

Acute Pulmonary Embolism: Imaging Techniques, Findings, Endovascular Treatment and Differential Diagnoses

Akute Lungenarterienembolie: Bildgebung, Bildbefunde, endovaskuläre Therapie und Differenzialdiagnosen

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ZUSAMMENFASSUNG

Hintergrund Die akute thrombotische Lungenarterienembolie (LAE) ist ein häufiges und potenziell tödliches Ereignis. Die Bildgebung spielt bei diesen Patienten für Diagnose und Management eine herausragende Rolle.

Method Dieser Übersichtsartikel diskutiert Bildgebung, diagnostische Vorgehensweisen, Bildbefunde und endovaskuläre Behandlungsmöglichkeiten der akuten thrombotischen LAE und illustriert wichtige Differenzialdiagnosen bezüglich des Spektrums akuter nicht thrombotischer LAE und nicht embolischer Lungenarterienpathologien. Der Artikel hebt Informationen mit Relevanz für den radiologischen Alltag besonders hervor und geht auch auf aktuelle Fortschritte ein, die heute in der klinischen Routine angewandt werden können. **Ergebnisse/Schlussfolgerung** Die computertomografische pulmonale Angiografie (CTPA) ist der aktuelle Referenzstandard für die Diagnose der akuten LAE. Die Ventilations-Perfusions- (VQ-) Bildgebung oder – in Zentren mit adäquater Expertise – die Magnetresonanztomografie (MRT) sind bei schwangeren oder jungen Patienten sowie Patienten mit Kontraindikationen für jodhaltige Kontrastmittel indiziert. Die invasive Angiografie bleibt Patienten mit der Intention einer endovaskulären Behandlung vorbehalten. Artefakte, akute nicht thrombotische LAE, chronische LAE und nicht embolische Lungenarterienpathologien sollten immer als Differenzialdiagnosen in Betracht gezogen werden.

Kernaussagen:

- CTPA ist Referenzstandard für die Diagnose der akuten LAE.
- MRT der akuten LAE sollte nur in Zentren mit adäquater Expertise durchgeführt werden.
- Invasive Angiografie bleibt Patienten mit endovaskulärer Behandlung vorbehalten.
- Artefakte und nicht embolische Lungenarterienpathologien können die akute LAE imitieren.
- Nicht thrombotische und chronische LAE sind weitere Differenzialdiagnosen der akuten thromboembolischen LAE.

ABSTRACT

Background Acute thrombotic pulmonary embolism (PE) is a common and potentially fatal event with imaging playing a pivotal role in the diagnosis and management of these patients. **Method** This review discusses imaging techniques, diagnostic algorithms, imaging findings and endovascular treatment of acute thrombotic PE, and illustrates important differential diagnoses relating to the spectrum of acute non-thrombotic PE and non-embolic pulmonary artery disease. The review emphasizes information relevant for everyday radiological

practice and highlights recent advances that can be readily applied in the clinical routine.

Results/Conclusion Computed tomography pulmonary angiography (CTPA) is the current reference standard for the diagnosis of acute PE. Ventilation and perfusion (VQ) scanning or – in centers with adequate expertise – magnetic resonance imaging (MRI) is indicated in pregnant or young patients and patients with contraindications to iodinated contrast. Invasive angiography is reserved for patients with intended endovascular treatment. Artifacts, acute non-thrombotic PE, chronic PE and non-embolic pulmonary artery diseases should always be considered as differential diagnoses.

Key points:

- CTPA is the reference standard for the diagnosis of acute PE.
- MRI for acute PE should only be performed in centers with adequate expertise.
- Invasive angiography is reserved for patients with intended endovascular treatment.
- Artifacts and non-embolic pulmonary artery diseases can mimic acute pulmonary thromboembolism.
- Non-thrombotic and chronic PE are also differential diagnoses of acute pulmonary thromboembolism.

Citation Format

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Introduction

Acute pulmonary embolism (PE) is a common and potentially fatal event with imaging playing a pivotal role in the diagnosis and management of these patients. The most common cause of acute PE is venous thromboembolism (VTE) from the lower extremity, referred to as acute thrombotic PE or acute pulmonary thromboembolism (PTE) [1]. Often, the term acute PE is used synonymously with acute PTE neglecting non-thrombotic causes of acute pulmonary embolism. Imaging differential diagnoses of acute PTE include the spectrum of acute non-thrombotic PE, chronic PE and non-embolic pulmonary artery disease. Endovascular treatment of acute PTE has emerged as a valuable treatment option in patients with compromised hemodynamics and right heart strain.

This review will discuss imaging techniques, diagnostic algorithms, imaging findings and endovascular treatment of acute PTE, and illustrate important differential diagnoses relating to the spectrum of acute non-thrombotic PE and non-embolic pulmonary artery disease. The review will emphasize information relevant for everyday radiological practice and highlight recent advances that can be readily applied in the clinical routine.

Epidemiology

Acute PE is a common and potentially life-threatening condition with an incidence of 50–200 per 100 000 [2, 3]. It is usually caused by detached thrombus material in 95% of cases from deep vein thrombosis (DVT) of the lower extremity inducing spontaneous, sometimes recurrent embolic events (venous thromboembolism, VTE) [4]. The overall mortality of acute PE is 10–30%, making it the third most common cause of cardiovascular death and accounting for 300 000–370 000 deaths in Europe every year [4, 5].

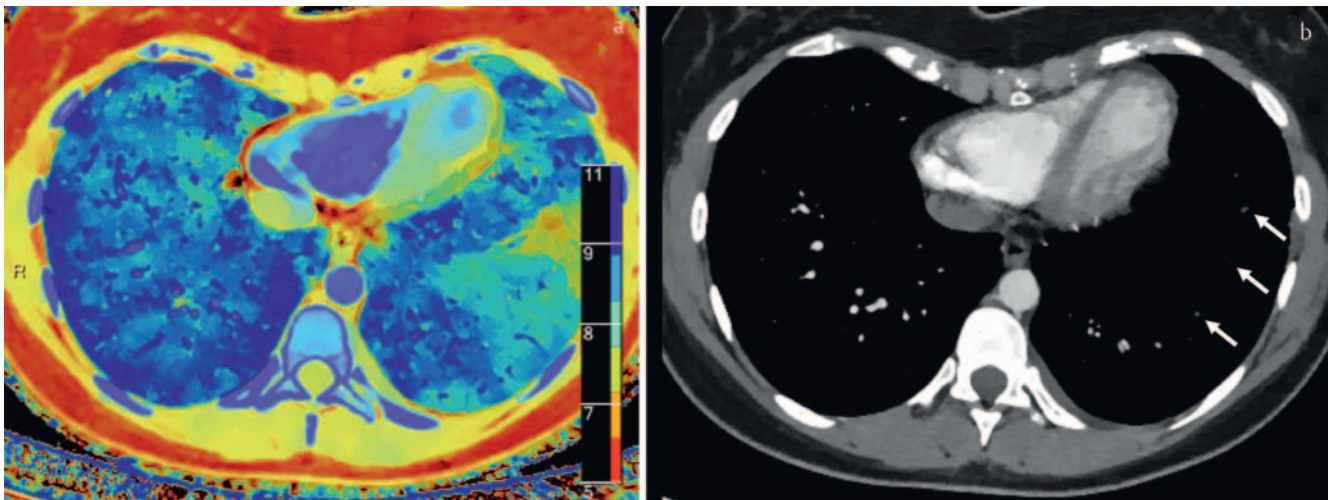
Imaging techniques

This section of this review article provides information related to imaging techniques and protocols most relevant for everyday radiological practice focusing on CT pulmonary angiography (CTPA), chest MRI, and catheter pulmonary angiography. Detailed imaging findings as well as further imaging modalities, i. e. chest X-ray, echocardiography, nuclear medicine imaging, ultrasound, and imaging of the pelvis and extremities will be discussed in the subsequent section.

Computed tomography

CTPA is the current reference standard in the evaluation of acute PE due to its excellent accuracy, wide availability, fast turnaround time, good spatial resolution and multi-planar reconstruction capabilities. CTPA is performed using multi-detector CT scanners after the administration of intravenous contrast. Typically, 50 to 100 ml of intravenous contrast are injected at 4–5 ml/s followed by a saline chaser at the same injection rate. The recommended volume of contrast depends on the body habitus as well as the type of scanner. The bolus tracking technique is used to time the study, when the acquisition initiated after the attenuation in the main pulmonary artery has reached a pre-determined threshold, typically 100 HU above the baseline. A timing bolus can also be used, albeit at an additional contrast and radiation dose. The scan is performed in a caudocranial direction to limit motion artifacts in the lung bases at the initiation of the study and at inspiratory breath-hold or resting expiratory position [6]. Careful breathing instructions are given to the patient prior to the acquisition to avoid a rapid inspiration of Valsalva maneuver during the acquisition, which can produce an artifactual defect due to transient contrast interruption [6, 7]. ECG-triggering is not necessary. The tube current and voltage are usually automatically selected based on patient size if the respective scanner setting is activated.

Arms should be placed above the head whenever possible even in emergency situations to improve image quality and reduce the



► **Fig. 1** **a** Z-effective map of a dual-energy CTPA in a 22-year-old female patient visualizes iodine distribution with blue colors representing high iodine concentration and yellow and red colors representing low iodine concentration. This axial plane shows a wedge-shaped area of low iodine concentration in the left lower lobe corresponding to an area of reduced perfusion. **b** CTPA demonstrates filling defects of subsegmental arteries in the left lower lobe (arrows) causing the perfusion deficit.

► **Abb. 1** **a** Die Z-effektive Karte einer Dual-Energy CTPA bei einer 22-jährigen Patientin visualisiert die Jod-Verteilung, wobei blaue Farben eine höhere Jod-Konzentration und gelbe oder rote Farben eine niedrigere Jod-Konzentration repräsentieren. Die axiale Ebene zeigt eine keilförmige Zone mit niedrigerer Jod-Konzentration im linken Unterlappen im Sinne einer Zone mit reduzierter Perfusion. **b** Die CTPA demonstriert Füllungsdefekte von Subsegmentarterien im linken Unterlappen (Pfeile), die das Perfusionsdefizit verursachen.

radiation dose. In cases where this is not possible, arms should be positioned in front of the abdomen and not at the side of the body.

A combination with a venous perfusion phase of the lower extremity has been proposed [8, 9]. Due to the additional radiation dose and greater volume of contrast material, routine application is currently not recommended. However, it may be useful in elderly patients with comorbidities in whom prompt diagnosis of DVT is more relevant for the outcome.

Wide-array scanners cover more length with each rotation, allowing less motion. High-pitch (up to 2) helical mode of a dual-source scanner also helps in reducing required breath-hold length and thus motion, resulting in better image quality along with lower radiation and contrast doses [10]. Depending on the patient weight, low tube voltage (70 or 80 kVp) techniques can be applied also reducing radiation and contrast doses due to the increased X-ray absorption by iodine at lower tube voltages [11]. Iterative reconstructive algorithms make it possible to lower the radiation dose even further [11].

Dual-energy CT, which can be performed using dual-source, dual-layer, dual-spin, dual-filter and rapid kVp switching technologies, collects data at two different energy levels [12]. This makes it possible to distinguish tissues with similar attenuation values using additional image sets such as iodine or Z-effective maps, virtual non-contrast and virtual monoenergetic images (VMI). Iodine or Z-effective maps highlight pixels containing iodine and can be used to generate perfusion blood volume (PBV) maps of lung perfusion (► **Fig. 1**). VMI at low energies (< 70 keV) are used to improve the signal from contrast, which can be used to salvage suboptimal vascular studies or prospectively use a lower dose of intravenous contrast [13]. High energy VMI can be used for decreasing artifacts, e. g. caused by metallic implants. Virtual

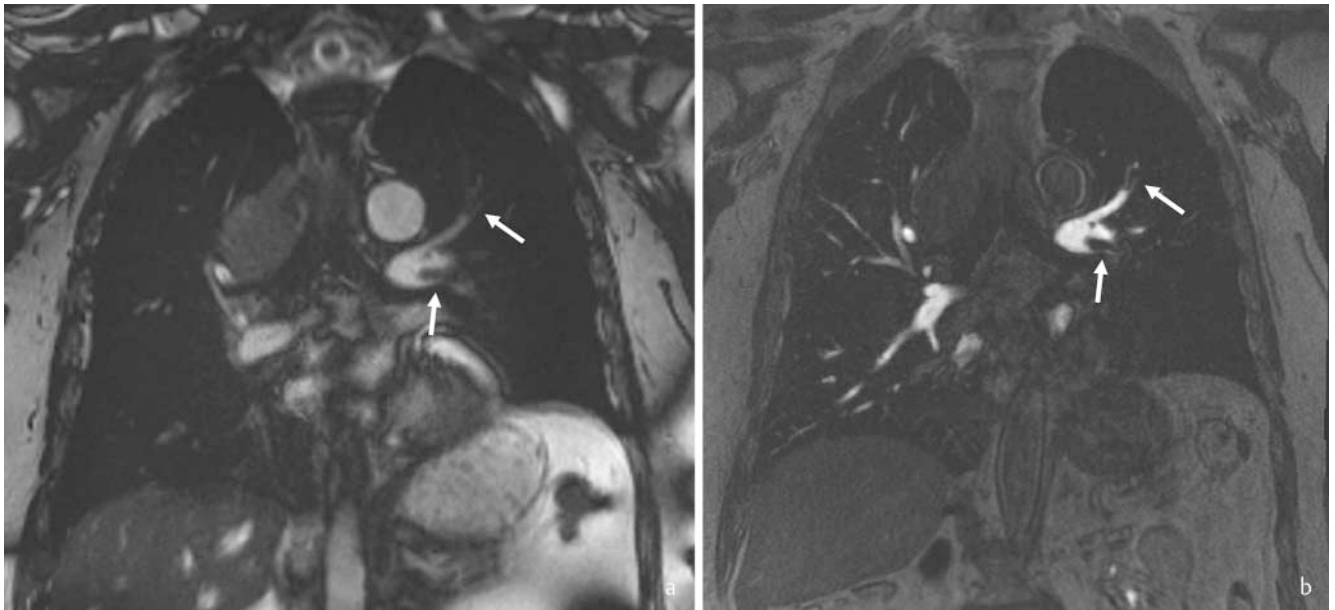
non-contrast images can be used to characterize incidentally seen lesions such as calcified granulomas.

Magnetic resonance imaging

Magnetic resonance imaging (MRI) has emerged as a valuable alternative to CTPA in the evaluation of acute PE particularly in patients with contraindications to iodinated contrast and in pregnant or young patients. The routine protocol includes static steady-state free precession (SSFP) sequences, contrast-enhanced 3 D magnetic resonance angiography (MRA) using a T1-weighted gradient-echo (GRE) sequence, and a 2 D axial or 3 D T1-weighted GRE sequence post-contrast. If the patient tolerates the flat positioning in the MRI scanner well, an additional time-resolved, contrast-enhanced 3 D (i. e. 4 D) MRA prior to the 3 D MRA sequence is helpful to obtain dynamic perfusion information [14].

Static SSFP sequences are acquired in axial and coronal orientation during free breathing or inspiratory breath-hold. The bright blood signal allows detection of pulmonary emboli even without intravenous contrast material (► **Fig. 2**). This is particularly valuable in pregnant patients. Contrast-enhanced 3 D MRA with high spatial resolution is obtained in coronal orientation during three inspiratory breath-holds for acquisition of pre-contrast images for subtraction purposes, arterial phase images and late arterial phase images (► **Fig. 2**) [14]. 0.1 mmol/kg gadolinium-based contrast agent is administered at a flow rate of 2 ml/s. Usually, a timing bolus is the preferred method to determine the time point with peak contrast enhancement of the pulmonary arteries. Alternatively, a bolus-tracking technique can be applied similarly to CTPA.

Time-resolved, contrast-enhanced 3 D MRA with lower spatial resolution is performed by repeated acquisitions of rapid volumetric sequences with parallel imaging and view-sharing techniques



► **Fig. 2** 69-year-old male patient with acute dyspnea. **a** Static SSFP sequence demonstrates a filling defect at the bifurcation of the left pulmonary artery with continuity into the left lower lobe artery (lower arrow) as well as another filling defect in the left upper lobe artery (upper arrow). **b** Contrast-enhanced 3 D MRA acquired in coronal orientation confirms the findings of the SSFP sequence.

► **Abb. 2** Ein 69-jähriger Patient mit akuter Dyspnoe. **a** Die statische SSFP Sequenz zeigt einen Füllungsdefekt an der Bifurkation der linken Pulmonalarterie mit Fortsetzung in die linke Unterlappenarterie (unterer Pfeil) sowie einen weiteren Füllungsdefekt in der linken Oberlappenarterie (oberer Pfeil). **b** Die Kontrastmittel-verstärkte 3D MRA, akquiriert in koronarer Orientierung, bestätigt die Befunde der SSFP Sequenz.

(e.g. TWIST, TRICKS or 4D-TRAK depending on the vendor) during shallow breathing following the first pass of a bolus of 0.05 mmol/kg gadolinium contrast agent at 4 ml/s. The temporal resolution should be about 1 frame/s. Subtraction images can be obtained for each time frame by subtracting the last non-enhanced frame. The technique enables visualization of perfusion defects allowing narrowing of the search for a pulmonary embolus [15].

The PIOPED III study was the largest study investigating the diagnostic accuracy of contrast-enhanced MRA for the detection of acute PTE compared to CTPA [16]. In technically adequate studies, the sensitivity and specificity of contrast-enhanced MRA for detecting acute PTE were 78 % and 99 %, respectively. However, the major limitation of MRA was the large number of technically inadequate studies (25 % of patients), mostly due to poor arterial opacification or motion artifacts, leading to the conclusion of this study that MRA should only be considered at institutions routinely performing MRA and routinely achieving good diagnostic quality, and only in patients with contraindications to CTPA.

More recent developments include a variety of non-contrast-enhanced techniques. 3 D SSFP sequences can be used to obtain non-contrast-enhanced 3 D MRA and yield similar diagnostic accuracy as contrast-enhanced MRA at least for the central and lobar arteries [17]. Fourier decomposition MRI allows assessment of pulmonary ventilation and perfusion without any contrast agent and provides information similar to a nuclear medicine ventilation/perfusion scan [18]. However, further clinical trials are warranted to assess the applicability and diagnostic accuracy of these techniques in the clinical routine.

Catheter pulmonary angiography

Catheter pulmonary angiography has been replaced by CTPA as the gold standard for the diagnosis of acute PE. However, catheter pulmonary angiography is still performed in patients in whom endovascular treatment is being considered. Both the right common femoral and right internal jugular vein can serve as access vessels via a 7 French introducer sheath. In our experience, a femoral access is better when treatment is planned in the same session. A femoral access enables better catheter and wire manipulation and torque-ability compared to an internal jugular access. The pulmonary trunk is reached through the right atrium and ventricle often causing transient arrhythmias. Therefore, continuous ECG monitoring is mandatory throughout the procedure. Readily available temporary pacing (either percutaneous or transvenous) is indicated in patients showing a left bundle branch block on ECG prior to the intervention because wire manipulation in the right heart can cause a right bundle branch block which would result in a life-threatening, complete heart block [19]. Therefore, a pre-procedural ECG is of utmost importance.

Pressure measurements are performed in the right atrium and pulmonary trunk prior to angiography for risk stratification. Routine settings for selective right and left pulmonary artery angiograms are 40 ml of iodinated contrast agent at an injection rate of 20 ml/s. These settings can be adjusted based on renal function and hemodynamic state. Besides, if only one lung is affected or intended for treatment, a unilateral pulmonary angiogram in the setting of acute PTE is sufficient in order to save contrast volume and time. Complications of catheter pulmonary angiography relate to the access site (bleeding, dissection, etc.), wire and cath-

eter manipulation injuries (e. g. arrhythmias, perforation) and the administration of iodinated contrast (contrast-induced nephropathy, thyrotoxicosis). Endovascular treatment options and their related complications are discussed in a separate section below.

Acute pulmonary thromboembolism

Clinical evaluation and diagnostic algorithm

Nonspecific or frequently missing clinical symptoms pose a diagnostic problem in acute PTE [2, 4]. The most common symptoms comprise chest pain, dyspnea, cough, hemoptysis and syncope [4]. Massive PTE can also lead to acute shock-inducing tachycardia, hypotension, tachy-/orthopnea, hypoxemia, hypocapnia, acute right heart failure and even sudden death [4, 5]. In hemodynamically unstable patients with suspected PTE, echocardiography is indicated to assess signs of right ventricular overload and to evaluate differential diagnoses of hemodynamic instability such as pericardial tamponade or valvular dysfunction. Positive findings of right ventricular overload justify emergency reperfusion treatment, e. g. by thrombolysis, if immediate CTPA is not feasible [4].

In hemodynamically stable patients, scoring systems such as the Wells score, simplified Wells score or revised Geneva score are applied to determine the pre-test probability for PTE allowing categorization into low, intermediate or high probability (► **Table 1**) [2, 4, 20]. For patients with low probability of PTE, the absence of all pulmonary embolism rule-out criteria (PERC) effectively excludes PTE with high sensitivity and a very low false-negative rate (► **Table 2**) [2, 21]. For patients with low or intermediate probability of PTE, D-dimer test is performed with a negative D-dimer safely excluding PTE. The performance of the D-dimer test in the elderly can be improved by using age-adjusted cut-offs [22]. Patients with a positive D-dimer test or high probability of PTE undergo CTPA as the imaging modality of choice to confirm or exclude PTE [4, 20, 23]. D-dimer may be nonspecifically elevated in oncologic, hospitalized and pregnant patients.

MRI should be considered if radiation is a concern, particularly in pregnant or young patients, as well as in patients with contraindications to iodinated contrast, mainly prior severe allergic reaction, severe renal insufficiency or untreated hyperthyroidism, provided that patients tolerate flat positioning and MRI is available on a routine basis. In the same group of patients, lung scintigraphy, i. e. ventilation (V) and perfusion (Q) scans, can also serve as an alternative to CTPA given the significantly lower radiation dose and the use of non-iodinated agents. In patients with relative contraindications to iodinated contrast, e. g. prior mild allergic reaction or mild renal insufficiency, CTPA is still the modality of choice after respective preventive measures, particularly for patients not tolerating flat positioning.

MRI can even be helpful without application of intravenous contrast material at the cost of lower sensitivity for segmental and subsegmental emboli. VQ scans have to be interpreted in combination with morphologic imaging such as a chest X-ray acquired on the same day because many lung diseases may result in impairment of regional pulmonary function. The sensitivity of

► **Table 1** Wells score to determine clinical probability for pulmonary embolism.

► **Tab. 1** Wells Score zur Bestimmung der klinischen Wahrscheinlichkeit für eine Lungenarterienembolie.

Items	Points
Previous PE or DVT	1.5
Heart rate \geq 100 beats per minute	1.5
Surgery or immobilization within the past four weeks	1.5
Hemoptysis	1
Active cancer	1
Clinical signs of DVT	3
Alternative diagnosis less likely than PE	3
Clinical probability	
Low	0 – 1
Intermediate	2 – 6
High	\geq 7

► **Table 2** Pulmonary Embolism Rule-out Criteria (PERC) for patients with low probability of PE.

► **Tab. 2** Ausschlusskriterien für eine Lungenarterienembolie (Pulmonary Embolism Rule-Out Criteria, PERC) für Patienten mit niedriger Wahrscheinlichkeit für eine Lungenarterienembolie.

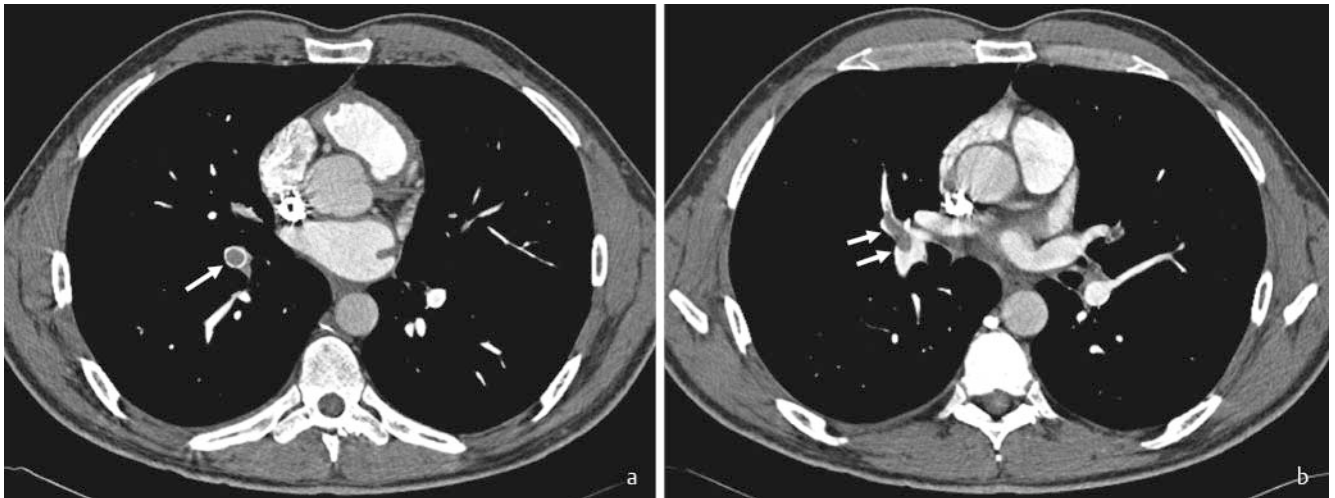
Pulmonary Embolism Rule-out Criteria (PERC)

Age \geq 50
Heart rate \geq 100 beats per minute
SaO ₂ on room air $<$ 95 %
Unilateral leg swelling
Hemoptysis
Surgery or trauma within the past four weeks
Previous PTE or DVT
Use of hormones (e. g. oral contraceptives, hormone replacement)

For patients with low clinical probability of acute PE, the absence of all of these criteria safely rules out acute PE.

VQ scanning can be improved by means of three-dimensional VQ single photon emission computed tomography (SPECT) or hybrid SPECT/CT achieving diagnostic accuracy similar to CTPA [24]. Chest X-ray alone has poor sensitivity for the detection of PTE and is only useful in combination with VQ scans or to suggest alternative causes of the symptoms such as pneumothorax, effusion, masses, pneumonia or pulmonary edema.

If PTE is confirmed and DVT is suspected, lower extremity ultrasound is the modality of choice for evaluating the femoral, popliteal and calf veins [23]. CT venography is particularly indicated if VET from the iliac veins or inferior vena cava are suspected



► **Fig. 3** CTPA in a 42-year-old male patient shows typical findings of acute PE with a filling defect surrounded by a rim of contrast appearing as a “polo mint sign” (a, arrow) and a further distal embolus at a vessel bifurcation forming acute angles with the vessel wall (b, arrows).

► **Abb. 3** Die CTPA bei einem 42-jährigen Patienten zeigt typische Befunde einer akuten Lungenarterienembolie mit einem Füllungsdefekt umgeben von einem schmalen Rand von Kontrastmittel, mit dem Bildeindruck eines „Polo Mint Zeichens“ (a, Pfeil) und einen weiter distal gelegenen Embolus an einer Arterienbifurkation, der spitze Winkel mit der Gefäßwand aufweist (b, Pfeile).

or if ultrasound of the lower extremity is not possible, e. g. due to casts or surgical dressings. Depending on the local standards of practice, lower extremity ultrasound can be performed as the initial imaging modality in pregnant patients with suspected PTE.

Imaging findings

Direct findings of acute PTE by CTPA or MRA comprise filling defects within pulmonary arteries often surrounded with a rim of contrast resulting in the “polo mint sign” in the plane perpendicular to the vessel course or the “railway sign” in the plane along the vessel course (► **Fig. 3**) [20, 23]. A clear advantage of CTPA compared to MRA is the signal of the embolus itself which shows soft-tissue density on CT as opposed to no signal on MRA sequences with a short echo time. Emboli in acute PTE tend to form acute angles with the vessel wall and are frequently located at vessel bifurcations (► **Fig. 3**) [20]. They can also be entirely occlusive and lead to an enlargement of the affected vessel while the arteries distal to the embolus can have a smaller caliber as perfusion is impaired. In contrast, chronic PTE exhibits filling defects adherent to the vessel wall forming obtuse angles as well as intraluminal webs or bands and recanalized thrombi (► **Fig. 4**) [25].

Complications of acute PTE include right ventricular dysfunction and pulmonary infarction. Signs of right heart strain on CTPA or MRI are an enlargement of the pulmonary trunk > 29 mm, an increased right-to-left ventricular diameter ratio > 1, flattening or inverse bowing of the interventricular septum and reflux of contrast material into the inferior vena cava and hepatic veins (► **Fig. 5**) [26]. Right heart strain is associated with higher mortality and a worse outcome with an increased right-to-left ventricular diameter ratio having the strongest predictive value and most robust evidence base for adverse clinical outcomes [23, 26, 27]. Pulmonary infarction can be identified on CT, MRI or chest X-ray as a wedge-shaped opacity in the lung periphery

(Hampton hump), often with central ground glass (“reversed halo” or “atoll” appearance) (► **Fig. 6**). Pulmonary infarction occurs in only 10–15% of patients with acute PTE, especially in patients with left-sided heart failure diminishing collateral blood supply via bronchial arteries.

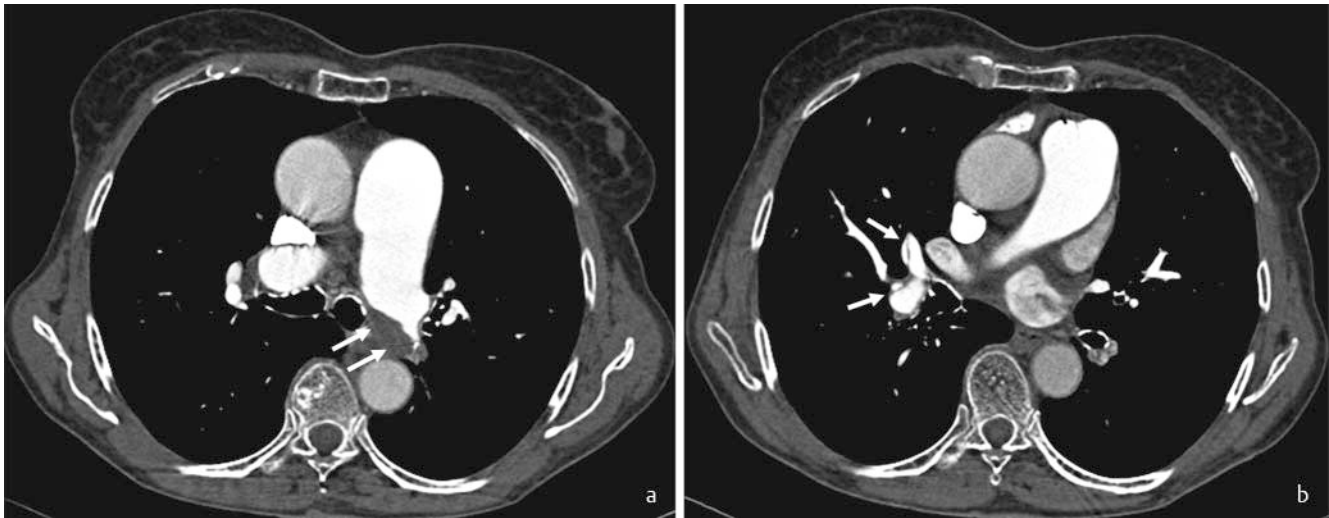
Iodine maps computed from dual-energy CT and time-resolved, contrast-enhanced MRA allow detection of wedge-shaped perfusion defects suggestive of acute PTE (► **Fig. 1**). Addition of these techniques to CTPA or MRA acquisition improves the sensitivity for detecting acute PTE particularly in cases of subsegmental emboli [28].

In patients with persistent foramen ovale, increasing right atrial pressure may account for paradoxical embolism with the risk of stroke or visceral infarction. Sometimes, a persistent foramen ovale can be directly seen on CTPA. Splenic or kidney infarcts detected on CTPA or MRI in the setting of acute PTE imply diagnosis of paradoxical embolism.

A variety of artifacts may imitate filling defects or abruptness of peripheral vessels. Breathing motion most commonly affects the lower zones, cardiac motion mainly the paracardial zones. Patient movement can cause artifacts within any lung region. Beam hardening artifacts from contrast material in the superior vena cava, catheters, wires, orthopedic prostheses or other medical devices can also lead to abrupt changes in attenuation along a vessel’s course.

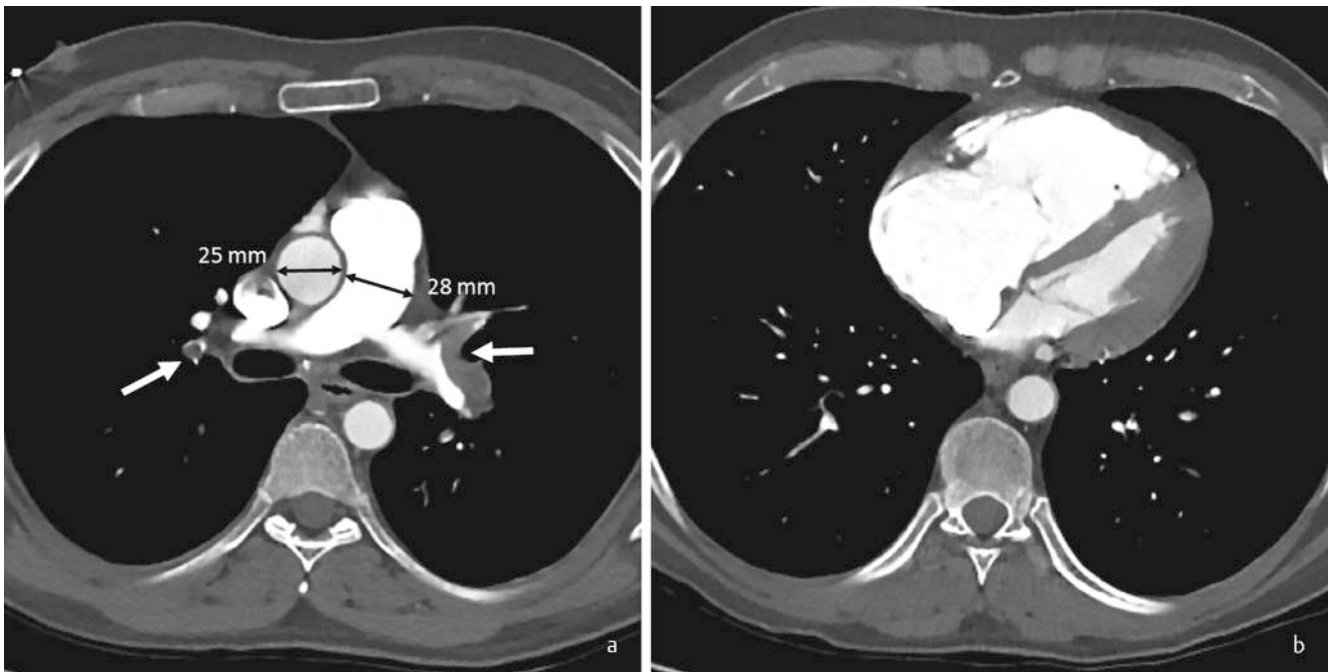
Endovascular treatment

Endovascular treatment of acute PTE is gaining increasing interest. The rationale behind removal of the thromboembolic burden in the pulmonary arterial circulation relates to improvement of right ventricular impairment in the setting of elevated pulmonary vascular resistance and to stabilization of the hemodynamics in the acute setting. Hypothetically, endovascular treatment may



► **Fig. 4** CTPA in a 51-year-old female patient demonstrates typical findings of chronic thromboembolic pulmonary hypertension with enlarged pulmonary trunk, a filling defect forming obtuse angles with the vessel wall (**a**, arrows) as well as intraluminal webs (**b**, arrows).

► **Abb. 4** Die CTPA bei einer 51-jährigen Patientin demonstriert typische Befunde einer chronisch thromboembolischen pulmonalen Hypertonie mit erweitertem Truncus pulmonalis, einem Füllungsdefekt, der stumpfe Winkel mit der Gefäßwand aufweist (**a**, Pfeile), sowie intraluminalen Strickleiter (**b**, Pfeile).

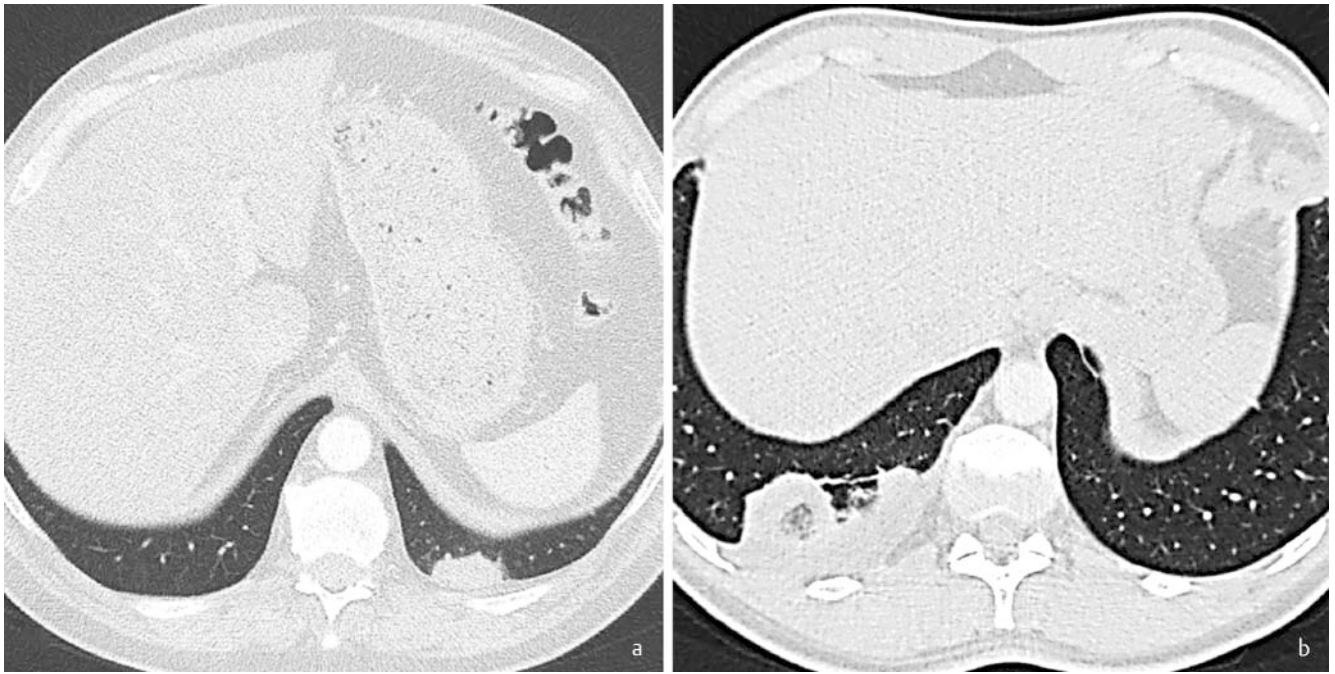


► **Fig. 5** CTPA in a 45-year-old male patient with acute PE (**a**, arrows) illustrates typical signs of right heart strain with a markedly increased right-to-left ventricular diameter ratio with flattening of the interventricular septum (**b**). The pulmonary trunk is mildly enlarged with the pulmonary trunk diameter exceeding the ascending aortic diameter.

► **Abb. 5** Die CTPA bei einem 45-jährigen Patienten mit akuter Lungenarterienembolie (**a**, Pfeile) illustriert typische Zeichen einer Rechtsherzbelastung mit in diesem Fall deutlich erhöhtem rechts-zu-linksventrikulärem Durchmesser-Verhältnis mit Abflachung des interventrikulären Septums (**b**). Der Truncus pulmonalis ist gering erweitert, was der im Vergleich zur aufsteigenden Aorta größere Durchmesser des Truncus pulmonalis zeigt.

decrease the future risk of developing chronic thromboembolic disease (CTED) as well as pulmonary hypertension secondary to chronic pulmonary thromboembolism (CTEPH). This potential

long-term benefit of endovascular treatment of PTE has not been demonstrated in studies yet. The long-term outcome analysis of the PEITHO trial failed to show benefits of systemic thrombolysis



► **Fig. 6 a** 59-year-old male patient with occlusion of the left posterior basal segment artery. Lung window of the CTPA reveals a wedge-shaped opacity in the lung periphery of the same segment representing pulmonary infarction. **b** Lung window of the CTPA in a different, 42-year-old male patient shows a different appearance of pulmonary infarction with a wedge-shaped opacity and central ground glass (“reversed halo” or “atoll” appearance) and accompanying pleural effusion.

► **Abb. 6 a** Ein 59-jähriger Patient mit Verschluss der linken posterioren basalen Segmentarterie. Das Lungenfenster der CTPA zeigt eine keilförmige Verdichtung in der Lungenperipherie desselben Segments im Sinne eines Infarkts. **b** Das Lungenfenster einer CTPA bei einem anderen, 42-jährigen Patienten zeigt ein anderes Erscheinungsbild eines Lungeninfarkts mit einer keilförmigen Verdichtung mit zentraler Milchglasdichte („umgekehrter Halo“ oder „Atoll“ Bild) und einen Begleiterrguss.

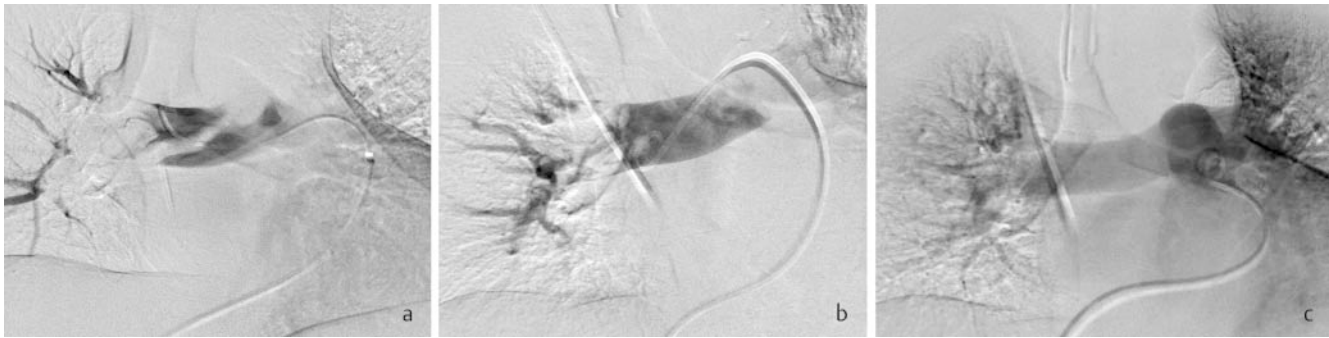
with tenecteplase with regard to functional impairment, risk of developing CTED or CTEPH and with regard to mortality [29]. Furthermore, systemic thrombolysis is accompanied by a significant risk of intracranial hemorrhage of 2% and of general major hemorrhage of up to 20% [30, 31].

There are different risk stratification systems for PTE and one of the established scoring systems following PTE diagnosis is the Simplified Pulmonary Embolism Severity Index (sPESI). The sPESI takes age, vital signs (heart rate, systolic blood pressure and oxygen saturation) as well as relevant clinical history (past medical history of cancer or cardiopulmonary pathology) into account. The resulting score gives an idea of the 30-day mortality risk [32]. The estimated mortality risk may help in deciding on the appropriate treatment.

Acute PTE patients with compromised hemodynamics and right heart strain as diagnosed by CTPA may benefit from endovascular treatment. Specifically, patients with submassive acute PTE as indicated by evidence of cardiac ischemia (elevated troponin and brain natriuretic peptide) and right heart strain are candidates for endovascular treatment or systemic thrombolysis. Patients with massive PTE may be better served by surgical thrombectomy [33]. The decision about the ideal therapeutic strategy in an individual patient in acute PTE should be made by a pulmonary embolism response team (PERT) [34, 35].

Endovascular treatment of acute PTE is typically pursued as a lysis predominant strategy infusing tissue plasminogen activator (tPA) via a side hole infusion catheter system. The catheter is placed across the pulmonary arterial thromboembolism (► **Fig. 7**). A typical dose of alteplase (recombinant tPA) is 1 mg per hour per catheter for a total of up to 24 mg. There are several options regarding delivery catheters. In our hospitals the Unifuse infusion catheter (Angiodynamics, Latham, NY) or the ultrasound-based EkoSonic infusion catheter (EKOS-BTG, Bothell, WA) is used. Different catheters may be used based on individual preferences and local availability. Ultrasound-based catheters have a core wire transmitting ultrasound waves and thereby leading to softening of the adjacent thromboembolic disease and improved delivery of the lytic agent into the thrombus [36]. Compared to systemic thrombolysis, the tPA dose used for endovascular treatment is lower and thus the risk of intracranial hemorrhage and other major bleeding events is decreased.

In selected patients mechanical thrombectomy can be pursued to quickly decrease the thromboembolic burden. Mechanical thrombectomy can be performed as the sole treatment in selected patients with a high bleeding risk not suitable for thrombolysis or combined with catheter-directed thrombolysis [37]. The underlying principle of mechanical thrombectomy in the pulmonary arterial circulation consists of maceration of the larger thrombus into smaller pieces that travel distally in the pulmonary arterial cir-



► **Fig. 7** 66-year-old male presenting from outside hospital as transfer due to massive pulmonary embolism with unstable hemodynamics. **a** a right-sided pulmonary angiogram via right common femoral access using 7 French sheath as well as 7 French APC catheter. There is a large thrombus seen in the distal right main pulmonary artery leading to near complete occlusion. Pressure measurements via the 7 French APC catheter revealed a mean pulmonary artery pressure of 51/19 mmHg with a mean pressure of 33 mmHg. Given the clinical status of the patient and the near occlusion of the right pulmonary artery, a decision was made to initiate ultrasound-assisted thrombolysis using the EkoSonic infusion system (EKOS-BTG, Bothell, WA). In addition to the tPA (1 mg/hour) given through the EkoSonic infusion catheter, the patient was also placed on systemic intravenous heparin infusion to normogram with a goal PTT of 50 to 70 sec. **b** 17 hours post-initiation of ultrasound-assisted pulmonary thrombolysis, the patient returned for repeat right-sided pulmonary angiogram via existing right common femoral vein access post-sheath exchange and new 7 French APC catheter. The pulmonary angiogram showed improving right pulmonary thrombus burden with resolution of thrombus in the right main pulmonary artery and residual thromboembolic disease at the proximal lobar level. However, the pressure was still elevated (repeat pressure measurements 57/14 mmHg with a mean pressure of 32 mmHg). A decision was made to proceed with ultrasound-assisted thrombolysis using the EkoSonic infusion system (EKOS-BTG, Bothell, WA) with infusion of 1 mg/hr of tPA along with systemic intravenous heparin infusion to normogram with a goal PTT of 50 to 70 sec. **c** re-assessment of right-sided pulmonary angiogram via existing right common femoral vein access post-sheath exchange and new 7 French APC catheter. There is complete resolution and re-perfusion of the right main pulmonary artery with residual thrombotic burden at the segmental level. This is a marked improvement compared to both baseline and 17 hours post-initiation of ultrasound-assisted pulmonary thrombolysis (compare to **b**). Repeat main pulmonary artery pressure measurements improved significantly as well, now measuring 43/8 mmHg with a mean pressure of 25 mmHg. Therefore, the decision was made to stop pulmonary thrombolysis at this point.

► **Abb. 7** Ein 66-jähriger Patient, der von einer anderen Klinik aufgrund einer schweren Lungenarterienembolie mit instabiler Hämodynamik eingewiesen wurde. **a** Pulmonale Angiographie rechts, durchgeführt über einen Zugang über die rechte Femoralvene mittels einer 7 French Schleuse mit einem 7 French APC Katheter. Ausgedehnter, nahezu komplett okklusiver Embolus in der rechten Pulmonalarterie und den nachgeschalteten Lappenarterien. Druckmessungen über den 7 French APC Katheter zeigen einen pulmonalarterien Druck von 51/19 mmHg mit einem Mittelwert von 33 mmHg. Aufgrund des klinischen Status und der schweren Embolie wurde die Entscheidung für eine Ultraschall-assistierte Thrombolysie mit dem EkoSonic infusion system (EKOS-BTG, Bothell, WA) getroffen. Zusätzlich zur Administration von 1 mg tPA pro Stunde wurde systemisch intravenös Heparin mit einer Ziel-PTT von 50 – 70 s verabreicht. **b** 17 Stunden nach Beginn der Ultraschall-assistierte Thrombolysie wurde die pulmonale Angiographie rechts wiederholt, über den existierenden Zugang in der rechten Femoralvene mittels eines neuen 7 French APC Katheters. Es zeigt sich eine deutliche Verringerung der Embolus-Masse, vor allem innerhalb der rechten Pulmonalarterie, mit jedoch noch wesentlicher Embolus-Masse in den Lappenarterien. Die erneute Druckmessung in der rechten Pulmonalarterie ergab 57/14 mmHg mit einem Mittelwert von 32 mmHg. Es wurde die Entscheidung getroffen, die Ultraschall-assistierte Thrombolysie einschließlich der systemischen Heparin-gabe fortzuführen. **c** Die folgende Darstellung der pulmonalen Angiographie rechts zeigt eine weitere Reduzierung der Embolus-Masse. Vor allem in der rechten Pulmonalarterie ist der Embolus nun nicht mehr sichtbar. Der Hauptteil des Embolus-Restes befindet sich nun auf Segmentarterienebene. Die erneute Druckmessung in der rechten Pulmonalarterie ergab 43/8 mmHg mit einem Mittelwert von 25 mmHg. Nach dieser erheblichen Verbesserung des Befundes wurde die Entscheidung getroffen, die Ultraschall-assistierte Thrombolysie zu beenden.

culatation, thereby relieving the proximal occlusive disease. This stabilizes the hemodynamics and makes smaller distal thromboembolic fragments more accessible to endogenous thrombolysis. One simple approach of mechanical thrombectomy for acute PTE is the rotating pigtail catheter technique which has been combined with lysis leading to decreased pulmonary artery pressure and high clinical success rates [38].

There is a lack of multicenter randomized controlled trials comparing catheter-directed versus systemic thrombolysis. From a technical standpoint there is also a lack of head-to-head comparisons between catheter-directed thrombolysis with or without ultrasound assistance. The current major trials used ultrasound-assisted catheter-directed thrombolysis techniques for the endovascular treatment of acute PTE.

The ULTIMA trial included 59 patients with acute PTE affecting the main pulmonary arteries or lower lobar arteries. The included

patients had evidence of right heart strain with a right ventricular to left ventricular ratio of 1.0 or higher. Patients were randomized into ultrasound-assisted catheter-directed thrombolysis plus anticoagulation (treatment group) with heparin versus heparin alone (control group). A statistically significant decrease in right ventricular to left ventricular ratio after 24 hours was observed in the treatment but not in the control group. No major hemorrhagic event was observed in either group. Three minor bleeding events occurred in the treatment group versus one minor bleeding event in the control group. The ULTIMA trial showed that ultrasound-assisted catheter-directed thrombolysis is safe and effective in decreasing right heart strain [39].

The SEATTLE II trial was a single-arm non-randomized study using ultrasound-assisted catheter-directed thrombolysis showing significant decreases in right ventricular to left ventricular ratio and pulmonary artery pressures 48 hours post-endovascular

treatment. None of the patients had intracranial hemorrhage. 1 severe and 15 moderate bleeding events were notified. The SEATTLE II trial showed again the effectiveness of ultrasound-assisted catheter-directed thrombolysis for endovascular treatment of acute PTE with a low risk of intracranial hemorrhage [40].

The PERFECT registry confirmed the results of the ULTIMA and SEATTLE II trials showing that catheter-directed treatment of PTE decreases both right ventricular strain and pulmonary artery pressures without major hemorrhagic events [41].

The most recent larger study published was the OPTALYSE PTE trial which included 101 patients treated with ultrasound-assisted catheter-directed thrombolysis. Patients were randomized to 4 different groups receiving different doses of tPA (4 to 12 mg) over infusion durations of 2 to 6 hours. Even with a decreased tPA dose and decreased infusion durations there was still a significant improvement in right ventricular to left ventricular ratio and thromboembolic burden. Ultrasound-assisted catheter-directed thrombolysis was safe in this study with a low major hemorrhage rate. However, one case of intracranial hemorrhage attributed to ultrasound-assisted catheter-directed thrombolysis was observed [42].

The short-term effectiveness of endovascular treatment of acute PTE has been demonstrated with the aforementioned trials and the registry. However, long-term data is warranted to assess whether catheter-directed treatment lowers the risk for developing sequelae of acute PTE, namely CTED and CTEPH with associated right ventricular failure.

Acute non-thrombotic pulmonary embolism

Imaging findings of acute non-thrombotic PE differ from those of acute PTE and are sometimes difficult to identify as such. Pulmonary fat embolism occurs after long bone fractures, soft tissue injuries or orthopedic surgery and has a mortality of about 20%. Lysis is obviously not an option. Bone marrow or soft tissue fragments reaching the pulmonary circulation cause toxic inflammation inducing microhemorrhage and edema [1]. Accordingly, imaging findings are oftentimes multifocal ground glass opacities and small nodules [43]. Fat containing filling defects are rarely seen.

Pulmonary gas embolism is a frequent incidental finding but can be lethal from 300–400 ml intravascular gas [1]. Possible causes are iatrogenic after surgery, interventions or injections, as well as trauma and decompression sickness. Typical imaging findings in CTPA are air-dense, well defined lucencies in the pulmonary circulation including the right heart, features of pulmonary edema, and focal peripheral oligemia [44].

Septic pulmonary emboli most often originate from right-sided infective endocarditis, infected catheters or wires, peripheral thrombophlebitis or infections elsewhere. The most common findings are lower lobe predominant, peripheral nodules with or without cavitation, often with clearly identifiable feeding vessels. Septic pulmonary emboli can be complicated by pulmonary abscess, empyema and pneumothorax.

Amniotic fluid embolism is a rare, but highly fatal (20–60% mortality rate) non-thrombotic PE [45]. Perinatal tears of uterine veins

cause amniotic fluid to reach the circulation inducing diffuse pulmonary ground glass opacities and often infarction of multiple organs [1]. Associated findings are pleural effusion and sometimes heterogeneous oligemia, though an intravascular filling defect can be missing [1].

Pulmonary cement embolism is an often asymptomatic complication of vertebroplasty or kyphoplasty [46]. It is caused by polymethyl methacrylate (an acrylic cement) leaking from the treated vertebral body into the epidural or paravertebral veins which ultimately can disconnect and reach the pulmonary arteries. Cement emboli appear as intravascular hyperdensities > 1000HU in CT or well defined, tubular or branching opacities visible even on chest X-ray [47].

Non-embolic pulmonary artery diseases

Non-embolic pulmonary artery diseases might mimic or go along with the appearance of PE. Pulmonary artery sarcoma is a very rare entity with the peak incidence between 40–50 years [48]. It appears as a filling defect within pulmonary arteries or along the artery walls. Features favoring the diagnosis of pulmonary artery sarcoma as opposed to PTE are extensive filling defects with complete occlusion of the pulmonary trunk or proximal pulmonary arteries, distension of the affected arteries, and extraluminal growth [48]. Occasionally heterogeneous late enhancement can be found. FDG PET-CT can help to identify pulmonary artery sarcomas as FDG attenuating lesions.

Takayasu arteritis is idiopathic large vessel inflammation with non-specific clinical manifestations [49]. In late stage disease, pulmonary artery involvement is possible. Concentric inflammation of the vessel wall and consecutive vessel wall thickening cause vessel stenosis or occlusion (► Fig. 8). Chronic progression often induces vessel collateralization. Evidence of further large vessel manifestations, in particular of the aorta and its proximal branches, favor this differential diagnosis [49].

Conclusion

Imaging plays a pivotal role in the diagnosis and management of acute PE. CTPA is considered the diagnostic reference standard and is indicated in all patients with a high probability of PTE as well as in patients with positive D-dimer test and intermediate or low probability of PTE. VQ scanning or MRI is indicated in pregnant or young patients and patients with non-correctable contraindications to iodinated contrast, provided that they tolerate flat positioning and the technique is available on a routine basis. In pregnant patients, lower extremity ultrasound can also serve as the initial imaging modality. Invasive catheter pulmonary angiography is reserved for patients with intended endovascular treatment. Artifacts, acute non-thrombotic PE, chronic PTE and non-embolic pulmonary artery diseases should always be considered as differential diagnoses of acute PTE.



► **Fig. 8** MRA demonstrates pulmonary artery involvement of Takayasu arteriitis with concentric wall thickening with vessel stenosis (e. g. arrows), as well as artery occlusion with large wedge-shaped areas with an absence of contrast enhancement.

► **Abb. 8** Eine MRA zeigt eine Beteiligung der Pulmonalarterie bei Takayasu-Arteriitis mit konzentrischer Wandverdickung mit Gefäßstenose (z.B. Pfeile), sowie einen Arterienverschluss mit großen keilförmigen Zonen ohne Kontrastmittelanreicherung.

Conflict of Interest

The authors declare that they have no conflict of interest.

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