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# Impact of CT venography added to CT pulmonary angiography for the detection of deep venous thrombosis and relevant incidental CT findings

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ABSTRACT

*Objectives:* To assess the additional diagnostic value of CT venography (CTV) simultaneously performed with CT pulmonary angiography (CTPA) in the context of thromboembolic disease for the detection of deep venous thrombosis (DVT) and other relevant incidental CT findings.

*Materials and Methods:* Retrospectively and consecutively, we included all patients referred to our emergency department within the last 24 months for suspected pulmonary embolism (PE) who underwent CTPA combined with CTV. Two radiologists blinded to clinical information and results independently analysed CTV images in the context of DVT of the lower extremities and other, unsuspected abdominal/pelvic findings. These latter were classified as relevant with therapeutic consequences or irrelevant. One radiologist reviewed patient clinical records. Inter-observer agreement for DVT detection was calculated.

*Results:* Of 696 patients, 119 had PE (17.1%) and 54 had DVT (7.8%), 16 (2.3%) of them without concomitant PE. Inter-observer agreement between the two readers was substantial (kappa = 0.78). CTV examinations led to diagnosis of relevant incidental abdominal/pelvic findings in 40 (5.7%) patients, including 11 with new malignant tumours, and 8 with progressive metastatic disease. The evaluated clinical and biological risk factors were not significantly associated with the presence of relevant incidental findings. CTV changed therapeutic management in 29 patients (4.3%): 15 had DVTs without PE, and 14 had abdominal/pelvic findings with therapeutic consequences.

*Conclusion:* CTV simultaneously performed with CTPA offers limited incremental value for detecting DVT. It may reveal other relevant findings leading to therapeutic changes, but the low rate does not justify screening patients with suspected PE.

## 1. Introduction

Venous thromboembolism (VTE) is a critical disease and a common cause of morbidity and mortality in developed countries, with an incidence of around 1.5 per 1000 person-years [1]. More than 90% of pulmonary emboli arise from leg and pelvic deep veins. Clinically suspected PE has become one of the most frequent indications for CT pulmonary angiography (CTPA) in emergency departments. The primary risk factor for recurrent pulmonary embolism (PE) is, among others [2], acute or residual venous thrombosis [3], and the incidence of both PE and DVT is steadily rising [4].

About 50% of patients with symptomatic PE have concomitant DVT [3,5]. Ultrasonography (US) offers high accuracy for detecting lower limb DVT, but remains a subjective operator-dependent examination, and the pelvic veins are often inadequately visualized, especially in obese patients. One suggestion to resolve this issue [6,7] is the addition

*Abbreviations:* BMI, Body mass index; $CTDI_{vol}$, Volume computed tomography dose index; CTPA, Computed tomography pulmonary angiography; CTV, Computed tomography venography; DLP, Dose length product; DVT, Deep vein thrombosis; PE, Pulmonary embolism; US, Ultrasonography; VTE, Venous thromboembolism.

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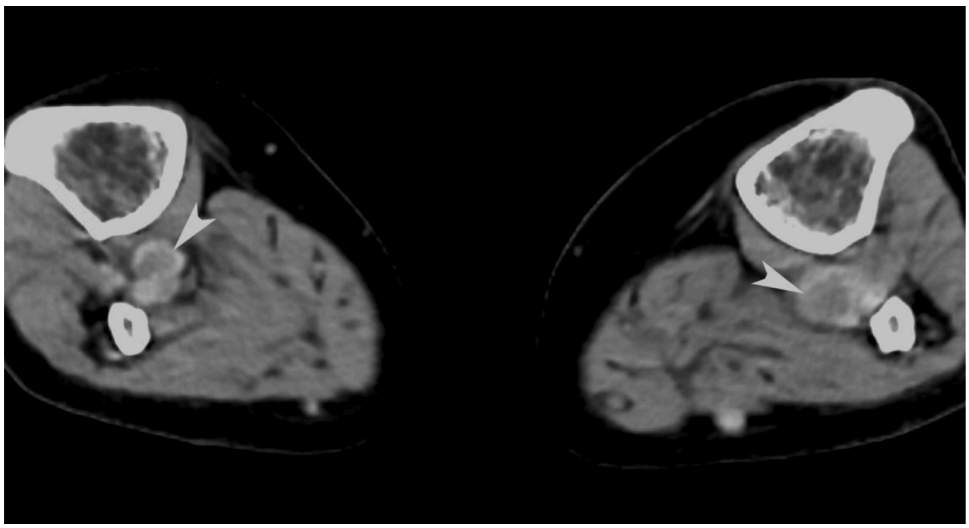

**Fig. 1.** Axial CT venography demonstrates bilateral popliteal DVT (arrows) detected in a 58-year-old man with no PE. The technical quality was rated 1 (excellent). DVT = deep vein thrombosis

of CT venography (CTV) of the lower extremities and pelvis to CTPA to improve DVT detection. Adding CTV to CTPA is straightforward: additional images are acquired from the popliteal fossa caudally to the inferior vena cava cranially during the same examination, using previously intravenously injected contrast agent. The data acquisition can thus be performed almost without any additional contrast medium injection, and the results are more objective and reproducible compared to US. The disadvantage is the radiation exposure of the patient, leading to a question of the benefit-risk balance of CTV performed simultaneously with CTPA for diagnosing DVT. Indeed, to reduce radiation exposure, Kalva et al. advocated limiting data acquisition with CTV to the lower extremities rather than including the pelvic veins, because including the latter does not significantly improve DVT detection [8]. However, extension of CTV to the pelvis could reveal other, unsuspected diseases, such as malignant pelvic tumors, inflammation or infection, that could even be the underlying cause for VTE [9].

There are few publications available to clarify the rate or value of incidental detection of relevant CT findings from simultaneous CTV [10]. Our aim therefore was to assess the additional diagnostic value of CTV simultaneously performed with CTPA in the context of thromboembolic disease, for the detection of DVT and other relevant, but unsuspected CT findings.

## 2. Materials and Methods

### 2.1. Patients

This retrospective study was conducted at the Lausanne University Hospital in Switzerland.

The institutional review board approved the study prior to our data collection. After entering the keywords “pulmonary embolism” and “deep venous thrombosis” into our comprehensive electronic database of examination reports, (search period from January 2015 to December 2016), we retrieved data for 725 patients who had undergone CTPA together with CTV for suspected PE. Patients under age 50 years were not eligible, because CTPA had always been performed without CTV in this younger age group in accordance with our local CT protocols and for radiation protection purposes.

### 2.2. CT parameters

We used a 256-row multidetector CT system (Revolution CT, GE Healthcare, Milwaukee, Wisconsin, USA). All examinations were performed in helical acquisition mode following the intravenous (IV) injection of 80 mL iodinated contrast medium (Accupaque®, 300 mg I/mL, GE Healthcare, Milwaukee, Wisconsin, USA) at a flow rate of 4 mL/s for CTPA into an antecubital vein using a power injector. Bolus tracking was used, with a region of interest centred on the main pulmonary artery. Acquisition was triggered when the CT attenuation exceeded 150 Hounsfield units. Immediately afterwards, we added IV injection of 40 mL of iodinated contrast medium at a flow rate of 1 mL/s for CTV, flushed with 40 mL of saline (NaCl) at a flow rate of 1 mL/s. CTV data acquisition was then performed after a delay of 210 seconds.

Patients were positioned supine with arms above the head and scanned in the cranio-caudal direction from the lung apices to the diaphragm, at full inspiration, and then from the popliteal fossa to the renal veins in the caudocranial direction. We used 120 kV for the CTV acquisition and three tube potential settings (80, 100, or 120 kV) for the CTPA acquisition depending on patient body mass index (BMI; <24, 24-26, or >26 $kg/m^2$, respectively). The tube current ranged from 100 to 580 mA with automatic tube current modulation in all three axes and a noise index of 25. The beam pitch was 0.992 and the gantry rotation time was 0.5 seconds. Image reconstruction parameters were as follows: section thickness 1.25 mm; section overlap 1 mm; soft tissue kernel algorithm, and adaptive statistical iterative reconstruction (ASiR-V) algorithm at 50%.

Volume CT dose indexes ($CTDI_{vol}$) and dose-length products (DLP) were retrieved from the dose exposure reports integrated into the DICOM structured report of each CT examination.

### 2.3. Image analysis and patient records

We did not re-evaluate CTPA images. Two independent and blinded radiologists (S.S and D.R) performed image analysis of CTV on our electronic picture archiving and communication system workstation (Carestream Vue, version11.4; Carestream Health, Rochester, NY, USA). They had respectively 20 and 10 years of expertise in thoracic imaging. The two readers were not aware of the CTPA results and did not analyse the CTPA images.

Each reader evaluated the technical quality of the CTV images, i.e., the contrast medium filling of the veins, according to a 3-point scale (1 = excellent, 2 = acceptable, 3 = non-acceptable) (Fig. 1). CT examinations that one or both readers considered to be technically non-acceptable were excluded from the analysis.

A third radiologist (P.D.), who was not involved in the image analysis, reviewed the clinical records of all patients, using the electronic

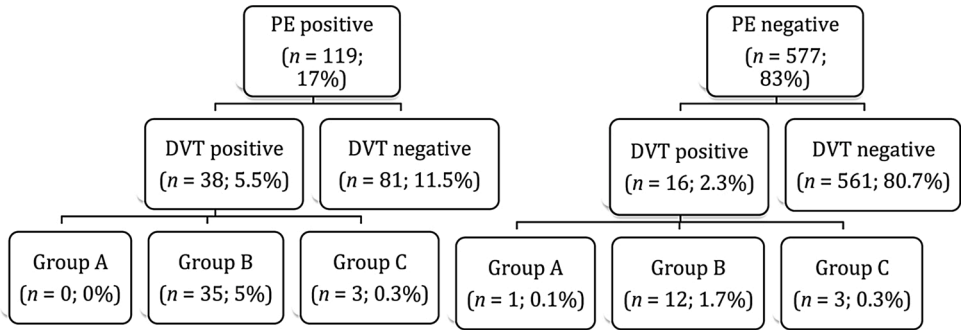


**Fig. 2.** Occurrence and localization of DVT in patients with and without PE.
Group A: patients with isolated DVT in the pelvic veins.
Group B: patients with DVT in the lower limb veins, from the femoral veins to the infra-popliteal veins unilaterally or bilaterally.
Group C: patients with DVT in both, pelvic and lower limb veins unilaterally or bilaterally.
PE = pulmonary embolism; DVT = deep vein thrombosis

database of the hospital. We recorded the symptoms and the D-dimer level of all patients, but did not consider the Wells Score, since the latter was not systematically calculated at our emergency department. The clinical symptoms leading to CTPA/CTV, and the incidence of PE and DVT in each of our patients was recorded. By correlating the relevant incidental CT findings detected by the two readers with the medical background of each patient, we distinguished the unknown and already known relevant CT findings. Furthermore, any diagnostic and/or therapeutic consequences resulting from the unknown relevant CT findings were recorded.

The CTV images were analysed in the context of DVT of the lower extremity, pelvic veins and the inferior vena cava. DVT was defined as a low-attenuating partial or complete intra-luminal filling defect surrounded by a high-attenuating ring of enhanced venous wall that was seen on at least two consecutive axial images [11]. Findings of chronic DVT (calcification within the venous wall, diffuse narrowing of the vein) were not considered because this diagnosis would not influence patient management[8].

Considering that some patients had multiple localisations of DVT, we classified these cases as follows: group A had isolated DVT in the pelvic veins; group B had DVT in the lower limb veins only, from the femoral veins to the infra-popliteal veins; and group C had DVT in both, the pelvic and lower limb veins.

In a second step, the two readers explored all abdominal and pelvic organs included in CTV images and classified any other pathological finding they detected as relevant or irrelevant. Examples of irrelevant CT findings were simple hepatic and renal cysts, hepatic and pancreatic calcifications, hepatic haemangiomas, calcified lymph nodes and colonic diverticulosis without acute inflammation. Examples of relevant findings were malignant tumors, acute inflammation or infection. After the independent image analysis, the two readers discussed any possible discordance regarding DVTs and incidental pelvic findings until they reached a consensus.

Finally, one of the two readers analysed CT dose indicators (CTDIvol and DLP) of CTV and CTPA. The radiation exposure necessary to perform CTV and CTPA was recorded (mean, median, range). The DLP served to estimate the effective dose using a specific conversion factor (0.015 mSv. $mGy^{-1}$ $cm^{-1}$ for the chest, and 0.0066 mSv. $mGy^{-1}$ $cm^{-1}$ for the pelvis) [12,13].

### 2.4. Statistical analysis

Statistical analyses were performed using the Stata 13.1 software (Stata Corporation, College Station, TX, USA). We evaluated the incidence of DVT in patients with and without PE, as well as the incidence of CT findings entailing relevant diagnostic and therapeutic consequences

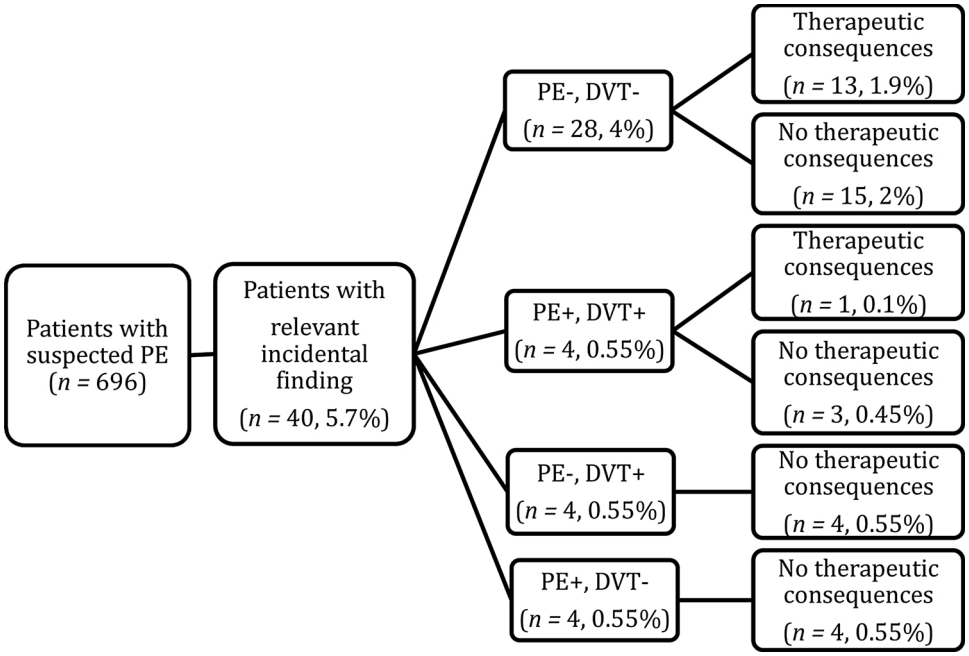


**Fig. 3.** Distribution of the incidental findings among the different patient groups and subsequent therapeutic consequences.
PE = pulmonary embolism; DVT = deep vein thrombosis
+ = present; - = absent.

**Table 1**
Overview of the relevant incidental findings with therapeutic consequences

| Relevant findings ($n = 14$) | | Therapeutic consequences | PE | DVT |
|---|---|---|---|---|
| New tumors ($n = 4$) | Retroperitoneal adenopathies | CT-guided biopsy, confirming metastatic pulmonary adenocarcinoma; oncological treatment | 0 | 0 |
| | Retroperitoneal adenopathies | Diagnosis of chronic lymphocytic leukemia and introduction of chemotherapy | 0 | 0 |
| | Bladder mass | Transurethral resection | 0 | 0 |
| | Pancreatic mass | Surgery after confirming adenocarcinoma by biopsy | 0 | 0 |
| New metastasis or increase in size ($n = 4$) | Abdominal metastases (liver, kidney and adrenal) and peritoneal carcinosis | New chemotherapy | 0 | 0 |
| | Bone metastasis | Increase of analgesia | 0 | 0 |
| | Bone metastasis | Lumbar magnetic resonance imaging followed by radiation therapy | 0 | 0 |
| | Sub-capsular hepatic metastasis | Increase of analgesics | 0 | 0 |
| Infection ($n = 4$) | Inguinal abscess | Drainage and antibiotics | 0 | 0 |
| | Pyelonephritis | Antibiotherapy | 1 | 1 |
| | Infectious hip arthritis after hip replacement with intramuscular abscess | Removal of the hip prosthesis and spacer insertion | 0 | 0 |
| | Knee bursitis | Final diagnosis of inflammatory arthritis confirmed by ultrasound, laboratory markers and intra-articular puncture; treatment by intra-articular cortisone injection | 0 | 0 |
| Vascular ($n = 2$) | Aneurysm of the abdominal aorta | Aortic prosthesis | 0 | 0 |
| | Suspicion of occlusion of femoral stent | Angioplasty and stenting of the left femoral artery | 0 | 0 |

0 = Absent; 1 = Present
PE: pulmonary embolism
DVT: deep venous thrombosis

detected on CTV. The inter-observer agreement between the two readers for the detection of DVT was evaluated using Cohen's kappa coefficient [14]. Categorical variables are reported as number or percentage and continuous variables as mean ± standard deviation. We compared results for patients with and without PE, and for patients with and without relevant incidental CT findings, using Fisher's exact test for categorical variables, and the Wilcoxon signed-rank sum test for continuous variables. Univariate and multivariate logistic regression analyses were also performed to find predictive factors for PE, DVT or relevant incidental CT findings. Statistical difference was considered significant at a $p$ value $<0.05$. When needed, the significance level was corrected for multiple comparisons using the Bonferroni method.

## 3. Results

Of the 725 initially retrieved consecutive CT examinations, the two readers considered CTV to be of non-adequate technical quality in 29 (4%) patients, mainly because of insufficient venous opacification. These cases were excluded from the statistical analysis. We finally analysed data for 696 patients who had CTV with CTPA, of whom 351 (50.4%) were women (age range, 50 - 99 years; mean age, 71.6 years ± 12 years).

Indications for CT examinations were principally dyspnoea ($n = 394$; 57%), chest pain ($n = 136$; 20%), hypoxia ($n = 118$; 17%), and other non-specific symptoms ($n = 48$; 6%). D-dimer level was available in 390 patients (56%), with a mean value of 5007 ng/mL (ranging from 700 to 36000 ng/mL) in patients with PE, and 2520 ng/mL (ranging from 110 to 17000 ng/mL) in patients without PE ($p < 0.001$).

PE was present in 119 patients (17%) and DVT in 54 patients (7.8%) (Fig. 1): 38 (5.5%) had both PE and DVT, 81 (11.5%) patients had only PE, and 16 (2.3%) patients had only DVT (Fig. 2). The localisation of DVT was distributed as follows: one patient (0.1%) was in group A, 47 patients (6.8%) were in group B, and six patients (0.9%) were in group C. Only one patient (0.1%) had thrombi isolated in the inferior vena cava with no extension to the lower limbs and no PE. Six patients (0.6%) had thrombi in both the pelvic and femoro-popliteal veins, of whom three (0.3%) had PE and three (0.3%) had no PE (Fig. 2). Inter-observer agreement between the two readers for DVT diagnosis was substantial (kappa = 0.78).

Of the 16 (2.3%) patients with isolated DVT, one (0.1%) was already on anticoagulation therapy. Therefore, the additional CTV led to a change in therapeutic management for 15 (2.1%) patients with the introduction of anticoagulation therapy.

Elevated D-dimer levels ($p < 0.001$), the presence of DVT ($p < 0.001$), and a medical history of PE or DVT ($p = 0.003$), were significantly associated with the presence of PE. Indeed, 27 (22%) patients with PE versus 71 (12%) patients with no PE had a history of PE or DVT ($p = 0.003$). No other clinical parameter showed a significant association with the presence of PE.

On multivariate analysis, the presence of DVT and higher D-dimer levels were independent predictive factors for PE on CTPA ($p < 0.001$).

CTV examinations led to identification of relevant incidental findings in 40 (5.7%) patients. Among these 40 patients, eight (20%) had PE (associated or not with DVT), four (10%) had DVT only, and 28 (70%) patients had neither PE nor DVT. There was no therapeutic consequence from the relevant incidental findings in 26 (65%) patients (Fig. 3). Table 1 shows the therapeutic consequences resulting from the relevant incidental findings in the remaining 14 (35%) patients. Four patients had an increase in number or size of known metastases (Fig. 4), and new malignant tumours were detected in four patients (Fig. 5), infection in four patients (Fig. 6), and vascular diseases in two patients. Of these 14 patients, one patient died 2 days after the CT evaluation. Using the Bonferroni method for multiple comparisons with a corrected $p < 0.0033$, we found no single statistically significant association between relevant incidental abdominal/pelvic findings and PE ($p = 0.37$) or DVT ($p = 0.008$) (Table 2). Moreover, no factor was found to be significantly predictive of a relevant incidental finding on multivariate analysis (data not shown).

The mean DLP resulting from CTV acquisition was 450 ± 195 mGy × cm (ranging from 150 to 848), corresponding to a mean effective dose of 2.97 mSv, and the mean CTDI was 5.6 ± 20.6 mGy (ranging from 1.6 to 9). The mean DLP resulting from the CTPA acquisition was 263 ± 101 mGy × cm (ranging from 109 to 812), corresponding to a mean effective dose of 3.95 mSv, and the mean CTDI was 9.9 ± 32 mGy (ranging from 2.8 to 19.7). Thus, CTV acquisition was responsible for about 43% of the effective radiation dose of a combined CTPA and CTV protocol.

## 4. Discussion

In our retrospective analysis including 696 patients with suspected PE, additional CTV led to a change in therapeutic management in 29 (4.1%), consisting of the introduction of anticoagulation therapy in 15 (2.1%) patients based on DVT without PE, and other treatments in 14 (2.0%) patients in whom we detected relevant incidental abdominal or pelvic findings. Although many papers have been focussed on CTV in the past, to the best of our knowledge, the detection of such unsuspected

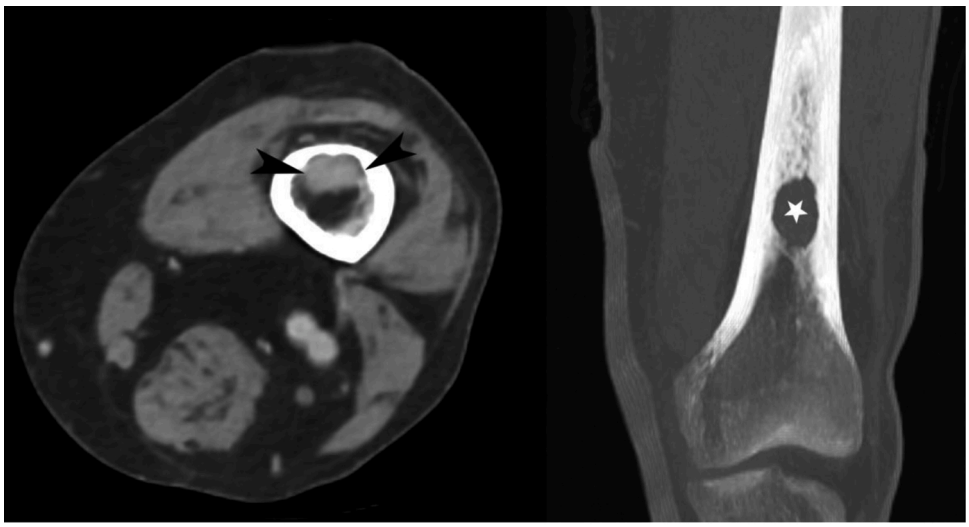

**Fig. 4.** Example of an incidental finding on an axial (a) and a coronal (b) reformatted maximum intensity projection CT venography image showing a bone metastasis of a breast cancer (arrow) in a 74-year-old woman without PE or DVT.
PE = pulmonary embolism; DVT = deep vein thrombosis

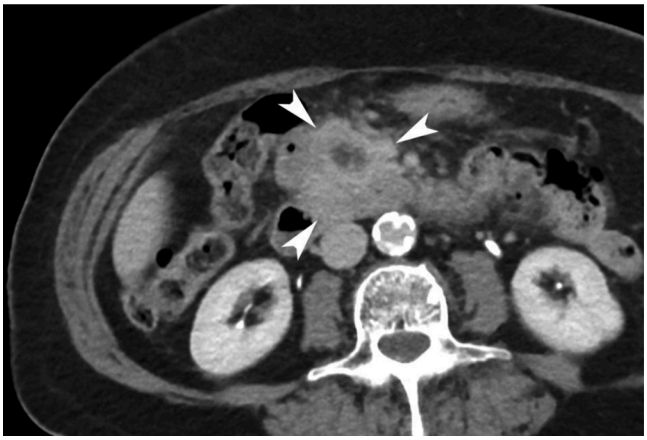

**Fig. 5.** Axial CT venography image showing pancreatic adenocarcinoma (arrow) incidentally detected in a 62-year-old man without PE and DVT.
PE = pulmonary embolism; DVT = deep vein thrombosis

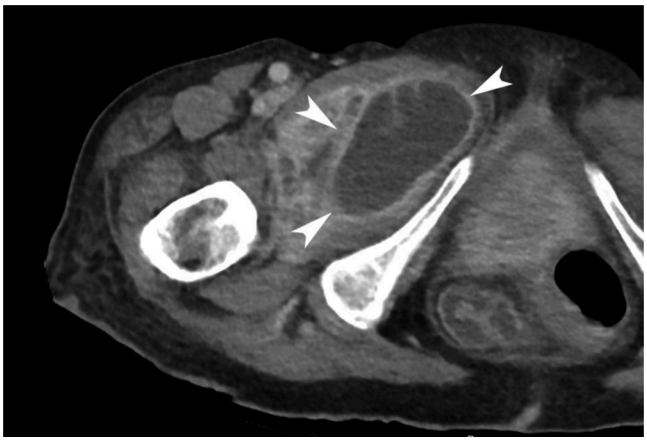

**Fig. 6.** Axial CT venography image showing an abscess of the obturator muscle (arrow) incidentally detected in a 79-year-old woman without PE neither DVT, treated by drainage and antibiotics.
PE = pulmonary embolism; DVT = deep vein thrombosis

**Table 2**
Risk factors of relevant incidental findings (IF)

| | Relevant IF $n = 40$ | Irrelevant or no IF $n = 656$ | $P$ * |
|---|---|---|---|
| Age (years) | 71.3 ± 12.0 | 75.7 ± 11.9 | *0.022* |
| Male | 21 | 324 | *0.41* |
| BMI (kg/m$^2$) | 26.3 ± 5.6 | 24.2 ± 4.9 | *0.011* |
| PE + | 8 | 111 | *0.37* |
| DVT + | 8 | 46 | *0.008* |
| History of PE or DVT + | 3 | 95 | *0.16* |
| History of cancer + | 20 | 234 | *0.05* |
| Anticoagulation + | 3 | 53 | *0.60* |
| Smoking + | 14 | 262 | *0.33* |
| Surgery + | 5 | 95 | *0.47* |
| Symptoms | | | |
| Dyspnea + | 27 | 367 | *0.10* |
| Chest pain + | 6 | 130 | *0.30* |
| Hypoxia + | 5 | 113 | *0.30* |
| Other + | 2 | 46 | *0.47* |
| Limb symptoms + | 3 | 18 | *0.11* |
| D-dimer level (ng/mL) | 4600 ± 3859 | 2850 ± 3435 | *0.011* |

*Significance level corrected for multiple comparisons using the Bonferroni method (corrected $p < 0.0033$)
+ = presence
BMI = body mass index
PE = pulmonary embolism
DVT = deep venous thrombosis of the lower extremities

findings thanks to CV has not been previously reported.

In 16 (2.3%) patients, we detected isolated DVT without associated PE. This rate is slightly lower that previously reported values [3,7,8,11,15]. Loud et al. found an incremental increase of almost 5% for the detection of VTE with the addition of CTV to CTPA [2]. Our lower rate may be explained by an improved CTPA acquisition technique. In particular, we reconstructed our images with a thickness of 1.25 mm, which may have led to better detection of pulmonary emboli, especially distally, compared to Cham et al. and Loud et al., who reconstructed CTPA images with a thickness of 3 - 5 mm [3,11].

After directly comparing the results of CTV with those for lower-extremity US, both simultaneously performed with CTPA, prior literature reported no significant advantage of combined CTPA/CTV, provided that lower-extremity US was regularly available [16–20]. The benefit of adding CTV to CTPA was minimal because the detection of isolated DVT was rare and not worth the cost and neither the additional

ionizing radiation [21,22]. US can be of limited use for detecting pelvic vein thrombosis [23], mainly because the compression technique cannot be applied, as it is done for the lower limbs. However, isolated DVT of the iliac veins or the inferior vena cava is extremely uncommon. Our study revealed only one patient with isolated pelvic thrombosis (0.1%), in agreement with other previous results [8,11,24]. Also, Stein et al. reported only 3% of isolated inferior vena cava or pelvic vein thromboses among 105 patients with positive results on CTV [25]. Thus, pelvic vein thrombosis is almost always associated with lower limb thrombosis, and the latter is easily detectable by US.

In 40 (5.7%) of our patients, CTV revealed relevant abdominal or pelvic findings, and 14 (2%) of these had therapeutic consequences. Bierry et al. explored incidental malignancies detected during CTPA combined with CTV, including thoracic tumours [10]. They reported the rate as high as 12.9% for incidental tumors detected in patients undergoing combined CTPA/CTV for suspicion of PE [10]; the addition of CTV to CTPA increased the incidence of relevant malignant findings from 23.7% to 32.8%. Furthermore, Bierry et al. found a correlation between DVT and malignancy [10]. In our series, we analysed only the CTV images, and we registered not only malignancies, but also other relevant incidental findings entailing therapeutic consequences. However, we found no significant association between present PE or DVT and relevant incidental findings on CTV images.

In a meta-analysis including 7122 cardiac magnetic resonance examinations performed in 7062 patients, Dunet et al. reported the detection of major incidental extra-cardiac findings in 12%, leading to management changes in only 1% [26]. Another meta-analysis quantified incidental findings detected on brain magnetic resonance examinations including 19.559 patients. Revealing 0.7% of neoplastic and 2% of non-neoplastic incidental findings, Morris et al. did not consider this low frequency as sufficient to justify screening healthy asymptomatic people [27]. Similarly, in a recent review of 1708 CTPA examinations leading to a detection rate of 1.7% ($n = 26$) for significant incidental findings, Anjum et al. concluded that this result does not justify CTPA [21].

In our study, 43% of the total radiation dose exposure was from CTV, which is lower than that previously reported by Bierry et al. in 2008 [10] and Reichert et al. in 2011 [24], where CTV caused 53% of the effective radiation dose in a combined CTPA and CTV protocol. This difference may be explained by recent technical advances in CT acquisition and, especially, our iterative reconstruction technique leading to a lower radiation exposure considering the large volume coverage. Indeed, our ASIR-V algorithm yields dose reductions of up to 40% compared to previous iterative reconstruction techniques while maintaining image quality in body CT [22].

Our study has several limitations. The first is the expected bias from its retrospective nature. Secondly, we did not compare CTV directly with US, although we consider US as effective as CTV for the detection of femoro-popliteal thrombosis [23]. However, this comparison was beyond the scope of our study design. Thirdly, we did not review the CTPA images, but instead recorded the reported findings and analysed only the CTV images. This approach may have led to a bias, because we could not conduct a global evaluation of all incidental findings discovered on CTPA and CTV. However, our study design permitted us to clearly assess the added value of CTV. Fourthly, the inclusion criterion that patients had to be age >50 years may also represent a bias, because incidental findings could be more often detected in elderly patients. However, our patients with relevant incidental findings were younger than the other patients, with a mean age of 71.3 and 75.7 years, respectively (Table 2).

In conclusion, the results of our study suggest that CTV routinely added to CTPA in patients age >50 years with suspected PE offers limited incremental value regarding the detection of venous thromboembolism. It may reveal other, unsuspected but relevant incidental CT findings leading to a change in therapeutic management in a few patients, but the low rate does not seem to justify screening all patients with suspected PE. Furthermore, no risk factor reliably identified patients who are likely to have incidental findings on CTV. Therefore, for radiation protection purposes, US may be preferable for detecting DVT of the lower extremities, especially considering the rare occurrence of isolated pelvic thrombosis, which is very difficult to detect with US.

## Declaration of Competing Interest

All authors declare that they have no potential conflicts of interest regarding this study.

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