diagnosed this way did not differ from the population diagnosed with CTPA. Some of such patients may have been also diagnosed with dual-modality scanners, partly caused by non-diagnostic scans. Unfortunately, the current data elements in RIETE do not allow for in-depth assessment of this issue. The study of factors influencing this practice could be the subject of further studies once dedicated data elements are available.

Our study has some limitations. First, data from RIETE do not include all centers in the enrolling countries and many centers are located in Western Europe. However, RIETE includes small and large, regional and referral centers. Previous studies have shown close resemblance of patients from RIETE to that of large administrative databases [31]. Second, RIETE lacks a core imaging laboratory for independent re-assessment of the images. Although lack of a core laboratory is a limitation in registry-based studies, including RIETE, our assessment of utilization rate of the technologies is less likely to be affected by this limitation. Third, as RIETE is based on real-life condition, each center is free to perform V/Q scan according to its own practices and possibilities. Even if the V/Q scan technology is now including CT [12, 29, 32, 33] the available data elements the registry do not make it feasible to distinguish planar or V/Q SPECT. Finally, even if our data suggest a low utilization rate of V/Q scan in diagnostic PE through RIETE, they do not prejudice the overall importance of scintigraphy in thrombosis disease. As RIETE only enrolls patients with objectively confirmed VTE, we were unable to explore the use of V/Q scan in patients with suspected PE (in whom the diagnosis was not confirmed). It also should be notice than V/Q scan currently have a valuable importance in post-embolic sequelae evaluation [5, 34, 35] and in pulmonary hypertension [36].

In conclusion, CTPA is the dominant modality for imaging PE. However, a significant minority of patients with PE still underwent V/Q scan. The study had population-level and patient-level goals to try to explore these results: at the patient level, we recognized the influence of some well-known clinical factors (such as diabetes or renal failure) but also highlighted additional comorbidities (as history of heart failure or prior VTE) to be among predictors of use of V/Q scanning. The presence of these factors should be considered in the decision for the choice of thoracic imaging modality for the diagnose PE. At the population-level, we noted regional and institutional variations in the use of VQ vs CTPA, partly explained by the availability of the modalities but also with an influence of regional practices. Health systems should optimize strategies to make V/Q scanning available (locally or nearby facility with regionalized transfer policies) among subgroups who may need the technology, especially over holiday periods and weekends.

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Authors contribution PBB substantially contributed to the conception and design of the work, write the manuscript, approved the final version of the manuscript and be accountable for the manuscript's contents. NP substantially contributed to the conception and design of the work, revise the manuscript, approved the final version of the manuscript and be accountable for the manuscript's contents. GM substantially contributed to the conception of the work, revise the manuscript, approved the final version of the manuscript and be accountable for the manuscript's contents. AS substantially contributed to the conception of the work, revise the manuscript, approved the final version of the manuscript and be accountable for the manuscript's contents. BB substantially contributed to the conception of the work, revise the manuscript, approved the final version of the manuscript and be accountable for the manuscript's contents. JL substantially contributed to the conception of the work, revise the manuscript, approved the final version of the manuscript and be accountable for the manuscript's contents. LF substantially contributed to the conception of the work, revise the manuscript, approved the final version of the manuscript and be accountable for the manuscript's contents. AGD substantially contributed to the conception of the work, revise the manuscript, approved the final version of the manuscript and be accountable for the manuscript's contents. PL substantially contributed to the conception of the work, revise the manuscript, approved the final version of the manuscript and be accountable for the manuscript's contents. JA substantially contributed to the conception of the work, revise the manuscript, approved the final version of the manuscript and be accountable for the manuscript's contents. LB substantially contributed to the conception and design of the work, revise the manuscript, approved the final version of the manuscript and be accountable for the manuscript's contents. MM substantially contributed to the conception and design of the work, revise the manuscript, approved the final version of the manuscript and be accountable for the manuscript's contents.

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Declarations

Conflict of interest Dr. Bikdeli reports that he is a consulting expert, on behalf of the plaintiff, for litigation related to two specific brand models of IVC filters. Dr. Bertoletti reports personal fees and other from Bayer, personal fees and other from BMS, personal fees and other from Pfizer, personal fees and other from Léo-Pharma, non-financial support from Sanofi, outside the submitted work. The others authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

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