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Multislice Computed Tomography Angiography as an Imaging Modality of Choice in Patients with Suspicion of Pulmonary Embolism – Own Experiences and Modern Imaging Techniques

Wielorzędowa angiografia tomografii komputerowej jako metoda obrazowania z wyboru u pacjentów z podejrzeniem zatorowości płucnej – doświadczenia własne i nowoczesne techniki obrazowania

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article; **G** – other

Abstract

Background. Pulmonary embolism (PE) is a relatively common and potentially life threatening clinical condition with estimated prevalence to be 0.4%. Early diagnosis of PE followed by adequate treatment reduces the risk of major complications. Multislice computed tomography pulmonary angiography (CTPA) currently constitutes an imaging modality of choice in patients with suspicion of PE. Computed tomography venography (CTV) of lower limb veins and CTPA can be performed simultaneously, allowing for visualization of lower limb deep vein thrombosis (DVT). Additionally, dual energy CT scanners enable the evaluation of lung perfusion which is of high value in indirect detection of pulmonary arterial microembolisms.
Objectives. The goal of the study was to assess the diagnostic value of a 64-detector CT scanner in the detection of both acute and chronic PE in patients with clinical suspicion of PE based on clinical scores.
Material and Methods. Retrospective analysis of CTPA performed between 2010 and 2012 in 102 consecutive patients (64 women, 38 men) with clinical suspicion of PE based on clinical scores (first of all the Wells score) and elevated D-dimer level was carried out. The patients' median age was 68.9 (range between 34 and 91). The examinations were carried out with a 64-detector CT scanner, using a "pulmonary embolism" protocol. The volume of contrast agent ranged from 60 to 70 mL, depending on the patient's body mass. The contrast medium was administered with an injection rate 4.0–5.0 mL/s. The concentration of the contrast medium in the main pulmonary artery (MPA) was monitored in every case with the use of a 'smart-prep' method. Scanning was started a few seconds (4–6) after reaching a plateau by the contrast medium in MPA. Additionally, in selected patients CTV was performed and/or lung perfusion was evaluated.
Results. Evidence of PE was demonstrated in 32 of 102 (31.4%) analyzed patients (pts). In 19 patients, centrally localized clots were visualized. Additionally, in 32 patients, lobar, segmental and proximal subsegmental filling defects corresponding to thrombo-embolic material were demonstrated. Moreover, in 14 patients, distal subsegmental filling defects were shown. Alternative diagnoses included: heart failure-related congestion (21 pts), pneumonia (19 pts) and malignancy (5 pts).
Conclusions. The multislice CTPA is an extremely useful imaging modality in patients with clinical suspicion of PE. The examination enables not only the analysis of pulmonary vessels but also evaluation of pulmonary parenchyma and mediastinum. The collimation of 0.625 mm makes it possible to detect the small foci of peripheral embolism (**Adv Clin Exp Med 2013, 22, 5, 705–713**).

Key words: pulmonary embolism, computed tomography pulmonary angiography, lung perfusion, dual energy computed tomography, computed tomography venography.

Streszczenie

Wprowadzenie. Zatorowość płucna (PE) jest częstą, potencjalnie zagrażającą życiu, chorobą. Wczesne rozpoznanie i wdrożenie stosownego leczenia u pacjentów z PE istotnie zmniejsza ryzyko poważnych powikłań. Obecnie angiografia tomografii komputerowej tętnic płucnych (CTPA) jest metodą obrazowania z wyboru u pacjentów z klinicznym podejrzeniem PE. Wielorzędowe skanery TK pozwalają na jednoczasowe wykonanie CTPA wraz z wenografią tomografii komputerowej (CTV) żył kończyn dolnych w diagnostyce zakrzepicy żył głębokich (DVT). Nowoczesne dwuenergetyczne skanery TK umożliwiają ilościową ocenę perfuzji płucnej, pomocnej w wykrywaniu mikrozatorowości płucnej.

Cel pracy. Ocena wartości diagnostycznej 64-rzędowej TK w wykrywaniu ostrej i przewlekłej PE u pacjentów z podejrzeniem PE w obrazie klinicznym.

Materiał i metody. Retrospektywnej ocenie poddano badania CTPA wykonane w latach 2010–2012 u 102 kolejnych pacjentów (64 kobiet; 38 mężczyzn) z klinicznym podejrzeniem PE. Średnia wieku w analizowanej grupie wyniosła 68,9 lat, zakres wiekowy 34–91 lat. Badania CTPA wykonano na 64-rzędowych skanerach TK za pomocą protokołu „zatorowości płucnej". Środek kontrastowy podawano dożylnie z prędkością 4,0–5,0 ml/s. Skanowanie wykonywano po 4–6 sekundach od uzyskania intensywnego zakontrastowania w obrębie pnia płucnego (MPA). Dodatkowo u wybranych pacjentów wykonywano CTV i/lub oceniano perfuzję miąższu płuc.

Wyniki. Cechy radiologiczne PE stwierdzono u 32 ze 102 (31,4%) analizowanych pacjentów. U 19 pacjentów uwidoczniono umiejscowione centralnie ubytki zakontrastowania. U 32 pacjentów stwierdzono ubytki zakontrastowania w gałęziach płatowych, segmentalnych oraz proksymalnych subsegmentalnych. U 14 pacjentów uwidoczniono ubytki zakontrastowania dystalnych odcinków gałęzi subsegmentalnych. Badanie CTPA pozwoliło na wykrycie innych chorób: zastoju w krążeniu płucnym (n = 21), zapalenia płuc (n = 19) oraz zmian nowotworowych (n = 5).

Wnioski. Wielorzędowa CTPA jest niezwykle przydatną techniką obrazowania u pacjentów z klinicznym podejrzeniem PE. Badanie to pozwala nie tylko na analizę zakontrastowania tętnic płucnych, lecz również na ocenę płuc i śródpiersia. Submilimetrowa rozdzielczość badania umożliwia wykrycie niewielkich obwodowych ubytków zakontrastowania (**Adv Clin Exp Med 2013, 22, 5, 705–713**).

Słowa kluczowe: zatorowość płucna, angiografia tomografii komputerowej tętnic płucnych, perfuzja płucna, dwuenergetyczna tomografia komputerowa, wenografia tomografii komputerowej.

Pulmonary embolism is a relatively common and potentially life threatening clinical entity with prevalence estimated to be 0.4% [1]. Risk factors include i.a. older age, history of previous deep vein thrombosis (DVT), prolonged bed rest (often associated with chronic orthopedic or neurological diseases), blood hypercoagulation disorders, recognized malignancy and surgery in the last 4 weeks [1, 2] In up to 30% of cases the cause of PE remains unknown with no recognized predisposing factors [2]. Pulmonary embolism is strongly associated with another vascular pathology – deep vein thrombosis (DVT). Acute PE is the third most common acute cardiovascular disorder, following heart infarction and cerebral stroke [3]. If PE is not diagnosed or is diagnosed too late, it is fatal in up to 30% of the patients [4]. However, early diagnosis followed by proper medical management decreases mortality rate to 2–10% [3]. There are three clinical scores based on clinical symptoms and laboratory tests which are used to assess the probability of PE. They include the Wells score, revised Geneva score and Pisa score [5–7].

Material and Methods

The authors retrospectively analyzed CTPA examinations performed between 2010 and 2012 in 102 consecutive patients with clinical suspicion of PE based on the clinical scores mentioned above (first of all, the Wells score) and elevated D-dimer level. The median age was 68.9 (range 34 to 91). A statistical analysis was performed using the chi-squared test and Fisher's exact test by means of Statistica software (StatSoft). Values of $p < 0.05$ were regarded as statistically significant.

The examinations were carried out with a 64-detector CT scanner, LightSpeed VCT (GE) and dual-energy Discovery 750HD (GE), using a "pulmonary embolism" protocol. The scan area covered the whole thorax with a slice thickness of 0.67 mm, pitch 0.9 and the tube rotation time of 0.4–0.8 s. The volume of the highly-iodinated contrast agent (iodine concentration 350–370 mg/mL; Iomeron (Bracco)) ranged from 60 to 70 mL, depending on the patient's body mass. The contrast medium was administrated with an injection rate of 4.0–5.0 mL/s using an automatic syringe via the cubital vein and was followed by an injection of 40 mL of saline as a so-called wash-out bolus. The concentration of the contrast medium in the lumen of the main pulmonary artery (MPA) was monitored in every case with the use of a 'smart-prep' method. Scanning was started a few seconds (4–6) after reaching a plateau by the contrast medium in MPA. Additionally, in selected patients, CTV was performed and/or lung perfusion was evaluated. The obtained images were analyzed using an AW4.4 workstation (GE). The protocol of CTPA is presented in Table 1.

Table 1. Acquisition parameters of the pulmonary embolism protocol of CT angiography

Tabela 1. Parametry akwizycji w protokole zatorowości płucnej angiografii TK

Contrast medium (Środek kontrastowy)	60–70 mL
Flow rate (Przepływ)	4–5 mL/s
Slice thickness (Grubość warstwy)	0.625 mm
Pitch (Współczynnik skoku)	0.9
Scan delay (Opóźnienie skanowania)	4–6 s
Time of scanning (Czas skanowania)	3.5 s
Voltage (Napięcie)	120 kV
Amperage (Natężenie)	modulated mAs
CTV of lower limbs (CTV kończyn dolnych)	200 s following contrast administration

CTV – computed tomography venography.
CTV – wenografia tomografii komputerowej.

Two radiologists (J.K. and A.C.) independently evaluated each examination. In cases of disconcordant reports, the authors challenged their opinions to work out an objective final report.

Results

The vast majority of CTPA (75/102; 73.5%) was performed as an emergency examination because of severe clinical symptoms and the need for a prompt diagnosis.

Generally in 32 of 102 (31.4%) patients analyzed the evidence of PE was demonstrated. The location of embolic material was classified as: central (pulmonary arteries, lobar branches), intermediate (segmental arteries and proximal subsegmental branches) and peripheral (distal subsegmental branches, tiny peripheral branches). Single location of thrombo-embolic material was found in 8 cases and double location in 15 patients, while in 9 patients triple location was found. Centrally localized filling defects (clots) were visualized in 19 patients. Segmental and proximal subsegmental filling defects corresponding to thrombo-embolic material were demonstrated in 32 patients. In 14 patients, peripheral filling defects were shown. Table 2 illustrates both the location and distribution of thrombo-embolic material in analyzed patients.

Thrombo-embolic material was observed in more than one region in 75% (24/32) of the patients with diagnosed PE. One anatomical location of the emboli was stated in only 25% of PE patients. It is worth stressing that the clots were visualized in the segmental arteries and proximal subsegmental branches (intermediate location) in all of the patients with CTPA confirmed PA. The central location of thrombo-embolic material was observed more often than the peripheral one (19 vs. 14). In only 9 patients (28.1%), the pulmonary artery filling defect was seen in all three anatomical locations.

In 14 of 32 patients (43.7%), on the basis of CTPA, acute PE was diagnosed. In the rest of the subset (n = 18; 56.2%), a chronic form of PE was detected. There was no significant difference in anatomical distribution of arterial emboli when comparing the subset with acute PE to the group with chronic PE.

Bilateral distribution of emboli was visualized in 25 out of 32 patients (78.1%). An analysis of the anatomical distribution of thrombo-embolic material did not demonstrate any statistically significant difference between pulmonary lobes and segments. Thrombo-embolic material was shown with higher incidence in the 2nd, 8th and 10th segments of both lungs, however, the difference was not significant.

An enlarged diameter of the MPA and pulmonary arteries (PA) was demonstrated in nearly all patients with diagnosed PE. However, enlargement

Table 2. The number of locations (1–3) and distribution (central, intermediate, peripheral) of thrombo-embolic material in analyzed patients

Tabela 2. Liczba lokalizacji (1–3) i rozmieszczenie (centralne, pośrednie, obwodowe) zmian zatorowo-zakrzepowych w analizowanej grupie

Number of locations (Liczba miejsc)	Number of patients (Liczba pacjentów)	Anatomical location (Umiejscowienie anatomiczne)	Number of locations (Liczba miejsc)
One (Pojedyncze)	8	central	19
Double (Podwójne)	15	intermediate	32
Triple (Potrójne)	9	peripheral	14
Total (Razem)	N = 32	total	N = 65

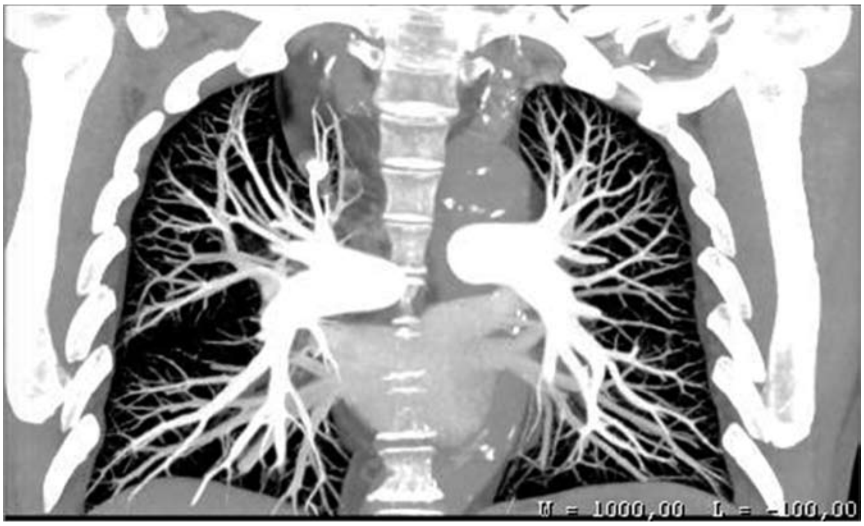

Fig. 1. Normally enhanced pulmonary arterial tree in maximal intensity projection (MIP) reconstruction

Ryc. 1. Prawidłowe zakontrastowanie gałęzi tętnic płucnych – rekonstrukcja projekcji maksymalnej intensywności (MIP)

Fig. 2. Thrombo-embolic material located in the central portions of both pulmonary arteries and at the division of the main pulmonary artery – the acute phase of pulmonary embolism

Ryc. 2. Materiał zatorowo-zakrzepowy umiejscowiony centralnie w świetle obu tętnic płucnych oraz w podziale pnia płucnego – ostra faza zatorowości płucnej

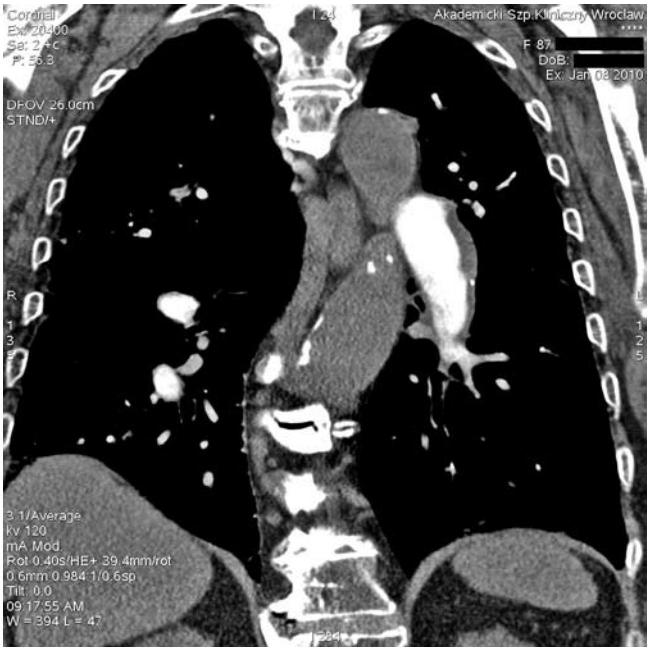

Fig. 3. Chronic phase of pulmonary embolism – the thrombo-embolic material with calcifications visible perimurally along the wall of the branch of the left pulmonary artery

Ryc. 3. Przewlekła faza zatorowości płucnej – materiał zakrzepowo-zatorowy ze zwapnieniami widoczny przyściennie w gałęzi lewej tętnicy płucnej

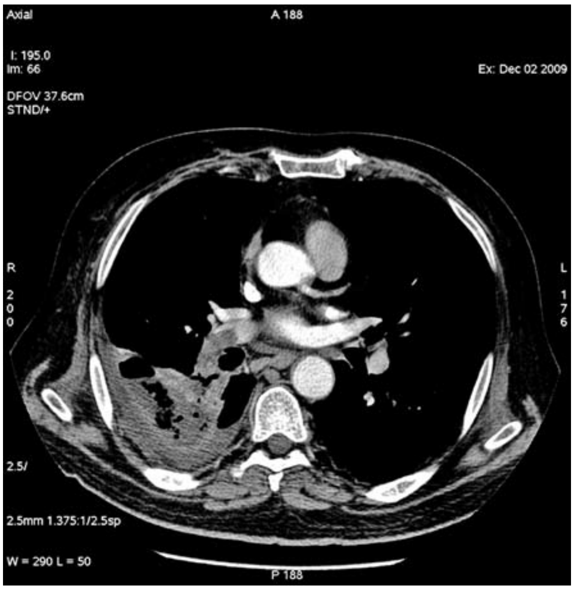

Fig. 4. The acute phase of pulmonary embolism complicated by right lung segmental infarction

Ryc. 4. Ostra faza zatorowości płucnej powikłana zawałem miąższu płuca prawego

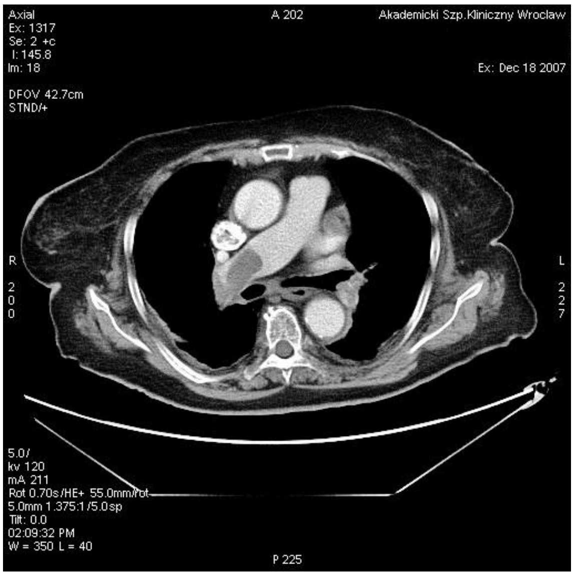

Fig. 5. The acute phase of pulmonary embolism – massive embolic material in the right pulmonary artery

Ryc. 5. Ostra faza zatorowości płucnej – masywny materiał zatorowy w prawej tętnicy płucnej

of the MPA and PA were also present in most of the patients with pulmonary venous congestion.

In 44 of 102 patients (43.1%), non-embolic pathologies were demonstrated including evidence of pulmonary venous congestion (n = 21), pneumonia (n = 19) and malignancy (n = 4). In 26 patients (25.5%) massive uni- or bilateral hydrothorax was shown, which required an emergency puncture of the pleural cavities.

Fig. 6. Ground-glass appearance in the course of chronic pulmonary embolism

Ryc. 6. Perfuzja mozaikowa (tzw. obraz mlecznej szyby) w przewlekłej zatorowości płucnej

The authors did not notice any statistically significant inter-observer discrepancies. The evaluation of the lobar, segmental and proximal subsegmental arterial branches showed no inter-observer differences. There was inter-observer discrepancy regarding the assessment of the peripheral subsegmental branches of 1–2 pulmonary segments in 2 of 32 patients with CTPA evidence of PE. The inter-observer discrepancy neither proved statistically significant nor influenced the radiological report and subsequent clinical management.

Discussion

Pulmonary embolism constitutes a common clinical problem particularly in older age group patients. This is in agreement with the present results – the median age in the subset with recognized PE was 73.4. In authors' material, PE was detected in nearly one third of the patients referred for CTPA with suspicion of either acute or chronic pulmonary embolism. However, in most of the patients who had undergone CTPA due to suspected PE, the result of the examination was negative. This is one of the reasons why conventional catheter digital subtraction angiography (DSA) should not be the imaging modality of choice and should be reserved for selected clinically severe life-threatening cases with strong clinical suspicion of PE to enable emergent thrombolysis and/or fragmentation of the main clots with the intention to cause distal migration of thrombo-embolic material [8–10].

Fig. 7. Dual energy CT – Color Z map of pulmonary embolism. Red color – normal perfusion, blue color – focal lung perfusion defect predominantly in the X segments of both lungs

Ryc. 7. Dwuenergetyczna tomografia komputerowa. Mapa Z zatorowości płucnej. Kolor czerwony – prawidłowa perfuzja; kolor niebieski – ogniskowe ubytki perfuzji płucnej głównie w segmentach 10. obu płuc

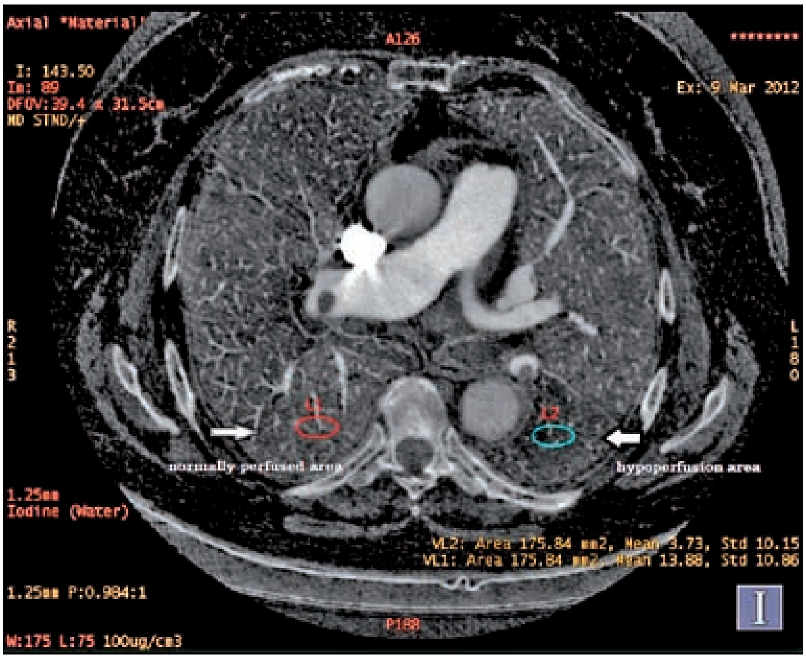

Fig. 8. Dual energy CT – the iodine/water ratio is significantly decreased, which reflects perfusion defects in the 10th segments of both lungs

Ryc. 8. Dwuenergetyczna tomografia komputerowa. Stosunek stężenia jod/woda jest wyraźnie obniżony w segmentach 10. obu płuc, co odzwierciedla zaburzenie perfuzji

Baile et al. regarded CTPA as comparable to traditional pulmonary angiography more than 10 years ago [11]. In 2007, Wittram et al. presented discrepancies between DSA and CTPA [12].

Pulmonary CTA does not take a long time, therefore it can be performed even in patients with a severe clinical state. The initial evaluation of obtained scans is also quick, which is worth emphasizing because prompt diagnosis leads to prompt proper treatment and improves clinical outcomes. Additionally, CTPA is a minimally invasive procedure – the only potential risk of adverse events is associated with intravenous contrast administration [13, 14]. However, there were no contrast-related complications in the present group. Generally, the currently widespread use of iso-osmolal and low viscosity non-ionic contrast media results in low risk of any CTA. Nevertheless, the authors always checked creatinine/GFR levels prior to CTPA [14]. Because of its high sensitivity in the detection of vascular anatomy and pathology, at present a sixty-four detector CTA is widely applied in diagnostic imaging of other vascular areas [15, 16].

Exposure to radiation constitutes a disadvantage of any CT examination. Therefore there are some strategies that are meant to reduce the radiation-associated risks. In the case of CTPA, one of the techniques is associated with the reduction of the radiation dose to superficial radiosensitive organs (female breasts and thyroid gland) without a negative impact on the quality of obtained scans [17]. Another technique is an application of bismuth-layered radioprotective shields placed on the superficial organs, which reduces breast radiation exposure by 57% and thyroid gland dose by 60% [18].

Based on authors' experience, evaluation of peripheral arterial branches should be carried out using thin slices to avoid missing small peripherally located thrombo-embolic material [19]. Simultaneous assessment of coronal and axial images makes it possible to avoid mistaking small pulmonary veins for distal arterial branches and to precisely assess the placement and extent of clots.

If a patient's condition is severe, a "first look" rough analysis should be performed directly following the scanning, at the radiographer's workstation, to make the further clinical decisions as prompt as possible. Afterwards, the images obtained should be analyzed in detail using first of all thin slices, followed by maximum intensity projections (MIP) and possibly VR (volume rendering) reconstructions. It is worth stressing, the CTPA enables a detailed analysis of pulmonary parenchyma, which makes it possible to detect peripheral pulmonary infarction as a typically cone-shaped peripheral zone of consolidation in the areas of occluded vessels. Pulmonary CTA also enables the detection of other chest pathologies such as coexisting alveolar/interstitial edema, atelectatic/inflammatory changes and enlargement of the right heart chambers as well as the main pulmonary artery (MPA) as a sign of right heart overload. Additionally, CTA allows assessment of any hilar or mediastinal pathology e.g. enlarged lymph nodes, malignant tumor.

In authors' opinion, evaluation of peripheral pulmonary arterial branches may be burdened with observer-dependent subjectivity [19]. It is mainly a consequence of the small lumen of peripheral pulmonary arterial branches – according to present observations, small peripheral branches should only be evaluated using thin submillimeter slices. Both thin and thick MIP reconstructions should be reserved for evaluation of large and medium-sized pulmonary arterial branches. Visualization of peripheral branches using MIP and VR reconstruction may demonstrate properly enhanced vessels whereas the same branches in submillimeter reconstructions show filling-defects corresponding to the presence of thrombo-embolic material. Average volume artifact is the cause of misleading images when using MIP or VR reconstruction. In spite of the limitations mentioned above, the authors regard CTPA as a highly sensitive and specific imaging diagnostic tool and thus a valuable imaging modality in the morphological presentation of the filling defects of pulmonary arterial branches.

The ventilation/perfusion (V/Q) scan is a potential alternative to CTPA [20, 21]. However, access to this diagnostic method is rather limited. Moreover, a relatively high rate of the V/Q scans is not conclusive, which decreases its cost-effectiveness. In contrast to this, CTPA is an easily accessible imaging diagnostic modality, allows rapid diagnosis and following emergent endovascular or open-surgery intervention when necessary. That is why it is reasonable to include pulmonary CTPA in the PE diagnostic protocols as the first-line imaging modality in this entity.

Additionally, when required, the area of examination of CTPA can be extended to enable evaluation of venous iliac axes which are often difficult to be visualized in Doppler ultrasound (Doppler-US) [22]. From authors' experience, the extended range of scan can be used when the implantation of a temporary or permanent IVC filter is considered.

When necessary, lower limb venous Doppler-US can be substituted by CT venography (CTV), which can be performed immediately after CTPA using one contrast medium administration (reduced nephrotoxicity). The method makes it possible to simultaneously visualize and assess both pulmonary circulation and the iliac and lower limb deep venous system. This seems to be the future of CTA in patients with suspicion of both PE and DVT [23, 24].

Advanced technology by means of dual-energy CT-scanners makes possible to perform CT-perfusion of the lungs, which is an additional advantage allowing for not only visualization but also quantitative assessment of contrast-deficit (hypoperfused) areas and thus detection of the regions of microembolism – which can be helpful in predicting potential respiratory complications [25, 26].

The application of magnetic resonance pulmonary angiography (MRPA) and magnetic resonance venography (MRV) in the diagnostic algorithm of PE seems to be the natural next step of development of advanced imaging modalities [27]. However, according to the results of a PIOPED III study, MRPA should be considered only at the centers which have a lot of experience in this modality and only for patients in whom CTA is contraindicated (i.a. pregnant women; allergy to iodine contrast media) [28]. On the other hand, it is more difficult to obtain simultaneously technically adequate MR-PA and MRV compared to CTPA/CTV [28].

Single photon emission computed tomography (SPECT) can constitute another alternative or supplementation to CTPA. According to Pilecki et al., SPECT in some cases may demonstrate a lack of perfusion or areas of hypoperfusion whereas the CTPA result was normal [29]. Therefore the authors think that it is crucial to implement a CT perfusion examination in the diagnostic protocol of PE [25, 26].

In conclusion, modern multidetector CT-scanners in association with the good quality of the exam and an experienced radiological team result in a highly conclusive CTPA report which is of the highest importance for a clinician and/or interventional specialist. Pulmonary CTA seems to be the method of choice in the routine imaging diagnostics of PE. Recent advances in modern CT-scanners enable quantitative analysis of lung parenchyma perfusion, which is an extremely useful tool in the detection and assessment of the extent of pulmonary microembolism. Additionally, the high speed of scanning makes it possible to scan the whole body following one contrast medium administration, which offers the possibility of simultaneous performance of 2 protocols, i.e. CTPA followed by CTV. This method, although associated with a higher dose of radiation, allows for both a detailed assessment of the deep lower leg venous system and pulmonary arterial tree.

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