LEK. KONSTANTIN SZEWCZUK

“PREDYKTORY PRZEWLEKŁEGO ZAKRZEPOWO-ZATOROWEGO NADCIŚNIENIA PŁUCNEGO W ANGIOGRAFII TOMOGRAFII KOMPUTEROWEJ W OCENIE JEDNEGO OŚRODKA”

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu w dyscyplinie nauki medyczne

Promotor: prof. dr hab. n. med. Marek Gołębiowski

I Zakład Radiologii Klinicznej
Warszawskiego Uniwersytetu Medycznego

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KEYWORDS: chronic thromboembolic pulmonary hypertension, computed tomography pulmonary angiography, pulmonary arteries, acute pulmonary embolism.

Żonie Alinie i synowi Ksaweremu

SPIS TREŚCI

1. WYKAZ PUBLIKACJI STANOWIĄCYCH PRACĘ DOKTORSKĄ

- Szewczuk, K, Dzikowska-Diduch O, Gołębiowski M. The use of imaging in the diagnosis and treatment of thromboembolic pulmonary hypertension. Cardiol J. 2025 May 29. doi: 10.5603/cj.102716. Epub ahead of print. PMID: 40439542.

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- Szewczuk, K., Dzikowska-Diduch O, Roik M, Pruszczyk P, Piotrowska-Kownacka D, Gołębiowski M. Chronic thromboembolic hypertension predictors in computed tomography angiography. Single-centre study. Polish Journal of Radiology. 2025;90:267-278. doi:10.5114/pjr/204159.

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3. WYKAZ SKRÓTÓW (alfabetycznie)

APE (ang. acute pulmonary embolism) – ostra zatorowość płucna

AUC (ang. Area Under the Curve) – pole pod krzywą ROC

BNP (ang. brain natriuretic peptide) – peptyd natriuretyczny typu B

BNP-PL (ang. Polish National Pulmonary Hypertension Registry) – ogólnopolska baza danych nadciśnienia płucnego

BPA (ang. balloon pulmonary angioplasty) –angioplastyka balonowa tętnic płucnych

cMR (ang. cardiac magnetic resonance) – rezonans magnetyczny serca

CTED (ang. chronic thromboembolic disease) – przewlekła zakrzepowo-zatorowa choroba

CTEPH (ang. chronic thromboembolic pulmonary hypertension) – przewlekłe zakrzepowo-zatorowe nadciśnienie płucne

CTPA (ang. computed tomography pulmonary angiography) – angiografia tomografii komputerowej tętnic płucnych

DECT (ang. dual-energy computed tomography) – dwuenergetyczna tomografia komputerowa

EKG – elektrokardiografia

ERS (ang. European Respiratory Society) – Europejskie Towarzystwo Chorób Płuc

ESC (ang. European Society of Cardiology) – Europejskie Towarzystwo Kardiologiczne

MDCT (ang. Multidetector Computed Tomography) – wielorzędowa tomografia komputerowa

mPAP (ang. mean pulmonary arterial pressure) – średnie ciśnienie w tętnicy płucnej

MRI (ang. magnetic resonance imaging) – obrazowanie metodą rezonansu magnetycznego

MRPA (ang. magnetic resonance pulmonary angiography) – angiografia rezonansu

magnetycznego tętnic płucnych

NPV (ang. negative predictive value) – wartość predykcyjna ujemna

NT-proBNP (ang. N-terminal pro-B-type natriuretic peptide) – N-końcowy propeptyd natriuretyczny typu B

PAH (ang. pulmonary arterial hypertension) – tętnicze nadciśnienie płucne

PAWP (ang. pulmonary arterial wedge pressure) – ciśnienie zaklinowania w tętnicy płucnej

PBV (ang. pulmonary blood volume) – objętość krwi płucnej

PDSA (ang. pulmonary digital subtraction angiography) – cyfrowa angiografia subtrakcyjna tętnic płucnych

PEA (ang. pulmonary endarterectomy) – endarterektomia płucna

PPV (ang. positive predictive value) – wartość predykcyjna dodatnia

PT/Ao (ang. pulmonary trunk to aorta ratio) – stosunek średnicy pnia płucnego do aorty

PSP (ang. poor subpleural perfusion) – osłabiona perfuzja podopłucnowa

PVR (ang. pulmonary vascular resistance) – opór naczyniowy płucny

RHC (ang. right heart catheterization) – cewnikowanie prawego serca

RV/LV (ang. right ventricle to left ventricle ratio) – stosunek średnicy prawej komory do lewej komory serca

SPECT (ang. single photon emission computed tomography) – tomografia emisyjna pojedynczego fotonu

TTE (ang. transthoracic echocardiography) – przezklatkowa echokardiografia serca

V/Q (ang. ventilation/perfusion scan) – scyntygrafia perfuzyjno-wentylacyjna

WU (ang. Wood units) – jednostki Wooda

3. PREDYKTORY PRZEWLEKŁEGO ZAKRZEPOWO-ZATOROWEGO NADCIŚNIENIA PŁUCNEGO W ANGIOGRAFII TOMOGRAFII KOMPUTEROWEJ W OCENIE JEDNEGO OŚRODKA [STRESZCZENIE]

Przewlekłe zakrzepowo-zatorowe nadciśnienie płucne (CTEPH, ang. chronic thromboembolic pulmonary hypertension) – potencjalnie zagrażający życiu stan kliniczny – zaliczane jest do grupy 4 nadciśnienia płucnego zgodnie z klasyfikacją Europejskiego Towarzystwa Kardiologicznego (ESC, ang. European Society of Cardiology) oraz Europejskiego Towarzystwa Chorób Płuc (ERS, ang. European Respiratory Society) [1,2].

CTEPH jest rzadkim powikłaniem ostrej zatorowości płucnej (APE, ang. acute pulmonary embolism), a jego patogeneza pozostaje nie do końca poznana. Obejmuje ona złożone zmiany strukturalne i czynnościowe w obrębie naczyń płucnych, prowadzące do wzrostu oporu naczyniowego (PVR, ang. pulmonary vascular resistance) oraz postępującej niewydolności prawej komory serca. Nieleczone CTEPH wiąże się z niekorzystnym rokowaniem, jednak rozwój nowoczesnych metod terapeutycznych znacząco poprawił przeżywalność chorych. Kluczowe znaczenie ma wczesne rozpoznanie, ponieważ pacjenci zdiagnozowani na wczesnym etapie choroby odnoszą największe korzyści z leczenia [1,2]. Diagnostyka obrazowa odgrywa zasadniczą rolę w pracy interdyscyplinarnego zespołu zajmującego się leczeniem CTEPH – umożliwia wczesne rozpoznanie, precyzyjne określenie lokalizacji i rozległości zmian, wybór odpowiedniej strategii terapeutycznej oraz monitorowanie skuteczności leczenia.

Niniejsza rozprawa doktorska oparta została na dwóch publikacjach: przeglądowej oraz oryginalnej.

Pierwsza z nich – artykuł przeglądowy – omawia aktualną rolę wielomodalnych technik obrazowania w diagnostyce CTEPH. Przedstawiono w nim najnowsze doniesienia dotyczące metod oceny perfuzji płucnej, takich jak scyntygrafia wentylacyjno-perfuzyjna (V/Q scan, ang. ventilation/perfusion scan), tomografia emisyjna pojedynczego fotonu (SPECT, ang. single photon emission computed tomography), tomografia komputerowa z podwójną energią (DECT, ang. dual-energy computed tomography) oraz rezonans magnetyczny z oceną perfuzji (MRI, ang. magnetic resonance imaging). Omówiono również techniki oceny zmian anatomicznych: angiografia tomografii komputerowej tętnic płucnych (CTPA, ang. computed tomography pulmonary angiography), angiografia rezonansu magnetycznego tętnic płucnych (MRPA, ang. magnetic resonance pulmonary angiography), cewnikowanie prawego serca (RHC, ang. right heart catheterization), cyfrowa angiografia subtrakcyjna (DSPA, ang. digital subtraction pulmonary

angiography) oraz klasyczne zdjęcie rentgenowskie klatki piersiowej. Ponadto, przedstawiono ocenę kardiologiczną w przebiegu CTEPH oraz rolę sztucznej inteligencji w obrazowaniu tej jednostki chorobowej.

Drugi artykuł – praca oryginalna – miał na celu ocenę częstości występowania charakterystycznych cech radiologicznych u chorych z potwierdzonym CTEPH i porównanie ich z częstością występowania z dowiedzionymi klinicznie: przewlekłej chorobie zakrzepowo-zatorowej (CTED, ang. chronic thromboembolic disease), tętniczym nadciśnieniem płucnym (PAH, ang. pulmonary arterial hypertension) oraz ostrą zatorowością płucną (APE ang acute pulmonary embolism), a następnie określenie ich wartości predykcyjnej.
W retrospektywnym badaniu przekrojowym przeanalizowano wyniki CTPA 115 pacjentów, podzielonych na cztery grupy kliniczne: CTEPH (n = 35), CTED (n = 20), PAH (n = 24) oraz APE (n = 36). Grupy były dobrane pod względem wieku i płci, a ostateczne rozpoznania ustalono zgodnie z aktualnymi wytycznymi. Badania wykonano przy użyciu 64-rzędowego tomografu komputerowego (64-MDCT, ang. 64-slice multidetector computed tomography) z bramkowaniem EKG, przy grubości warstwy 0,625 mm i czasie obrotu 0,5 sekundy. Zanonimizowane obrazy oceniono losowo pod kątem obecności cech CTEPH, które sklasyfikowano w trzech grupach: cechy przewlekłej zatorowości płucnej, cechy nadciśnienia płucnego oraz cechy przeciążenia prawej komory serca. Wartość predykcyjną analizowanych cech radiologicznych ustalono na podstawie wskaźnika AUC (ang. Area Under the Curve), wyznaczanego z analizy krzywych ROC, wraz z obliczeniem czułości, swoistości, trafności diagnostycznej, wartości predykcyjnej dodatniej (PPV, ang. Positive Predictive Value) oraz wartości predykcyjnej ujemnej (NPV, ang. Negative Predictive Value).
Najwyższą wartość predykcyjną wykazały cechy należące do grupy przewlekłej zatorowości płucnej, takie jak zwężenie naczyń, nieregularności błony wewnętrznej oraz pasma i przegrody naczyniowe (ang. bands and webs), szczególnie na poziomie segmentalnym (AUC = 0,906; 95% CI: 0,863–0,950). W ocenie całościowej naczyń płucnych zmiany te uzyskały AUC = 0,894 (95% CI: 0,850–0,938). Umiarkowaną wartość predykcyjną wykazały natomiast: mozaikowa perfuzja miąższu płucnego (AUC = 0,740), zmienność średnicy naczyń płatowych i segmentalnych (AUC = 0,788), a także zwężenia, nieregularności ścian naczyń oraz obecność pasm i przegród na poziomie płatowym (AUC = 0,785). Cechy przeciążenia prawej komory serca, takie jak stosunek średnic RV/LV ≥ 1 (AUC = 0,641), spłaszczenie lub przemieszczenie przegrody międzykomorowej (AUC = 0,621), refluks kontrastu do żyły głównej dolnej (AUC = 0,504) oraz przerost ściany prawej komory (AUC = 0,546), wykazywały niższą wartość predykcyjną. Podobnie, parametry sugerujące obecność nadciśnienia płucnego – wskaźnik PT/Ao ≥ 1 (AUC = 0,671), poszerzenie naczyń oskrzelowych (AUC = 0,661), powiększone lub zwapniałe węzły chłonne śródpiersia (AUC = 0,555) oraz obecność płynu osierdziowego lub pogrubienia osierdzia

(AUC = 0,550) – również charakteryzowały się ograniczoną wartością diagnostyczną.

Niniejsza rozprawa doktorska umożliwiła kompleksowe podsumowanie aktualnego stanu wiedzy na temat roli obrazowania w diagnostyce CTEPH oraz analizę oryginalnych danych klinicznych, oceniając częstość występowania i znaczenie diagnostyczne wybranych cech radiologicznych CTPA. Uzyskane wyniki mogą przyczynić się do poprawy precyzji i szybkości rozpoznawania CTEPH w codziennej praktyce klinicznej.

4. PREDICTORS OF CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION IN COMPUTED TOMOGRAPHY ANGIOGRAPHY IN A SINGLE-CENTER STUD [SUMMARY]

Chronic thromboembolic pulmonary hypertension (CTEPH) is a potentially life-threatening clinical condition classified under Group 4 of pulmonary hypertension according to the guidelines of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS) [1,2]. CTEPH is a rare complication of acute pulmonary embolism (APE), and its pathogenesis remains not fully understood. It involves complex structural and functional changes within the pulmonary vasculature, leading to increased pulmonary vascular resistance (PVR) and progressive right ventricular failure. If left untreated, CTEPH is associated with poor prognosis; however, the development of modern therapeutic strategies has significantly improved patient survival. Early diagnosis is crucial, as patients diagnosed at an early disease stage benefit most from available treatments [1,2]. Imaging plays a key role in the work of the multidisciplinary team managing CTEPH—it enables early detection, precise assessment of the location and extent of vascular changes, appropriate treatment planning, and monitoring of therapeutic outcomes.

This doctoral dissertation is based on two publications: one review article and one original research article.

The first, a review article, discusses the current role of multimodal imaging techniques in the diagnosis of CTEPH. It presents the latest findings on lung perfusion assessment methods, including ventilation/perfusion scintigraphy (V/Q scan), single photon emission computed tomography (SPECT), dual-energy computed tomography (DECT), and perfusion magnetic resonance imaging (MRI). It also discusses techniques for anatomical evaluation, such as computed tomography pulmonary angiography (CTPA), magnetic resonance pulmonary angiography (MRPA), right heart catheterization (RHC), digital subtraction pulmonary angiography (DSPA), and standard chest X-ray. Furthermore, it outlines cardiological assessment in the course of CTEPH and highlights the role of artificial intelligence in imaging of this condition.

The second, original article, aimed to evaluate the frequency of characteristic radiological features in patients with confirmed CTEPH and compare them with their prevalence in clinically established cases of chronic thromboembolic disease (CTED), pulmonary arterial hypertension (PAH), and acute pulmonary embolism (APE). The study also assessed the predictive value of these features.

This retrospective cross-sectional study analyzed CTPA results from 115 patients divided into four clinical groups: CTEPH (n = 35), CTED (n = 20), PAH (n = 24), and APE (n = 36). The groups were matched by age and sex, and final diagnoses were established according to current clinical guidelines. Examinations were performed using a 64-slice multidetector computed tomography

(64-MDCT) scanner with ECG gating, 0.625 mm slice thickness, and a 0.5-second rotation time. The anonymized images were reviewed randomly for the presence of CTEPH-related features, which were categorized into three groups: features of chronic pulmonary embolism, features of pulmonary hypertension, and signs of right heart overload. The predictive value of the radiological findings was assessed using area under the curve (AUC) values derived ROC analysis, with sensitivity, specificity, diagnostic accuracy, positive predictive value (PPV), and negative predictive value (NPV) also calculated.

The highest predictive value was demonstrated by features associated with chronic pulmonary embolism, such as vessel narrowing, intimal irregularities, and the presence of bands and webs, particularly at the segmental level (AUC = 0.906; 95% CI: 0.863–0.950). When assessed across the pulmonary vasculature as a whole, these changes yielded an AUC of 0.894 (95% CI: 0.850–0.938).

Moderate predictive value was observed for mosaic perfusion of the lung parenchyma (AUC = 0.740), variability in the diameter of lobar and segmental vessels (AUC = 0.788), and bands and webs at the lobar level (AUC = 0.785).

Features of right ventricular overload, such as an RV/LV diameter ratio ≥ 1 (AUC = 0.641), interventricular septal flattening or bowing (AUC = 0.621), contrast reflux into the inferior vena cava (AUC = 0.504), and right ventricular wall hypertrophy (AUC = 0.546), showed lower predictive value in ROC-based diagnostic assessment.

Similarly, parameters indicative of pulmonary hypertension — including a pulmonary trunk-to-aorta diameter ratio (PT/Ao) ≥ 1 (AUC = 0.671), bronchial artery enlargement (AUC = 0.661), enlarged or calcified mediastinal lymph nodes (AUC = 0.555), and pericardial effusion or thickening (AUC = 0.550) — also demonstrated limited predictive value.

This doctoral dissertation enabled a comprehensive summary of the current state of knowledge on the role of imaging in CTEPH diagnostics and provided an original analysis of clinical data, assessing the prevalence and diagnostic significance of selected CTPA radiological features. The findings may contribute to improving the precision and timeliness of CTEPH diagnosis in everyday clinical practice.

5. WSTĘP

5.1. Przewlekłe zakrzepowo-zatorowe nadciśnienie płucne – zarys problematyki.

Przewlekłe zakrzepowo-zatorowe nadciśnienie płucne (CTEPH, ang. *chronic thromboembolic pulmonary hypertension*) jest formą przedwłośniczkowego nadciśnienia płucnego, stanowiącą potencjalnie zagrażający życiu stan kliniczny. Klasyfikowane jest jako grupa 4 nadciśnienia płucnego według wytycznych Europejskiego Towarzystwa Kardiologicznego (ESC, ang. European Society of Cardiology) oraz Europejskiego Towarzystwa Chorób Płuc (ERS, ang. European Respiratory Society) [1,2].

CTEPH jest rzadkim powikłaniem ostrej zatorowości płucnej (APE, ang. acute pulmonary embolism). Badania szacują, że częstość jego występowania wynosi od 0,5% do 9% po przebytym epizodzie APE, w zależności od zastosowanej metodologii, strategii przesiewowych oraz różnic w populacjach badanych [2-5]. Przeprowadzona w 2017 roku metaanaliza wykazała, że CTEPH rozwija się u około 3,2% pacjentów, którzy przeżyli ostrą zatorowość płucną [6]. W momencie rozpoznania średni wiek pacjentów wynosi 63 lata, a choroba występuje z podobną częstością u kobiet i mężczyzn [1].

Roczna zapadalność na CTEPH różni się geograficznie – w USA i Europie wynosi od 3 do 5 przypadków na 100 000 mieszkańców, podczas gdy w Japonii odnotowano zapadalność na poziomie 1,9 przypadków na 100 000 osób [7].

W Polsce, od momentu utworzenia krajowego rejestru nadciśnienia płucnego (BNP-PL) w 2018 roku, zarejestrowano łącznie 876 przypadków CTEPH, w tym 550 nowo rozpoznanych, co odpowiada średniej częstości około 8,3 nowych przypadków miesięcznie [8].

Warto podkreślić, że nie u wszystkich pacjentów z CTEPH udaje się potwierdzić przebycie APE. Dane retrospektywne wskazują, że nawet 40–60% pacjentów nie miało wcześniej rozpoznanej żylnej choroby zakrzepowo-zatorowej [9-11].

Rozpoznanie CTEPH potwierdza się na podstawie cewnikowania prawego serca (RHC, ang. right heart catheterization) oraz badań obrazowych układu naczyniowego płuc. Kryteria diagnostyczne CTEPH obejmują średnie ciśnienie w tętnicy płucnej (mPAP, ang. mean pulmonary arterial pressure) przekraczające 20 mmHg, opór naczyniowy płucny (PVR, ang. pulmonary vascular resistance) wynoszący co najmniej 2 jednostki Wooda (WU, ang. Wood units) oraz ciśnienie zaklinowania w tętnicy płucnej (PAWP, ang. pulmonary arterial wedge pressure) nieprzekraczające 15 mmHg. Konieczne jest również stwierdzenie niejednorodnych ubytków perfuzji w scyntygrafii płuc oraz specyficznych objawów radiologicznych CTEPH w badaniach obrazowych. Przed rozpoczęciem pełnej diagnostyki wymagana jest co najmniej trzymiesięczna

skuteczna antykoagulacja [1].

Co istotne, wykazano, że u 22% pacjentów z APE w CTPA obecna była co najmniej jedna cecha radiologiczna sugerująca przewlekłą chorobę zakrzepowo-zatorową, a jej obecność niemal ośmiokrotnie zwiększała ryzyko rozwoju CTEPH. Jednak obecnie obowiązujące wytyczne ESC dotyczące postępowania w APE nie rekomendują rutynowego badania w kierunku CTEPH u wszystkich pacjentów po ostrym epizodzie, lecz wyłącznie u tych, którzy mimo trzymiesięcznej skutecznej antykoagulacji nadal odczuwają duszność wysiłkową lub obniżenie tolerancji wysiłku względem stanu sprzed epizodu [12].

Patogeneza CTEPH ma charakter wieloczynnikowy i nie została jeszcze w pełni poznana; obejmuje ona złożone procesy zachodzące zarówno na poziomie makroskopowym, jak i mikroskopowym.

Bezpośrednią przyczyną CTEPH jest zwężenie lub zamknięcie podsegmentalnych, segmentalnych oraz głównych odgałęzień tętnic płucnych, wynikające z niecałkowitego ustąpienia materiału zatorowo-zakrzepowego oraz przekształcenia się skrzeplin w przewlekłe, zorganizowane zmiany włókniste, ograniczające przepływ krwi [2,13,14]. U większości pacjentów z APE mechanizmy endogennej trombolizy prowadzą do całkowitej rekanalizacji naczyń i przywrócenia prawidłowego przepływu [14,15]. U części chorych jednak materiał zatorowy nie ulega resorpcji, lecz ulega organizacji i przekształceniu w tkankę włóknistą [1,16].

Dokładny mechanizm tego procesu nie został w pełni wyjaśniony, jednak badania wskazują na szereg czynników ryzyka predysponujących do jego rozwoju, takich jak przewlekłe stany zapalne, przebyta splenektomia, obecność przeciwciał antyfosfolipidowych lub antykoagulantu toczniowego, podwyższone stężenie czynnika VIII, nawrotowa choroba zakrzepowo-zatorowa czy stosowanie hormonów tarczycy [2,13,17,18].

Utrzymująca się niedrożność naczyń płucnych prowadzi do wzrostu oporu naczyniowego oraz ciśnienia w krążeniu płucnym. Wzmożony przepływ przez drożne naczynia wywołuje znaczny stres ścinający (shear stress) [1,19], co inicjuje procesy remodelingu ścian drobnych naczyń obwodowych i rozwój wtórnej mikroangiopatii. W rezultacie dochodzi do dalszego wzrostu oporu naczyniowego oraz postępującej niewydolności prawej komory serca.

Opisano różne typy remodelingu, obejmujące m.in. zamknięcie małych tętniczek podsegmentalnych, pogrubienie błony wewnętrznej oraz przerost błony środkowej, z tworzeniem zmian typu splotowego w obrębie tętniczek [1,16,19,20]. Co istotne, zmiany mikroangiopatyczne obserwuje się również w rejonach płuc pozbawionych bezpośredniego dopływu krwi z tętnic płucnych [21]. Sugeruje się, że może to być związane z przepływem krwi przez krążenie oboczne,

głównie za pośrednictwem przerośniętych tętnic oskrzelowych. Choć mechanizm ten pełni funkcję kompensacyjną, może jednocześnie sprzyjać remodelingowi mikrokrążenia [22].

Opisane wyżej procesy prowadzą do dalszego wzrostu oporu PVR oraz pogłębiającej się niewydolności prawej komory serca. Rokowanie u nieleczonych pacjentów z CTEPH jest niekorzystne – pięcioletni wskaźnik przeżycia wynosi około 30% przy mPAP powyżej 40 mmHg i jedynie 10% przy mPAP przekraczającym 50 mmHg [23].

Postęp w zakresie terapii CTEPH znacząco poprawił rokowanie oraz wyniki leczenia pacjentów [2,19,20]. Zgodnie z zaleceniami 7. Światowego Sympozjum Nadciśnienia Płucnego, endarterektomia płucna (PEA, ang. pulmonary endarterectomy) stanowi leczenie z wyboru u pacjentów kwalifikujących się do zabiegu chirurgicznego. W przypadkach, w których interwencja operacyjna nie jest możliwa, skuteczną alternatywę stanowi leczenie farmakologiczne oraz przezskórna angioplastyka balonowa (BPA, ang. balloon pulmonary angioplasty) [19,20].

Wszyscy pacjenci z rozpoznanym CTEPH powinni zostać ocenieni przez wielodyscyplinarny zespół specjalistów w celu ustalenia optymalnej, indywidualnie dostosowanej strategii terapeutycznej, uwzględniającej zarówno stan ogólny chorego, jak i współistniejące choroby. Według ostatnio publikowanych danych, leczenie chirurgiczne pozwala osiągnąć pięcioletnie przeżycie u około 90% pacjentów, podczas gdy leczenie farmakologiczne zapewnia trzyletnie przeżycie na poziomie 70% [2]

Wczesne rozpoznanie CTEPH ma kluczowe znaczenie, ponieważ pacjenci zdiagnozowani na wczesnym etapie choroby odnoszą największe korzyści z leczenia [24]. Niestety, diagnostyka CTEPH jest trudna, głównie ze względu na bezobjawowy początek (tzw. „okres miesiąca miodowego" po przebytej zatorowości płucnej) [13,16], powolną progresję objawów oraz ich niespecyficzny charakter. Do najczęstszych objawów należą duszność (99,1%), obrzęki kończyn dolnych (40,5%), zmęczenie (31,5%), ból w klatce piersiowej (15,3%) oraz omdlenia (13,7%) [2, 24, 25]. Objawy te są jednak mało charakterystyczne i często przypisywane innym jednostkom chorobowym, co utrudnia postawienie właściwego rozpoznania.

Dodatkowym problemem w procesie diagnostycznym jest brak udokumentowanej przeszłości choroby zakrzepowo-zatorowej u części pacjentów, co opóźnia ich skierowanie do wyspecjalizowanych ośrodków [13,16]. Diagnoza CTEPH bywa również opóźniona lub błędna z powodu niskiego poziomu świadomości klinicznej dotyczącej tej jednostki chorobowej[13,24]. Badania wykazują, że średni czas od pojawienia się pierwszych objawów do postawienia rozpoznania wynosi od 14 do 24 miesięcy [26].

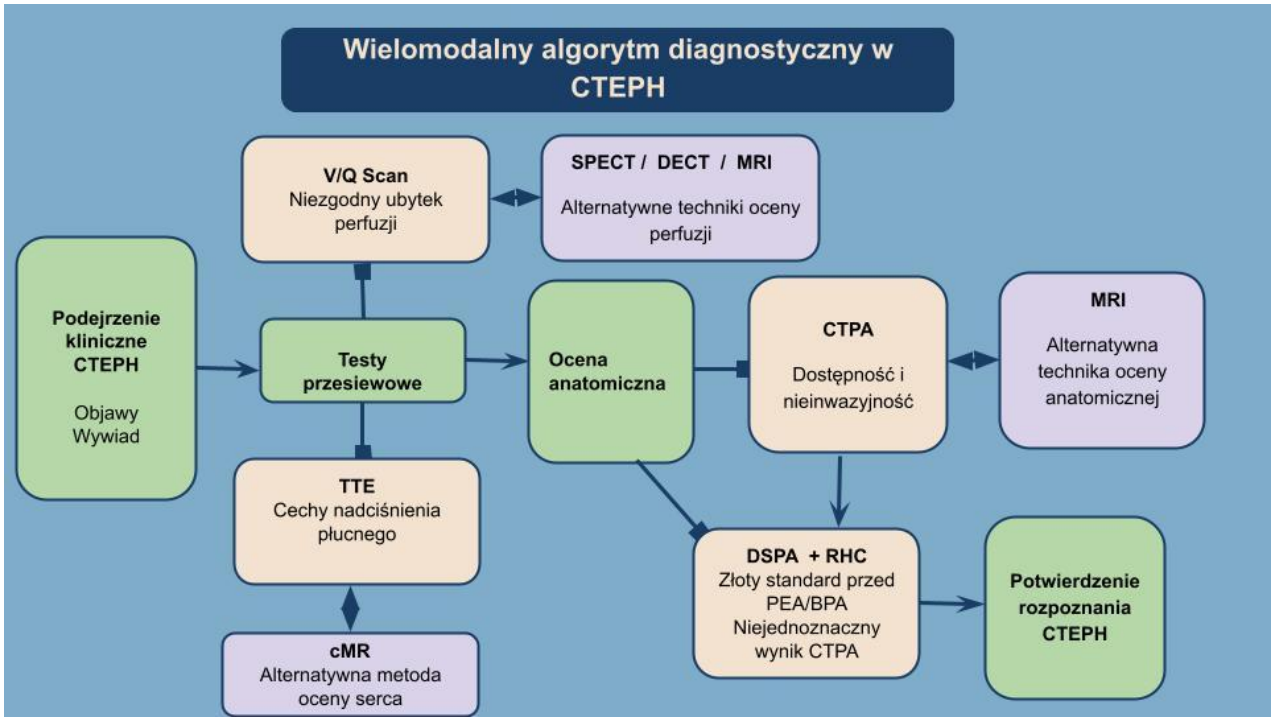
Jednym z narzędzi wspomagających proces diagnostyczny jest akronim SCAR (Suspect, Confirm,

Assess Risk), który promuje systematyczne podejście do rozpoznawania CTEPH, podkreślając konieczność wczesnego podejrzenia choroby, potwierdzenia diagnozy i oceny ryzyka [27].

Zastosowanie wielomodalnych technik obrazowania odgrywa kluczową rolę w diagnostyce CTEPH, umożliwiając wczesne rozpoznanie choroby, precyzyjne określenie lokalizacji i rozległości zmian, dobór odpowiedniej strategii terapeutycznej oraz ocenę skuteczności leczenia. Dynamiczny rozwój technologii obrazowania pozwala na uzyskiwanie obrazów o wysokiej rozdzielczości oraz ocenę specyficznych parametrów hemodynamicznych, co przekłada się na wcześniejsze rozpoznanie i bardziej trafne decyzje kliniczne.

5.2. Miejsce obrazowania w diagnostyce przewlekłego zakrzepowo-zatorowego nadciśnienia płucnego.

Zgodnie z wytycznymi ESC/ERS z 2022 roku, podstawowym badaniem przesiewowym u pacjentów z objawami oraz czynnikami ryzyka CTEPH jest przezklatkowa echokardiografia serca (TTE, ang. transthoracic echocardiography), pozwalająca na wstępną ocenę obecności nadciśnienia płucnego . W przypadku niskiego prawdopodobieństwa nadciśnienia płucnego należy rozważyć inne przyczyny zgłaszanych dolegliwości [1,27]. Przy pośrednim prawdopodobieństwie wskazane jest wykonanie dodatkowych badań, takich jak oznaczenie stężenia peptydów natriuretycznych (BNP (ang. brain natriuretic peptide) lub NT-proBNP (ang. N-terminal pro-B-type natriuretic peptide)) [1,27]. W procesie stratyfikacji ryzyka pomocne są również narzędzia diagnostyczne, takie jak kryteria wykluczenia CTEPH według Leiden (łączące EKG i poziom NT-proBNP) [28] oraz algorytm InShape II, uwzględniający parametry kliniczne, zapis EKG i NT-proBNP [29]. Oba wykazują wysoką czułość i swoistość w wykluczaniu CTEPH [27]. U pacjentów z wysokim prawdopodobieństwem choroby zaleca się wykonanie scyntygrafii perfuzyjno-wentylacyjnej (V/Q, ang. ventilation/perfusion scan) lub alternatywnych technik obrazowania w celu oceny zaburzeń perfuzji płucnej [1]. W przypadkach podejrzenia CTEPH konieczne jest rozszerzenie diagnostyki o badania umożliwiające szczegółową ocenę anatomiczną, potwierdzenie rozpoznania oraz wybór optymalnej strategii terapeutycznej. Należą do nich CTPA oraz RHC z cyfrową angiografią subtrakcyjną tętnic płucnych (PDSA, ang. pulmonary digital subtraction angiography) [1]. (Rycina 1)



Rycina 1. **Wielomodalny algorytm diagnostyczny w CTEPH**

W diagnostyce CTEPH kluczową rolę odgrywa ocena perfuzji płucnej. Scyntygrafia V/Q pozostaje złotym standardem w wykrywaniu zaburzeń perfuzji, wykazując bardzo wysoką czułość (96–97,4%) oraz swoistość (94–100%) [1,30]. Prawidłowy wynik badania praktycznie wyklucza CTEPH, osiągając ujemną wartość predykcyjną bliską 100% [13,24,31]. W badaniu ocenia się zarówno wentylację, jak i perfuzję płucną w celu wykrycia charakterystycznych dla CTEPH niezgodnych ubytków perfuzji, najczęściej mnogich, klinowatych, średniego i dużego stopnia, przy zachowanej wentylacji [33]. Dodatni wynik wymaga jednak potwierdzenia innymi technikami obrazowania, gdyż podobne zmiany mogą występować w innych chorobach naczyń płucnych [32].

Tradycyjną dwuwymiarową scyntygrafię V/Q coraz częściej zastępuje obrazowanie trójwymiarowe z wykorzystaniem tomografii emisyjnej pojedynczego fotonu (SPECT, ang. single photon emission computed tomography), które cechuje się wyższą czułością, swoistością oraz wartością predykcyjną ujemną [13,34,35].

Alternatywną metodą oceny perfuzji płucnej jest tomografia komputerowa z podwójną energią (DECT, ang. dual-energy computed tomogra), pozwalająca na ilościową analizę tkanek na podstawie różnic w pochłanianiu promieniowania [13]. W diagnostyce CTEPH metoda ta wykazuje wysoką zgodność ze scyntygrafią V/Q, osiągając czułość 97–100% i swoistość 86–92% [36,37]. DECT umożliwia ocenę objętości krwi płucnej (PBV, ang. pulmonary blood volume), a także jakościową analizę mikroangiopatii płucnej poprzez identyfikację obszarów osłabionej perfuzji podopłucnowej (PSP, ang. poor subpleural perfusion) [38,39,40].

Perfuzja płucna może być również oceniana za pomocą rezonansu magnetycznego (MRI, ang. magnetic resonance imaging), który umożliwia kompleksową ocenę jakościową i ilościową przepływu płucnego [41]. Nowoczesne techniki, takie jak ultra-short echo time, poprawiają jakość obrazów, skracają czas akwizycji oraz ograniczają artefakty [42–45]. MRI pozwala na automatyczną ocenę parametrów hemodynamicznych [41,46] i wykazuje wysoką czułość (97–100%) oraz swoistość (90–95%) w wykrywaniu CTEPH – porównywalną lub przewyższającą klasyczną scyntygrafię V/Q [47,48]. Ze względu na brak ekspozycji na promieniowanie MRI znajduje szczególne zastosowanie w monitorowaniu pacjentów wymagających wielokrotnej kontroli.

Metodą referencyjną w potwierdzaniu rozpoznania CTEPH i kwalifikacji do leczenia chirurgicznego są RHC z DSPA [1]. W Polsce, zgodnie z danymi rejestru BNP-PL, badanie DSPA potwierdziło CTEPH u 96,1% pacjentów, a w pozostałych przypadkach diagnostyka oparta była na wynikach badania CTPA [49]. DSPA umożliwia dokładną ocenę lokalizacji, rozległości oraz morfologii przewlekłych materiałów zatorowych [50], lecz ze względu na inwazyjność, nie

jest stosowana rutynowo [1].

Do nieinwazyjnych metod obrazowania strukturalnego w CTEPH są CTPA i MRI. Angiografia rezonansu magnetycznego tętnic płucnych (MRPA, (ang. magnetic resonance pulmonary angiography), zarówno z kontrastem gadolinowym, jak i bez niego, umożliwia ocenę unaczynienia bez narażenia pacjenta na promieniowanie oraz jodowe środki kontrastowe. Obrazowe cechy CTEPH w MRPA są porównywalne z tymi uzyskiwanymi w CTPA i obejmują zarówno zmiany naczyniowe, jak i śródmiąższowe [51–54]. Czułość i swoistość MRPA w wykrywaniu CTEPH wynoszą odpowiednio: dla poziomu płatowego 83,1% i 98,6%, a dla segmentalnego 87,7% i 98,1% [13,55,56].

W związku z powyższym, rola radiologa w interdyscyplinarnym zespole zajmującym się diagnostyką i leczeniem CTEPH jest kluczowa. Wymaga ona przy tym nieustannego aktualizowania wiedzy o możliwościach poszczególnych metod obrazowych oraz ich prawidłowej interpretacji.

Doniesienia zawarte w artykule przeglądowym stanowiącym rozdział 7.1 niniejszej rozprawy doktorskiej prezentują jedno z najbardziej kompleksowych opracowań dotyczących zastosowania technik obrazowania w diagnostyce CTEPH dostępnych w aktualnej literaturze.

5.3 Angiografia tomografii komputerowej w przewlekłym zakrzepowo-zatorowym nadciśnieniu płucnym.

CTPA stanowi istotne narzędzie w CTEPH oraz w ocenie kwalifikacji pacjentów do leczenia operacyjnego. Badania wykazują wysoką czułość i swoistość tej metody w wykrywaniu charakterystycznych cech CTEPH: czułość na poziomie płatowym wynosi 89–100%, a segmentalnym 84–91%; swoistość odpowiednio 96–100% i 92–99% [57–59].

Zgodnie z obowiązującymi wytycznymi, ujemny wynik CTPA nie wyklucza obecności CTEPH, ponieważ zmiany w dystalnych odcinkach naczyń płucnych mogą pozostać niewidoczne [60]. Mimo tego CTPA dostarcza kluczowych informacji dotyczących lokalizacji i morfologii materiału zatorowego, niezbędnych do planowania leczenia chirurgicznego lub interwencyjnego.

CTPA jest powszechnie dostępna i stanowi badanie pierwszego rzutu w APE, umożliwiając jednocześnie identyfikację cech sugerujących współistnienie przewlekłych zmian zakrzepowo-zatorowych [32]. Dodatkowo umożliwia wykrycie współistniejących patologii miąższu płucnego i struktur śródpiersia, a także wspomaga różnicowanie z innymi chorobami naczyń płucnych [2].

Typowe cechy obrazowe CTEPH w CTPA obejmują zmiany naczyniowe charakterystyczne dla przewlekłej zatorowości, takie jak częściowe zamknięcie światła naczynia, skrzepliny (także zwapniałe), przegrody wewnątrznaczyniowe, pasma i przegrody. Widoczne są również objawy nadciśnienia płucnego – poszerzenie pnia oraz tętnic płucnych oraz tętnic oskrzelowych i piersiowych wewnętrznych [61,62]. Obrazowanie pozwala także ocenić zmiany miąższowe (np. blizny włókniste, mozaikową perfuzję miąższu płucnego, anomalie oskrzeli) oraz objawy przeciążenia prawej komory serca, takie jak jej przerost i powiększenie prawej komory [61,62]. Wygląd radiologiczny może się różnić w zależności od stopnia zaawansowania choroby, rozległości zmian naczyniowych i nasilenia nadciśnienia płucnego [63].

Wysoka dostępność, nieinwazyjność, możliwość diagnostyki różnicowej oraz jednoczesna ocena zmian naczyniowych, miąższowych i sercowych czynią CTPA metodą o wyjątkowym znaczeniu w diagnostyce CTEPH. Należy jednak podkreślić, że skuteczność diagnostyczna metody, a zwłaszcza jej czułość zależy w dużej mierze od doświadczenia osoby interpretującej wyniki. Ważna jest przy tym odpowiednia jakość techniczna ocenianych obrazów. Dodatkowo obrazowe cechy CTEPH nie są specyficzne wyłącznie dla tej jednostki chorobowej wymagając odpowiedniej analizy w kontekście klinicznym. Podnoszenie kompetencji w zakresie uzyskiwania wysokiej jakości technicznej i interpretacji CTPA może przyczynić się do poprawy wykrywalności CTEPH, zmniejszenia konieczności dalszej diagnostyki, skrócenia czasu do rozpoznania oraz optymalizacji wyników leczenia.

Ze względu na ograniczoną liczbę dostępnych doniesień naukowych analizujących częstość występowania oraz wartość predykcyjną cech radiologicznych charakterystycznych dla CTEPH w badaniu CTPA, przeprowadziłem kompleksową ocenę częstości występowania tych cech w badaniu CTPA. Porównałem uzyskane wyniki z obrazem radiologicznym jednostek chorobowych najczęściej uwzględnianych w diagnostyce różnicowej CTEPH, takich jak przewlekła zakrzepowo-zatorowa choroba (CTED, ang. chronic thromboembolic disease), tętnicze nadciśnienie płucne (PAH, ang. pulmonary arterial hypertension) oraz APE. Na podstawie przeprowadzonej analizy dokonałem oceny wartości diagnostycznej tych cech w rozpoznaniu CTEPH. Szczegółowe wyniki badania przedstawiono w rozdziale 7.2 niniejszej rozprawy doktorskiej.

6. CELE PRACY

1. Ocena częstości występowania cech radiologicznych charakterystycznych dla CTEPH w CTPA, z uwzględnieniem trzech kategorii zmian: przewlekłej zatorowości płucnej, nadciśnienia płucnego oraz przeciążenia prawej komory serca , u chorych z potwierdzonym rozpoznaniem CTEPH.

2. Porównanie częstości występowania wybranych cech obrazowych charakterystycznych dla CTEPH z ich obecnością w chorobach naczyń płucnych (CTED, APE oraz PAH) o zbliżonej symptomatologii klinicznej i podobnych cechach radiologicznych

3. Ocena przydatności diagnostycznej wybranych cech radiologicznych w różnicowaniu pacjentów z CTEPH, z wykorzystaniem parametrów takich jak: wskaźnik AUC, czułość, swoistość, wartość predykcyjna dodatnia, wartość predykcyjna ujemna oraz trafność diagnostyczna,

4. Przedstawienie miejsca CTPA wśród innych metod obrazowania CTEPH

7. PRACE TWORZĄCE CYKL PUBLIKACJI

Rozdziały 7.1. – 7. 2. stanowią cykl publikacji wchodzących w skład prezentowanej rozprawy doktorskiej.

7.1. The use of imaging in the diagnosis and treatment of thromboembolic pulmonary hypertension

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Authors: Konstantin Szewczuk, Olga Dzikowska-Diduch, Marek Gołębiowski

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The use of imaging in the diagnosis and treatment of thromboembolic pulmonary hypertension

Short title: The role of imaging in thromboembolic pulmonary hypertension

Konstantin Szewczuk[1], Olga Dzikowska-Diduch[2], Marek Gołębiowski[1]

[1]1st Department of Clinical Radiology Medical University of Warsaw, Warsaw, Poland

[2] Department of Internal Medicine and Cardiology with the Center for Diagnosis and Treatment of Venous Thromboembolism, Medical University of Warsaw, Poland

Corresponding Author: Konstantin Szewczuk, 1st Department of Clinical Radiology Medical University of Warsaw, 5 Chałubińskiego St., 02–004 Warsaw, Poland, tel: +48791944648, e-mail: konstantin.szewczuk@uckwum.pl

Abstract

Chronic thromboembolic pulmonary hypertension (CTEPH) is a potentially life-threatening condition, classified as group 4 pulmonary hypertension (PH), caused by stenosis or occlusion of the pulmonary arteries due to unresolved thromboembolic material. The prognosis for untreated CTEPH patients is poor because it leads to elevated pulmonary artery pressure and

right heart failure. Early and accurate diagnosis of CTEPH is crucial because it remains the only form of PH that is potentially curable. However, diagnosing CTEPH is often challenging and frequently delayed or misdiagnosed. This review discusses the current role of multimodal imaging in diagnosing CTEPH, guiding clinical decision-making, and monitoring post-treatment outcomes. The characteristic findings, strengths, and limitations of various imaging modalities, such as computed tomography, ventilation-perfusion lung scintigraphy, digital subtraction pulmonary angiography, and magnetic resonance imaging, are evaluated. Additionally, the role of artificial intelligence in improving the diagnosis and treatment outcomes of CTEPH is explored. Optimal patient assessment and therapeutic decision-making should ideally be conducted in specialized centers by a multidisciplinary team, utilizing data from imaging, pulmonary hemodynamics, and patient comorbidities.

Keywords: chronic thromboembolic pulmonary hypertension, computed tomography angiography, dual-energy CT, V/Q scintigraphy, magnetic resonance imaging

Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is a potentially life-threatening condition classified as group 4 pulmonary hypertension (PH) according to the European Society of Cardiology (ESC) and European Respiratory Society (ERS) guidelines (i.e., PH secondary to pulmonary artery obstruction). It represents a form of precapillary PH [1, 2]. CTEPH is caused by stenosis or occlusion of the subsegmental, segmental, and main branches of the pulmonary arteries (PA) due to incomplete resolution of pulmonary thromboembolic material and formation of chronic, flow-limiting, organized thrombi [1, 2].

In Poland, since the establishment of the national pulmonary hypertension registry (BNP-PL) in 2018, a total of 876 CTEPH patients have been recorded, including 550 newly diagnosed cases, with an average incidence rate of approximately 8.3 new cases per month [3]. The diagnosis of CTEPH is confirmed by right heart catheterization (RHC) and pulmonary vascular imaging. The diagnostic criteria for PH are a mean pulmonary artery pressure (mPAP) greater than 20 mmHg, a pulmonary vascular resistance (PVR) of 2 or more Wood units (WU), and a pulmonary artery wedge pressure (PAWP) of 15 mmHg or less and mismatched perfusion defects on lung scan and specific diagnostic signs for CTEPH seen by

multidetector computed tomography pulmonary angiography (CTPA). At least three months of effective anticoagulation is required before diagnostic workup [2, 4, 5].

CTEPH is a rare complication of acute pulmonary embolism (APE), although one in four patients with CTEPH has not had a previously diagnosed episode of venous thromboembolism. The incidence of CTEPH is not well defined, but prospective observational studies estimate the range from 0.5% to 9% after APE [2, 6–8]. This wide range is due to different study designs and screening methods. From a clinical perspective, it is believed that about 3–5% of APE cases lead to CTEPH due to incomplete clot resolution, with an incidence of 3 to 5 cases per 100,000 people per year [1, 9]. Notably, it has been demonstrated that in 22% of patients with APE, at least one radiological feature suggestive of chronic thromboembolic disease was present on CTPA, and its presence increased the likelihood of developing CTEPH nearly eightfold. However, the current ESC guidelines for the management of APE do not recommend testing for CTEPH in all patients after an acute episode, but specifically in those who, despite at least three months of effective anticoagulation therapy, continue to experience exertional dyspnea or reduced physical capacity compared to their condition prior to the event [10].

However, not all patients with CTEPH have a documented history of APE. Some studies indicate that only about 60% of CTEPH patients have a confirmed history of venous thromboembolism [11], while others show that 74.8% had APE and 56.1% had deep vein thrombosis [12].

Although CTEPH is caused by obstructions in the pulmonary arteries, its pathophysiology is complex and not yet fully understood [2, 13]. In most patients with PE, endogenous thrombolytic mechanisms are effective, resulting in complete thrombus resolution and the restoration of normal blood flow [13, 14]. However, in a subset of patients, the embolism fails to resolve and instead progresses to fibrous tissue formation [2, 15]. The exact mechanism of this process remains unclear, but study results have shown several risk factors, including chronic inflammatory processes, splenectomy, the presence of circulating antiphospholipid antibodies or lupus anticoagulants, elevated factor VIII levels, and recurrent venous thromboembolism or thyroid replacement therapy. [1, 2, 16, 17].

Persistent occlusion of pulmonary blood flow due to non-absorbed material raises resistance and pressure. The increased flow in the unobstructed vessels, leading to considerable “shear stress” [2, 5]. This stress triggers remodeling of the walls of small distal vessels with a

secondary microvasculopathy, which leads to increased pulmonary vascular resistance and progressive right heart failure.

Different types of remodeling have been observed, including obstruction of small subsegmental arteries, thickening of the intima, and hypertrophy of the media with plexiform lesions in the arterioles [2, 5, 15, 18].

The natural progression of CTEPH results in elevated PVR and worsening right ventricular (RV) failure. The prognosis for untreated CTEPH patients is poor, with a five-year survival rate of 30% for those with mPAP exceeding 40 mmHg and only 10% for those with mPAP over 50 mmHg [19]. The development of therapeutic options for patients with CTEPH, including pulmonary endarterectomy (PEA), pulmonary hypertension-targeted medical therapy, and balloon pulmonary angioplasty (BPA), has significantly improved patient outcomes [2, 5, 18]. Following the recommendations of the 7th World Symposium on Pulmonary Hypertension, PEA is the preferred treatment for operable CTEPH patients. For those who are inoperable, targeted medical therapy and balloon pulmonary angioplasty are promising alternative treatments [5, 18]. Surgical treatment has been shown to achieve a five-year survival rate of 90%, whereas medical therapy has a three-year survival rate of 70% [2].

Early diagnosis of CTEPH is crucial because patients diagnosed at an early stage are likely to benefit the most from treatment [20]. However, diagnosing CTEPH remains challenging and is frequently delayed or misdiagnosed [1, 20]. On average, it takes approximately 14–24 months from the onset of symptoms to reach a diagnosis in expert centers [21]. Misdiagnosis and delayed diagnosis of CTEPH can be attributed to several factors. Diagnostic difficulties are determined by the silent onset (asymptomatic period after APE so-called “honeymoon period”) [1, 15], slow progression of symptoms, and nonspecific clinical presentation including symptoms such as shortness of breath, edema, fatigue, asthenia, chest pain, and syncope [2, 20]. Furthermore, insufficient awareness of CTEPH among many physicians and the absence of a documented history of thromboembolic disease contribute to delays in referring patients to specialized centers [1, 15]. The complex diagnostic workup, which involves evaluating clinical and physical signs, extensive imaging studies, as well as hemodynamic evaluation, requires expert centers with multidisciplinary teams [1, 15].

The role of radiologists in a multidisciplinary team is indispensable because imaging is pivotal not only in the initial assessment but also in identifying alternative diagnoses, delineating the extent and topography of lesions, and detecting additional abnormalities.

Radiologists face significant challenges in diagnosing CTEPH. Studies indicate that only 26% of radiologists accurately diagnosed CTEPH in original routine CT scans, in contrast to experts who identified all cases correctly [22]. The inability to effectively utilize and interpret various imaging modalities contributes substantially to delays in the diagnosis and treatment of CTEPH [23].

In this article we discuss the current role of multimodal imaging in the diagnosis of CTEPH, emphasizing the characteristic findings associated with each imaging modality (Table 1). (**Central illustration**).

Accurate knowledge of the role of multimodal imaging in CTEPH is essential for the precise interpretation of results, enabling early diagnosis, the selection of appropriate treatment strategies, and the evaluation of treatment efficacy

Chest radiography

Chest radiography is often performed as a part of baseline evaluation, but for the detection of CTEPH it is of limited value. In the early stages of disease, it may be normal. In advanced cases, chest radiography can depict findings related to PH and thromboembolic disease. Among the most commonly observed findings in studies are cardiomegaly, oligemia, right descending pulmonary artery dilatation, and pleural effusion and thickening [24]. Chest radiography may show differential areas of hypoperfusion, hyperperfusion, and parenchymal scarring. It is vital to pay attention to radiological clues in a patient with clinical symptoms, which should alert to the possible presence of PH [18, 25, 26].

Ventilation-perfusion lung scintigraphy

Ventilation-perfusion lung scintigraphy (ventilation/perfusion scan -V/Q scan) according to the guidelines is a first-line imaging technique for the diagnosis of CTEPH [27]. V/Q scanning is highly sensitive, ranging from 96% to 97.4%, and highly specific, ranging from 94 to 100%, in identifying perfusion abnormalities.

While a normal V/Q scan effectively rules out the diagnosis of CTEPH, with a negative predictive value approaching 100% [1, 20, 28], a positive result cannot be used as a standalone tool for clinical decision-making. It always requires confirmation through additional diagnostic imaging because other pulmonary vascular diseases can cause unmatched perfusion defects [29].

The V/Q scan comprises both ventilation and perfusion assessments to detect the mismatched perfusion defect characteristic of CTEPH. During the ventilation phase, the patient inhales an aerosol containing diethylenetriaminepentaacetic acid labeled with technetium-99m (99mTc), which allows the aerosol particles to reach the distal segments of the respiratory tract. In the perfusion phase, technetium-99m-labeled microaggregated albumin (MAA) is administered via a peripheral vein, where it becomes lodged in the precapillary arterioles [27, 30]. The most characteristic findings in CTEPH are multiple, moderate to large, wedge-shaped perfusion defects, while ventilation remains intact (Figure 1 A, B) [31]. These defects correspond to the size of the lobar, segmental, or subsegmental regions of the lung, which correspond to the thrombotic occlusion of a specific artery [1, 23, 32]. However, it is important to remember that various other pathological conditions can result in similar patterns of vascular obstruction in a V/Q scan. These include vasculitis, pulmonary artery sarcoma, external vascular compression due to bronchial carcinoma, mediastinal adenocarcinoma, fibrosis, or congenital abnormalities of the pulmonary vasculature [1, 25]. Therefore, additional imaging is necessary following an abnormal V/Q scan to assess disease morphology, evaluate lung parenchymal abnormalities, and establish a differential diagnosis. It should be noted that the extent of perfusion defects does not correlate with the severity of CTEPH [33], and there is a possibility of underestimating the degree of obstruction because radioisotope-labeled particles can pass through partially occluded vessels [25]. Conventional V/Q scan imaging involves two-dimensional planar acquisition using a gamma camera. In clinical practice, there is an increasing trend to replace traditional 2D V/Q scintigraphic imaging, especially for perfusion scans (where segmental defects may be overlooked or underestimated due to segment overlap and adjacent lung masking in a specific camera position), with 3D V/Q lung imaging using single-photon emission computed tomography (SPECT). This method can overcome the aforementioned limitations providing images with higher sensitivity, specificity, and negative predictive value [1, 27, 34, 35].

Right heart catheterization with pulmonary angiography

Right Heart Catheterization (RHC) with digital subtraction pulmonary angiography (DSPA) is the reference standard for the assessment of CTEPH and evaluating surgical eligibility [2]. In Poland, based on data from the study by Kopeć et al., derived from the BNP-PL registry and covering the period between March 2018 and August 2019, CTEPH was confirmed by pulmonary artery angiography in most patients (96.1%), while in 3.9% of cases the diagnosis was confirmed using CTPA [36].

If CTEPH is suspected on the basis of clinical and imaging findings, the patient should be referred to a pulmonary hypertension center for confirmation of pre-capillary PH. The hemodynamic characteristics of pre-capillary PH, including CTEPH, are described earlier in this paper [31].

Although DSPA has traditionally been the standard for diagnosing and confirming CTEPH, it is now primarily used for diagnosing and evaluating treatment options when CTPA results are inconclusive [37]. Multiplanar imaging in DSPA allows precise visualization of lobar and segmental branches, with the lateral view being helpful in overcoming the limitations of overlapping vessels [25]. DSPA enables the assessment of the extent, location, and morphology of chronic emboli, distinguishing them from the well-defined filling defects observed during APE [25]. Angiographic findings consistent with CTEPH include lucent intravascular lines (webs and bands), irregular vessel wall contour, stenoses and post-stenotic dilatation, angular narrowing, and complete obstructions – so called “pouch defects” (Figure 2) [18, 31, 38]. The latter is caused by a complex restructuring process involving organization, recanalization, and clot retraction, which leads to a concave configuration in obstructing thrombi [25, 38]. DSPA also enables the exclusion of increased PVR secondary to distal vascular disease, arteriopathy, or pulmonary venous hypertension [39, 40]. However, as previously noted, DSPA is not routinely used for the diagnosis of CTEPH in all patients due to its invasiveness, the limitations of two-dimensional projection images, and the benefits offered by non-invasive imaging modalities [1]. The latter, such as advanced computed tomography technologies (including dual-energy CT, electrocardiogram gated area detector CT) offer greater resolution and detailed assessment, particularly in distal vessels, compared to DSPA. This enhanced imaging capability is especially significant in the context of rapidly evolving treatment modalities, such as TPE and BPA [40, 41].

Computed tomography pulmonary angiography

According to ECG guidelines, (CTPA) is recommended and widely used for diagnosing CTEPH and evaluating operability. Although CTPA may not be the initial test for the evaluation of CTEPH, it is important in the next steps of diagnostics and for treatment decision-making. Moreover, CTPA is easily available and is the initial imaging test of choice for APE, which enables the detection of features suggestive of pre-existing CTEPH [29].

However, the guidelines also note that a negative CTPA result does not rule out CTEPH because distal disease might be missed [37]. The results of studies describe the high

sensitivity and specificity of CTPA in detecting features of CTEPH: sensitivity (lobar 89–100%; segmental 84–91%) and specificity (lobar 96–100%; segmental 92–99%) [42–44].

CTPA provides detailed anatomical assessment of the pulmonary vasculature, revealing endovascular thrombi, complete obstructions, vascular wall thickening, intimal irregularities, abrupt stenosis, webs, bands, and bronchial artery collaterals (Figure 3) [1, 25]. This enables both qualitative and quantitative evaluation of vascular changes typical for CTEPH, such as distal vessel pruning and increased arterial tortuosity [45]. Importantly, CTPA can differentiate APE from chronic thromboembolic lesions [25]. Detection of CTEPH features during an APE suggests an acute-on-chronic presentation [4].

Mosaic perfusion, seen in over 94% of CTEPH cases [27, 46], reflects vascular redistribution and is more frequent than in other PH types [47], supporting the diagnosis when distal occlusion is uncertain. In severe forms, hyperperfused areas with dilated arteries and increased density may appear [27, 48]. Pulmonary infarctions—present in 10–15% of cases—manifest as subpleural opacities, fibrotic scars, or cavitations, depending on chronicity [25]. Bronchiectasis is also more prevalent in CTEPH than in other forms of thromboembolic PH [38, 49].

Additional CT signs of PH include main pulmonary artery dilatation and calcification, right ventricular hypertrophy, septal flattening, right atrial enlargement, and pericardial effusion [37, 47].

CTPA also offers the advantage of providing structural and differentiating information about potential underlying lung and mediastinal diseases. This capability helps distinguish between CTEPH mimics that present with perfusion defects on a V/Q scan, such as pulmonary artery sarcoma, large vessel vasculitis, fibrosing mediastinitis, and congenital pulmonary vascular abnormalities [27, 47]. While CTPA is considered less effective than DSA in identifying subsegmental lesions, advancements in CT imaging technology, such as electrocardiogram-gated scans, are expected to address this limitation [1, 50, 51]. Electrocardiogram-gated computed tomography (ECG-gated CT), which improves resolution and reduces artifacts caused by cardiac motion, is a very promising diagnostic technique for CTEPH [27]. Studies have shown higher sensitivity of ECG-gated CT angiography in assessing pulmonary arteries for signs of CTEPH compared to contrast-enhanced magnetic resonance angiography (MRA) and DSPA [53]. ECG-gated CT allows for accurate evaluation of segmental and subsegmental

vessels, lung parenchyma, as well as anatomical and functional parameters of the heart [20, 27].

Dual-energy computed tomography

Dual-energy computed tomography (DECT) has recently emerged as a CT technique for quantitative analysis of tissues and materials based on the different absorption characteristics of the materials [1]. Lung DECT is an effective technology for mapping the distribution of iodine in the lung after administration of an iodine-based contrast agent [52]. This method uses low- and high-tube-voltage X-rays to simultaneously capture two different datasets. The spatial distribution of the iodine in the lung parenchyma reflects pulmonary perfusion [53]. The results of studies demonstrate a strong correlation between DECT perfusion imaging and V/Q scintigraphy with DECT sensitivity ranging from 97% to 100% and a specificity ranging from 86% to 92% in diagnosing CTEPH [54, 55]. The significant advantage of DECT is the ability to evaluate quantitative lung perfusion using the lung perfusion blood volume (PBV) score. The PBV parameter is calculated as the sum of the iodine density scores in each lung segment (Figure 1. C, D) [53]. It has been shown that PBV correlates with the qualitative and quantitative perfusion assessment data provided by multiplanar scintigraphy and SPECT-CT [55, 56]. Furthermore, DECT results in patients with CTEPH correlates with hemodynamic parameters [57, 58]. Several studies have demonstrated that DECT allows for the qualitative evaluation of microvasculopathy through a sensitive analysis of poor subpleural perfusion (PSP) [53, 59]. DECT, in addition to functional assessment, enables simultaneous evaluation of cardiac, vascular, and pulmonary morphology within a single examination, making it a one-stop-shop modality. Furthermore, the radiation doses required for DECT are significantly lower compared to V/Q-SPECT [60]. However, unlike perfusion SPECT, it should be noted that in DECT, late-phase lung PBV reflects perfusion from both the pulmonary arteries and systemic collaterals, which may affect the interpretation of results [61]. In addition, knowledge of focal iodine defects unrelated to pulmonary embolism that occur in DECT scans mainly due to beam-hardening artifacts or artifacts due to motion may help to interpret the scans more accurately [62]. Other limitations of this method include its high cost and the limited availability of scanners equipped with this technique [1].

Magnetic resonance imaging

Magnetic resonance imaging (MRI) is playing an increasingly important role in the diagnosis of CTEPH. MR angiography (MRA) techniques provide morphological evaluation of the

pulmonary vasculature, while MR perfusion techniques provide information of the pulmonary tissue perfusion at the capillary level. MR pulmonary angiography (MRPA) either with or without the use of gadolinium-based contrast is the only method that can assess vascularization without exposure to ionizing radiation and iodine contrast agents. Contrast-enhanced MRA can be performed at high spatial resolution using 3D, T1-weighted, spoiled gradient echo sequence or at high temporal resolution (up to one second) using time-resolved techniques (like TWIST – time-resolved imaging with stochastic trajectories [Siemens Healthcare, Erlangen, Deutschland], or TRICKS – time-resolved imaging of contrast kinetics [General Electric Healthcare, Milwaukee, WI, USA]) [63]. Non-contrast MRA techniques include 3D steady-state free precession, 3D partial Fourier Fast spin echo (FSE), arterial spin labelling (ASL), or phase contrast sequences [63]. CTEPH features observed in MRPA are comparable to those seen on CTA and encompass both non-occlusive and occlusive symptoms [26, 64–66]. The sensitivity and specificity of MRPA in detecting CTEPH at the lobar level were reported to be 83.1% and 98.6%, respectively, while at the segmental level they were 87.7% and 98.1%, respectively [1, 67]. Studies comparing the diagnostic performance of MRPA with CTPA indicate that both methods are equally effective in detecting CTEPH at the lobar and segmental level of pulmonary artery obstruction. However, CTPA is superior to MRPA in imaging sub-segmental artery obstructions due to its higher spatial resolution, better contrast-to-noise ratio, and shorter imaging time, which facilitates better breath-hold [25, 38, 66].

Another application of MR in CTEPH is the evaluation of perfusion defects. Pulmonary perfusion MRI is a valuable tool in the differential diagnosis of PH, including CTEPH, offering both qualitative and quantitative assessment [68, 69]. Challenges in lung MRI imaging arise from magnetic susceptibility differences between air and tissue, leading to image noise. This is mitigated by advanced techniques such as ultra-short echo time, zero echo time acquisitions, and simultaneous multi-slice balanced steady-state free precession (SMS b-SSFP) imaging, which improve resolution and anatomical coverage, and reduce scan times [68, 70–73].

Dynamic MRI enables real-time visualization of pulmonary perfusion: areas with normal perfusion show uniform enhancement, while obstructed segments exhibit delayed or reduced contrast flow, often appearing as wedge-shaped or mottled defects in CTEPH [68, 63,74]. Post-processing allows user-independent quantification of pulmonary blood volume (PBV),

flow (PBF), mean transit time (MTT), and time to peak (TTP) at multiple anatomical levels [68, 74].

Perfusion MRI has demonstrated high sensitivity (97–100%) and specificity (90–95%) in CTEPH detection, comparable or superior to V/Q scans [75–77]. Quantitative perfusion parameters have also shown strong correlation with pulmonary function tests and Doppler echocardiography, reflecting disease severity and treatment response [78–81]. Improvements in perfusion following endarterectomy further support its role in disease monitoring, with the added advantage of no radiation exposure [82]. Limitations include limited availability, the need for expert interpretation, specialized software, and susceptibility to motion artifacts [63, 68]

Evaluation of cardiac structure and function in CTEPH

While CTEPH results from disruption of the pulmonary vascular bed, RV function and anatomical changes are crucial in determining patient symptoms and prognosis. Right heart catheterization (RHC) remains the gold standard for diagnosing PH and is essential for confirming CTEPH. RHC provides direct measurements of pressures in the pulmonary artery and right atrium (RAP), as well as cardiac output (CO) and RV volumes. These measurements are used to calculate additional parameters such as PVR, cardiac index (CI), stroke volume (SV), pulmonary vascular compliance (PVC), and pulmonary artery impedance [83–85]. Transthoracic echocardiography (TTE) is the most important non-invasive tool for diagnosing CTEPH and assessing the impact of CTEPH treatment on right heart function due to its wide availability, low cost, and safety [1, 83]. TTE estimates systolic pulmonary arterial pressure (sPAP) based on the velocity of tricuspid regurgitation [86]. It also detects signs of RV overload, such as thickening of the RV free wall, RV dilation, and flattening of the interventricular septum. Advanced disease symptoms may include dilation of the right atrium and inferior vena cava, as well as pericardial effusion [1, 83, 87, 88]. Cardiac magnetic resonance (cMR) is a valuable method for assessing RV morphology and function in the diagnosis and monitoring of CTEPH [1, 83, 89]. cMR cine images provide precise information on RV volumetric parameters, RV mass, and wall motion. Additionally, cMR offers a non-invasive evaluation of blood flow, including SV, CO, and pulmonary artery distensibility [83, 89]. Interestingly, cMR can demonstrate regional myocardial fibrosis,

helping to differentiate various cardiomyopathies [90], and it can assess subtle changes in the myocardial substrate, identifying myocardial injury (Figure 4) [1, 91].

The role of CTEPH imaging in clinical decision-making and post-treatment follow-up

Assessment of operability is often influenced by many factors, such as anatomic findings, patient history, age, condition, and degree of hemodynamic impairment. A multidisciplinary team approach, including a PEA surgeon, BPA interventionist, PH specialist, and thoracic radiologist, is often required when making clinical decisions. If hemodynamic parameters do not correlate (PVR is disproportionately elevated) with anatomic imaging findings, microvascular arteriopathy may be advanced [38]. Studies show that accurate radiological evaluation helps to estimate the stage of disease in patients with CTEPH, predict surgical findings and the level of disease, and predict hemodynamic changes after surgery [92, 93]. In addition, evaluation of other lung and mediastinal changes as well as coronary alterations is particularly important for assessing the risks and contraindications for the treatment procedures. Post-operative imaging evaluation is also essential. Various imaging methods are being used to monitor patients to assess response to treatment. Echocardiography is the easiest readily available test demonstrating improved right ventricular contractility and systolic pressures with right and left ventricular post-therapy remodeling [26, 38]. MRI is also a noninvasive, extremely helpful tool in assessing functional recovery [94,]. V/Q scan and DECT are used to assess improvements in perfusion in treated areas [38]. However, the primary role of postoperative imaging is the assessment of complications. Perioperative complications after PEA may include reperfusion pulmonary edema, which manifests as asymmetric parenchymal opacities in treated areas [26, 38]. Airway hemorrhage can appear on CT as hazy ground-glass opacities with ill-defined margins [26]. Pulmonary artery steal syndrome, observed in approximately 70% of patients after PEA, results from the redistribution of perfusion from previously normal vessels to endarterectomized arteries, leading to impaired gas exchange and manifesting as mismatch on V/Q scan [26, 38, 95]. Residual PH, occurring in between 16% and 51% of patients, is caused by inoperable macrovascular subsegmental lesions or from the presence of microvascular disease [95, 96]. Previously difficult to detect, these complications are now observable with advanced technologies such as lung perfusion MRI and ECG-CTPA [96].

The role of artificial intelligence in CTEPH diagnosis

Currently, there are limited data on the use of artificial intelligence (AI) in characterizing CTEPH imaging. To date, only a few studies using AI in this disease have been published. Vainio et al. and Bird et al. evaluated hypoperfusion areas affected by CTEPH specifically on CTPA images using a DL model [97, 98]. The studies by Joshua Gawlitza et al. and Sumer Shikhare et al. describe the development of a supervised machine learning (ML) model trained on various quantitative and qualitative CT imaging features for noninvasive preoperative baseline risk stratification of preoperative patients [99, 100]. In contrast, Kogan et al. developed a ML model to identify patients with likely PH, using a large patient-level, US-based electronic health record database. The above-mentioned studies highlight possible potential expansion in the field of AI in the interpretation of medical images. In the future, automated interpretation of imaging results using AI tools may have the potential to improve diagnostic accuracy, reducing delays in diagnosis and providing new information about CTEPH.

Conclusions

CTEPH is relatively rare, but it has poor outcomes if untreated. The diagnosis of CTEPH is often inaccurate and delayed, resulting in treatment delays and a worsening prognosis. Assessment of each patient and therapeutic decision-making should ideally be conducted in specialized reference centers by a multidisciplinary team, based on data from comorbidities, imaging, and pulmonary hemodynamics. Imaging plays a pivotal role in the diagnosis of CTEPH, preoperative assessment, and treatment monitoring. Radiologists thus play a crucial role in the care of patients with CTEPH. Understanding the usefulness and limitations of different imaging modalities, being aware of the imaging characteristics of CTEPH and conditions that can mimic it, as well as identifying complications, is essential in radiological assessment. Rapidly advancing imaging techniques provide superior image quality and evaluation of specific parameters, enabling earlier diagnosis and accurate clinical decision-making. Therefore, it is imperative to continuously update our knowledge about the role of each method, the appropriate use of imaging, and the accurate interpretation of results.

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References

1. Higuchi S, Ota H, Yaoita N, et al. Update on the roles of imaging in the management of chronic thromboembolic pulmonary hypertension. J Cardiol. 2023; 81(3): 297–306, doi: 10.1016/j.jjcc.2022.03.001, indexed in Pubmed: 35490106.
2. Ruaro B, Baratella E, Caforio G, et al. Chronic Thromboembolic Pulmonary Hypertension: An Update. Diagnostics (Basel). 2022; 12(2), doi: 10.3390/diagnostics12020235, indexed in Pubmed: 35204326.
3. Darocha S. Epidemiologia CTEPH. Presented at: 13. Konferencja Sekcji Krążenia Płucnego Polskiego Towarzystwa Kardiologicznego; 2023 Oct; Warsaw, Poland. Dane z Bazy BNP-PL.
4. Teerapuncharoen K, Bag R. Chronic Thromboembolic Pulmonary Hypertension. Lung. 2022; 200(3): 283–299, doi: 10.1007/s00408-022-00539-w, indexed in Pubmed: 35643802.
5. Otani N, Watanabe R, Tomoe T, et al. Pathophysiology and Treatment of Chronic Thromboembolic Pulmonary Hypertension. Int J Mol Sci. 2023; 24(4), doi: 10.3390/ijms24043979, indexed in Pubmed: 36835383.
6. Ende-Verhaar YM, Cannegieter SC, Vonk Noordegraaf A, et al. Incidence of chronic thromboembolic pulmonary hypertension after acute pulmonary embolism: a contemporary view of the published literature. Eur Respir J. 2017; 49(2), doi: 10.1183/13993003.01792-2016, indexed in Pubmed: 28232411.
7. Pengo V, Lensing AWA, Prins MH, et al. Thromboembolic Pulmonary Hypertension Study Group. Incidence of chronic thromboembolic pulmonary hypertension after

pulmonary embolism. N Engl J Med. 2004; 350(22): 2257–2264, doi: 10.1056/NEJMoa032274, indexed in Pubmed: 15163775.

8. Valerio L, Mavromanoli AC, Barco S, et al. FOCUS Investigators. Chronic thromboembolic pulmonary hypertension and impairment after pulmonary embolism: the FOCUS study. Eur Heart J. 2022; 43(36): 3387–3398, doi: 10.1093/eurheartj/ehac206, indexed in Pubmed: 35484821.
9. Gall H, Hoeper MM, Richter MJ, et al. An epidemiological analysis of the burden of chronic thromboembolic pulmonary hypertension in the USA, Europe and Japan. Eur Respir Rev. 2017; 26(143), doi: 10.1183/16000617.0121-2016, indexed in Pubmed: 28356407.
10. Ciurzyński M, Kurzyna M, Kopeć G, et al. An expert opinion of the Polish Cardiac Society Working Group on Pulmonary Circulation on screening for chronic thromboembolic pulmonary hypertension patients after acute pulmonary embolism: Update. Kardiol Pol. 2022; 80(6): 723–732, doi: 10.33963/KP.a2022.0141, indexed in Pubmed: 35665906.
11. Lang IM, Madani M. Update on chronic thromboembolic pulmonary hypertension. Circulation. 2014; 130(6): 508–518, doi: 10.1161/CIRCULATIONAHA.114.009309, indexed in Pubmed: 25092279.
12. Pepke-Zaba J, Hoeper MM, Humbert M. Chronic thromboembolic pulmonary hypertension: advances from bench to patient management. Eur Respir J. 2013; 41(1): 8–9, doi: 10.1183/09031936.00181212, indexed in Pubmed: 23277517.
13. Blauwet LA, Edwards WD, Tazelaar HD, et al. Surgical pathology of pulmonary thromboendarterectomy: a study of 54 cases from 1990 to 2001. Hum Pathol. 2003; 34(12): 1290–1298, doi: 10.1016/j.humpath.2003.07.003, indexed in Pubmed: 14691915.
14. Auger WR, Kerr KM, Kim NHS, et al. Chronic thromboembolic pulmonary hypertension. Cardiol Clin. 2004; 22(3): 453–66, vii, doi: 10.1016/j.ccl.2004.04.006, indexed in Pubmed: 15302364.
15. Guérin L, Couturaud F, Parent F, et al. Prevalence of chronic thromboembolic pulmonary hypertension after acute pulmonary embolism. Prevalence of CTEPH after

pulmonary embolism. Thromb Haemost. 2014; 112(3): 598–605, doi: 10.1160/TH13-07-0538, indexed in Pubmed: 24898545.

16. Delcroix M, Kerr K, Fedullo P. Chronic Thromboembolic Pulmonary Hypertension. Epidemiology and Risk Factors. Ann Am Thorac Soc. 2016; 13 Suppl 3: S201–S206, doi: 10.1513/AnnalsATS.201509-621AS, indexed in Pubmed: 27571001.
17. Lang IM, Pesavento R, Bonderman D, et al. Risk factors and basic mechanisms of chronic thromboembolic pulmonary hypertension: a current understanding. Eur Respir J. 2013; 41(2): 462–468, doi: 10.1183/09031936.00049312, indexed in Pubmed: 22700839.
18. Yang J, Madani MM, Mahmud E, et al. Evaluation and Management of Chronic Thromboembolic Pulmonary Hypertension. Chest. 2023; 164(2): 490–502, doi: 10.1016/j.chest.2023.03.029, indexed in Pubmed: 36990148.
19. Fedullo P, Kerr KM, Kim NH, et al. Chronic thromboembolic pulmonary hypertension. Am J Respir Crit Care Med. 2011; 183(12): 1605–1613, doi: 10.1164/rccm.201011-1854CI, indexed in Pubmed: 21330453.
20. Verbelen T, Godinas L, Maleux G, et al. Chronic thromboembolic pulmonary hypertension: diagnosis, operability assessment and patient selection for pulmonary endarterectomy. Ann Cardiothorac Surg. 2022; 11(2): 82–97, doi: 10.21037/acs-2021-pte-12, indexed in Pubmed: 35433370.
21. Zhang Yi, Yu X, Jin Qi, et al. Advances in targeted therapy for chronic thromboembolic pulmonary hypertension. Heart Fail Rev. 2019; 24(6): 949–965, doi: 10.1007/s10741-019-09798-x, indexed in Pubmed: 31044326.
22. Rogberg AN, Gopalan D, Westerlund E, et al. Do radiologists detect chronic thromboembolic disease on computed tomography? Acta Radiol. 2019; 60(11): 1576–1583, doi: 10.1177/0284185119836232, indexed in Pubmed: 30897932.
23. Gopalan D, Delcroix M, Held M. Diagnosis of chronic thromboembolic pulmonary hypertension. Eur Respir Rev. 2017; 26(143), doi: 10.1183/16000617.0108-2016, indexed in Pubmed: 28298387.

24. Woodruff WW, Hoeck BE, Chitwood WR, et al. Radiographic findings in pulmonary hypertension from unresolved embolism. AJR Am J Roentgenol. 1985; 144(4): 681–686, doi: 10.2214/ajr.144.4.681, indexed in Pubmed: 3872021.

25. Gopalan D, Blanchard D, Auger WR. Diagnostic Evaluation of Chronic Thromboembolic Pulmonary Hypertension. Ann Am Thorac Soc. 2016; 13 Suppl 3: S222–S239, doi: 10.1513/AnnalsATS.201509-623AS, indexed in Pubmed: 27571004.

26. Renapurkar RD, Shrikanthan S, Heresi GA, et al. Imaging in Chronic Thromboembolic Pulmonary Hypertension. J Thorac Imaging. 2017; 32(2): 71–88, doi: 10.1097/RTI.0000000000000256, indexed in Pubmed: 28060193.

27. Kligerman S, Hsiao A. Optimizing the diagnosis and assessment of chronic thromboembolic pulmonary hypertension with advancing imaging modalities. Pulm Circ. 2021; 11(2): 20458940211007375, doi: 10.1177/20458940211007375, indexed in Pubmed: 34104420.

28. Tunariu N, Gibbs SJR, Win Z, et al. Ventilation-perfusion scintigraphy is more sensitive than multidetector CTPA in detecting chronic thromboembolic pulmonary disease as a treatable cause of pulmonary hypertension. J Nucl Med. 2007; 48(5): 680–684, doi: 10.2967/jnumed.106.039438, indexed in Pubmed: 17475953.

29. Kim NH, D'Armini AM, Delcroix M, et al. Chronic thromboembolic pulmonary disease. Eur Respir J. 2024; 64(4), doi: 10.1183/13993003.01294-2024, indexed in Pubmed: 39209473.

30. Ruggiero A, Screaton NJ. Imaging of acute and chronic thromboembolic disease: state of the art. Clin Radiol. 2017; 72(5): 375–388, doi: 10.1016/j.crad.2017.02.011, indexed in Pubmed: 28330686.

31. Ribas Sola J, Sánchez-Corral Mena MÁ, Riera-Mestre A. Update in the management of chronic thrombo-embolic pulmonary hypertension. Med Clin (Barc). 2024; 162(3): 126–133, doi: 10.1016/j.medcli.2023.08.006, indexed in Pubmed: 37925273.

32. Miniati M, Pistolesi M, Marini C, et al. Value of perfusion lung scan in the diagnosis of pulmonary embolism: results of the Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis (PISA-PED). Am J Respir Crit Care Med. 1996;

154(5): 1387–1393, doi: 10.1164/ajrccm.154.5.8912753, indexed in Pubmed: 8912753.

33. Azarian R, Wartski M, Collignon MA, et al. Lung perfusion scans and hemodynamics in acute and chronic pulmonary embolism. J Nucl Med. 1997 Jun; 38(6): 980–983, indexed in Pubmed: 9189155.

34. Soler X, Hoh CK, Test VJ, et al. Single photon emission computed tomography in chronic thromboembolic pulmonary hypertension. Respirology. 2011; 16(1): 131–137, doi: 10.1111/j.1440-1843.2010.01867.x, indexed in Pubmed: 20920137.

35. Frost A, Badesch D, Gibbs JS, et al. Diagnosis of pulmonary hypertension. Eur Respir J. 2019; 53(1), doi: 10.1183/13993003.01904-2018, indexed in Pubmed: 30545972.

36. Kopeć G, Dzikowska-Diduch O, Mroczek E, et al. Characteristics and outcomes of patients with chronic thromboembolic pulmonary hypertension in the era of modern therapeutic approaches: data from the Polish multicenter registry (BNP-PL). Ther Adv Chronic Dis. 2021; 12: 20406223211002961, doi: 10.1177/20406223211002961, indexed in Pubmed: 33854746.

37. Humbert M, Kovacs G, Hoeper MM, et al. ESC/ERS Scientific Document Group. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Respir J. 2023; 61(1), doi: 10.1183/13993003.00879-2022, indexed in Pubmed: 36028254.

38. Hahn LD, Papamatheakis DG, Fernandes TM, et al. Multidisciplinary Approach to Chronic Thromboembolic Pulmonary Hypertension: Role of Radiologists. Radiographics. 2023; 43(2): e220078, doi: 10.1148/rg.220078, indexed in Pubmed: 36525366.

39. Hinrichs JB, Marquardt S, von Falck C, et al. Comparison of C-arm Computed Tomography and Digital Subtraction Angiography in Patients with Chronic Thromboembolic Pulmonary Hypertension. Cardiovasc Intervent Radiol. 2016; 39(1): 53–63, doi: 10.1007/s00270-015-1090-7, indexed in Pubmed: 25828726.

40. Tyagi S, Batra V, Gautam A. Review of Advances on Management of Chronic Thromboembolic Pulmonary Hypertension. International Journal of Angiology. 2023; 32(04): 207–214, doi: 10.1055/s-0043-1767759.

41. Ogo T, Fukuda T, Tsuji A, et al. Efficacy and safety of balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension guided by cone-beam computed tomography and electrocardiogram-gated area detector computed tomography. Eur J Radiol. 2017; 89: 270–276, doi: 10.1016/j.ejrad.2016.12.013, indexed in Pubmed: 28034568.

42. Reichelt A, Hoeper MM, Galanski M, et al. Chronic thromboembolic pulmonary hypertension: evaluation with 64-detector row CT versus digital substraction angiography. Eur J Radiol. 2009; 71(1): 49–54, doi: 10.1016/j.ejrad.2008.03.016, indexed in Pubmed: 18462902.

43. Ley S, Ley-Zaporozhan J, Pitton MB, et al. Diagnostic performance of state-of-the-art imaging techniques for morphological assessment of vascular abnormalities in patients with chronic thromboembolic pulmonary hypertension (CTEPH). Eur Radiol. 2012; 22(3): 607–616, doi: 10.1007/s00330-011-2290-4, indexed in Pubmed: 21947513.

44. Sugiura T, Tanabe N, Matsuura Y, et al. Role of 320-slice CT imaging in the diagnostic workup of patients with chronic thromboembolic pulmonary hypertension. Chest. 2013; 143(4): 1070–1077, doi: 10.1378/chest.12-0407, indexed in Pubmed: 23100061.

45. Rahaghi FN, Ross JC, Agarwal M, et al. Pulmonary vascular morphology as an imaging biomarker in chronic thromboembolic pulmonary hypertension. Pulm Circ. 2016; 6(1): 70–81, doi: 10.1086/685081, indexed in Pubmed: 27162616.

46. Rahaghi FN, Ross JC, Agarwal M, et al. Pulmonary vascular morphology as an imaging biomarker in chronic thromboembolic pulmonary hypertension. Pulm Circ. 2016; 6(1): 70–81, doi: 10.1086/685081, indexed in Pubmed: 27162616.

47. Verbelen T, Godinas L, Dorfmüller P, et al. Clinical-radiological-pathological correlation in chronic thromboembolic pulmonary hypertension. Eur Respir Rev. 2023; 32(170), doi: 10.1183/16000617.0149-2023, indexed in Pubmed: 38123236.

48. Kligerman SJ, Henry T, Lin CT, et al. Mosaic Attenuation: Etiology, Methods of Differentiation, and Pitfalls. Radiographics. 2015; 35(5): 1360–1380, doi: 10.1148/rg.2015140308, indexed in Pubmed: 26274445.

49. Grosse A, Grosse C, Lang IM. Distinguishing Chronic Thromboembolic Pulmonary Hypertension From Other Causes of Pulmonary Hypertension Using CT. AJR Am J

Roentgenol. 2017; 209(6): 1228–1238, doi: 10.2214/AJR.17.17871, indexed in Pubmed: 28981358.

50. Murayama K, Suzuki S, Nagata H, et al. Visualization of Lenticulostriate Arteries on CT Angiography Using Ultra-High-Resolution CT Compared with Conventional-Detector CT. AJNR Am J Neuroradiol. 2020; 41(2): 219–223, doi: 10.3174/ajnr.A6377, indexed in Pubmed: 31857330.

51. Ogo T, Fukuda T, Tsuji A, et al. Efficacy and safety of balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension guided by cone-beam computed tomography and electrocardiogram-gated area detector computed tomography. Eur J Radiol. 2017; 89: 270–276, doi: 10.1016/j.ejrad.2016.12.013, indexed in Pubmed: 28034568.

52. Schüßler A, Richter M, Tello K, et al. Evaluation of Diagnostic Accuracy and Radiation Exposure of Dual-Energy Computed Tomography (DECT) in the Course of Chronic Thromboembolic Pulmonary Hypertension (CTEPH). Rofo. 2021; 193(11): 1318–1326, doi: 10.1055/a-1502-7541, indexed in Pubmed: 34139779.

53. Miwa K, Taniguchi Yu, Fujii H, et al. Microvasculopathy Evaluated by Dual-Energy Computed Tomography in Patients with Chronic Thromboembolic Pulmonary Hypertension and Pulmonary Arterial Hypertension. Life (Basel). 2022; 12(8), doi: 10.3390/life12081232, indexed in Pubmed: 36013412.

54. Masy M, Giordano J, Petyt G, et al. Dual-energy CT (DECT) lung perfusion in pulmonary hypertension: concordance rate with V/Q scintigraphy in diagnosing chronic thromboembolic pulmonary hypertension (CTEPH). Eur Radiol. 2018; 28(12): 5100–5110, doi: 10.1007/s00330-018-5467-2, indexed in Pubmed: 29846802.

55. Dournes G, Verdier D, Montaudon M, et al. Dual-energy CT perfusion and angiography in chronic thromboembolic pulmonary hypertension: diagnostic accuracy and concordance with radionuclide scintigraphy. Eur Radiol. 2014; 24(1): 42–51, doi: 10.1007/s00330-013-2975-y, indexed in Pubmed: 23982287.

56. Si-Mohamed S, Moreau-Triby C, Tylski P, et al. Head-to-head comparison of lung perfusion with dual-energy CT and SPECT-CT. Diagn Interv Imaging. 2020; 101(5): 299–310, doi: 10.1016/j.diii.2020.02.006, indexed in Pubmed: 32173289.

57. Si-Mohamed SA, Zumbihl L, Turquier S, et al. Lung Dual-Energy CT Perfusion Blood Volume as a Marker of Severity in Chronic Thromboembolic Pulmonary Hypertension. Diagnostics (Basel). 2023; 13(4), doi: 10.3390/diagnostics13040769, indexed in Pubmed: 36832256.

58. Abozeed M, Conic S, Bullen J, et al. Dual energy CT based scoring in chronic thromboembolic pulmonary hypertension and correlation with clinical and hemodynamic parameters: a retrospective cross-sectional study. Cardiovasc Diagn Ther. 2022; 12(3): 305–313, doi: 10.21037/cdt-21-686, indexed in Pubmed: 35800352.

59. Onishi H, Taniguchi Yu, Matsuoka Y, et al. Evaluation of microvasculopathy using dual-energy computed tomography in patients with chronic thromboembolic pulmonary hypertension. Pulm Circ. 2021; 11(1): 2045894020983162, doi: 10.1177/2045894020983162, indexed in Pubmed: 33532057.

60. Schüssler A, Lug Q, Kremer N, et al. Evaluation of diagnostic accuracy of dual-energy computed tomography in patients with chronic thromboembolic pulmonary hypertension compared to V/Q-SPECT and pulmonary angiogram. Front Med (Lausanne). 2023; 10: 1194272, doi: 10.3389/fmed.2023.1194272, indexed in Pubmed: 37425315.

61. Koike H, Sueyoshi E, Sakamoto I, et al. Clinical Significance of Late Phase of Lung Perfusion Blood Volume (Lung Perfusion Blood Volume) Quantified by Dual-Energy Computed Tomography in Patients With Pulmonary Thromboembolism. J Thorac Imaging. 2017; 32(1): 43–49, doi: 10.1097/RTI.0000000000000250, indexed in Pubmed: 27846051.

62. Kang MJ, Park CM, Lee CH, et al. Focal iodine defects on color-coded iodine perfusion maps of dual-energy pulmonary CT angiography images: a potential diagnostic pitfall. AJR Am J Roentgenol. 2010; 195(5): W325–W330, doi: 10.2214/AJR.09.3241, indexed in Pubmed: 20966296.

63. Aziz M, Krishnam M, Madhuranthakam AJ, et al. Update on MR imaging of the pulmonary vasculature. Int J Cardiovasc Imaging. 2019; 35(8): 1483–1497, doi: 10.1007/s10554-019-01603-y, indexed in Pubmed: 31030315.

64. Ley S, Grünig E, Kiely DG, et al. Computed tomography and magnetic resonance imaging of pulmonary hypertension: Pulmonary vessels and right ventricle. J Magn

Reson Imaging. 2010; 32(6): 1313–1324, doi: 10.1002/jmri.22373, indexed in Pubmed: 21105137.

65. Kreitner KF, Kunz RP, Ley S, et al. Chronic thromboembolic pulmonary hypertension - assessment by magnetic resonance imaging. Eur Radiol. 2007; 17(1): 11–21, doi: 10.1007/s00330-006-0327-x, indexed in Pubmed: 16838142.

66. Ley S, Kauczor HU, Heussel CP, et al. Value of contrast-enhanced MR angiography and helical CT angiography in chronic thromboembolic pulmonary hypertension. Eur Radiol. 2003; 13(10): 2365–2371, doi: 10.1007/s00330-003-1878-8, indexed in Pubmed: 12712256.

67. Ley S, Ley-Zaporozhan J, Pitton MB, et al. Diagnostic performance of state-of-the-art imaging techniques for morphological assessment of vascular abnormalities in patients with chronic thromboembolic pulmonary hypertension (CTEPH). Eur Radiol. 2012; 22(3): 607–616, doi: 10.1007/s00330-011-2290-4, indexed in Pubmed: 21947513.

68. Lacharie M, Villa A, Milidonis X, et al. Role of pulmonary perfusion magnetic resonance imaging for the diagnosis of pulmonary hypertension: A review. World J Radiol. 2023; 15(9): 256–273, doi: 10.4329/wjr.v15.i9.256, indexed in Pubmed: 37823020.

69. Hopkins SR, Wielpütz MO, Kauczor HU. Imaging lung perfusion. J Appl Physiol (1985). 2012; 113(2): 328–339, doi: 10.1152/japplphysiol.00320.2012, indexed in Pubmed: 22604884.

70. Hatabu H, Ohno Y, Gefter WB, et al. Fleischner Society. Expanding Applications of Pulmonary MRI in the Clinical Evaluation of Lung Disorders: Fleischner Society Position Paper. Radiology. 2020; 297(2): 286–301, doi: 10.1148/radiol.2020201138, indexed in Pubmed: 32870136.

71. Alsop DC, Hatabu H, Bonnet M, et al. Multi-slice, breathhold imaging of the lung with submillisecond echo times. Magn Reson Med. 1995; 33(5): 678–682, doi: 10.1002/mrm.1910330513, indexed in Pubmed: 7596272.

72. Mayo JR, MacKay A, Müller NL. MR imaging of the lungs: value of short TE spin-echo pulse sequences. AJR Am J Roentgenol. 1992; 159(5): 951–956, doi: 10.2214/ajr.159.5.1414805, indexed in Pubmed: 1414805.

73. Nazir MS, Neji R, Speier P, et al. Simultaneous multi slice (SMS) balanced steady state free precession first-pass myocardial perfusion cardiovascular magnetic resonance with iterative reconstruction at 1.5 T. J Cardiovasc Magn Reson. 2018; 20(1): 84, doi: 10.1186/s12968-018-0502-7, indexed in Pubmed: 30526627.

74. Johns CS, Swift AJ, Hughes PJC, et al. Pulmonary MR angiography and perfusion imaging-A review of methods and applications. Eur J Radiol. 2017; 86: 361–370, doi: 10.1016/j.ejrad.2016.10.003, indexed in Pubmed: 28341390.

75. Johns CS, Swift AJ, Rajaram S, et al. Lung perfusion: MRI vs. SPECT for screening in suspected chronic thromboembolic pulmonary hypertension. J Magn Reson Imaging. 2017; 46(6): 1693–1697, doi: 10.1002/jmri.25714, indexed in Pubmed: 28376242.

76. Rajaram S, Swift AJ, Telfer A, et al. 3D contrast-enhanced lung perfusion MRI is an effective screening tool for chronic thromboembolic pulmonary hypertension: results from the ASPIRE Registry. Thorax. 2013; 68(7): 677–678, doi: 10.1136/thoraxjnl-2012-203020, indexed in Pubmed: 23349220.

77. Ingrisch M, Maxien D, Meinel FG, et al. Detection of pulmonary embolism with free-breathing dynamic contrast-enhanced MRI. J Magn Reson Imaging. 2016; 43(4): 887–893, doi: 10.1002/jmri.25050, indexed in Pubmed: 26391931.

78. Ohno Y, Hatabu H, Murase K, et al. Primary pulmonary hypertension: 3D dynamic perfusion MRI for quantitative analysis of regional pulmonary perfusion. AJR Am J Roentgenol. 2007; 188(1): 48–56, doi: 10.2214/AJR.05.0135, indexed in Pubmed: 17179345.

79. Ohno Y, Koyama H, Nogami M, et al. Dynamic perfusion MRI: capability for evaluation of disease severity and progression of pulmonary arterial hypertension in patients with connective tissue disease. J Magn Reson Imaging. 2008; 28(4): 887–899, doi: 10.1002/jmri.21550, indexed in Pubmed: 18821609.

80. Ohno Y, Koyama H, Yoshikawa T, et al. Contrast-enhanced multidetector-row computed tomography vs. Time-resolved magnetic resonance angiography vs. contrast-enhanced perfusion MRI: assessment of treatment response by patients with inoperable chronic thromboembolic pulmonary hypertension. J Magn Reson Imaging. 2012; 36(3): 612–623, doi: 10.1002/jmri.23680, indexed in Pubmed: 22566188.

81. Gordon Y, Partovi S, Müller-Eschner M, et al. Dynamic contrast-enhanced magnetic resonance imaging: fundamentals and application to the evaluation of the peripheral perfusion. Cardiovasc Diagn Ther. 2014; 4(2): 147–164, doi: 10.3978/j.issn.2223-3652.2014.03.01, indexed in Pubmed: 24834412.

82. Lacharie M, Villa A, Milidonis X, et al. Role of pulmonary perfusion magnetic resonance imaging for the diagnosis of pulmonary hypertension: A review. World J Radiol. 2023; 15(9): 256–273, doi: 10.4329/wjr.v15.i9.256, indexed in Pubmed: 37823020.

83. Marchetta S, Verbelen T, Claessen G, et al. A Comprehensive Assessment of Right Ventricular Function in Chronic Thromboembolic Pulmonary Hypertension. J Clin Med. 2022; 12(1), doi: 10.3390/jcm12010047, indexed in Pubmed: 36614845.

84. Bonno E, Viray M, Jackson G, et al. Modern Right Heart Catheterization: Beyond Simple Hemodynamics. Advances in Pulmonary Hypertension. 2020; 19(1): 6–15, doi: 10.21693/1933-088x-19.1.6.

85. Richter MJ, Hsu S, Yogeswaran A, et al. Right ventricular pressure-volume loop shape and systolic pressure change in pulmonary hypertension. Am J Physiol Lung Cell Mol Physiol. 2021; 320(5): L715–L725, doi: 10.1152/ajplung.00583.2020, indexed in Pubmed: 33655769.

86. Parasuraman S, Walker S, Loudon BL, et al. Assessment of pulmonary artery pressure by echocardiography-A comprehensive review. Int J Cardiol Heart Vasc. 2016; 12: 45–51, doi: 10.1016/j.ijcha.2016.05.011, indexed in Pubmed: 28616542.

87. Rudski L, Lai W, Afilalo J, et al. Guidelines for the Echocardiographic Assessment of the Right Heart in Adults: A Report from the American Society of Echocardiography. Journal of the American Society of Echocardiography. 2010; 23(7): 685–713, doi: 10.1016/j.echo.2010.05.010.

88. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015; 28(1): 1–39.e14, doi: 10.1016/j.echo.2014.10.003, indexed in Pubmed: 25559473.

89. Erley J, Tanacli R, Genovese D, et al. Myocardial strain analysis of the right ventricle: comparison of different cardiovascular magnetic resonance and echocardiographic techniques. J Cardiovasc Magn Reson. 2020; 22(1): 51, doi: 10.1186/s12968-020-00647-7, indexed in Pubmed: 32698811.

90. Swift AJ, Rajaram S, Capener D, et al. LGE patterns in pulmonary hypertension do not impact overall mortality. JACC Cardiovasc Imaging. 2014; 7(12): 1209–1217, doi: 10.1016/j.jcmg.2014.08.014, indexed in Pubmed: 25496540.

91. Roller FC, Wiedenroth C, Breithecker A, et al. Native T1 mapping and extracellular volume fraction measurement for assessment of right ventricular insertion point and septal fibrosis in chronic thromboembolic pulmonary hypertension. Eur Radiol. 2017; 27(5): 1980–1991, doi: 10.1007/s00330-016-4585-y, indexed in Pubmed: 27651142.

92. McInnis MC, Wang D, Donahoe L, et al. Importance of computed tomography in defining segmental disease in chronic thromboembolic pulmonary hypertension. ERJ Open Res. 2020; 6(4), doi: 10.1183/23120541.00461-2020, indexed in Pubmed: 33313309.

93. Eberhard M, McInnis M, de Perrot M, et al. Dual-Energy CT Pulmonary Angiography for the Assessment of Surgical Accessibility in Patients with Chronic Thromboembolic Pulmonary Hypertension. Diagnostics (Basel). 2022; 12(2), doi: 10.3390/diagnostics12020228, indexed in Pubmed: 35204319.

94. Rolf A, Rixe J, Kim WK, et al. Pulmonary vascular remodeling before and after pulmonary endarterectomy in patients with chronic thromboembolic pulmonary hypertension: a cardiac magnetic resonance study. Int J Cardiovasc Imaging. 2015; 31(3): 613–619, doi: 10.1007/s10554-014-0580-z, indexed in Pubmed: 25519191.

95. Jenkins DP, Madani M, Mayer E, et al. Surgical treatment of chronic thromboembolic pulmonary hypertension. Eur Respir J. 2013; 41(3): 735–742, doi: 10.1183/09031936.00058112, indexed in Pubmed: 23143539.

96. Braams NJ, Ruigrok D, Schokker MGM, et al. Pulmonary vascular imaging characteristics after pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension. J Heart Lung Transplant. 2020; 39(3): 248–256, doi: 10.1016/j.healun.2019.11.020, indexed in Pubmed: 31866175.

97. Vainio T, Mäkelä T, Savolainen S, et al. Performance of a 3D convolutional neural network in the detection of hypoperfusion at CT pulmonary angiography in patients with chronic pulmonary embolism: a feasibility study. Eur Radiol Exp. 2021; 5(1): 45, doi: 10.1186/s41747-021-00235-z, indexed in Pubmed: 34557979.

98. Bird E, Hasenstab K, Kim N, et al. Mapping the Spatial Extent of Hypoperfusion in Chronic Thromboembolic Pulmonary Hypertension Using Multienergy CT. Radiol Cardiothorac Imaging. 2023; 5(4): e220221, doi: 10.1148/ryct.220221, indexed in Pubmed: 37693197.

99. Gawlitza J, Endres S, Fries P, et al. Machine learning assisted feature identification and prediction of hemodynamic endpoints using computed tomography in patients with CTEPH. Int J Cardiovasc Imaging. 2024; 40(3): 569–577, doi: 10.1007/s10554-023-03026-2, indexed in Pubmed: 38143250.

100. Shikhare S, Balki I, Shi Y, et al. Right-to-left ventricle ratio determined by machine learning algorithms on CT pulmonary angiography images predicts prolonged ICU length of stay in operated chronic thromboembolic pulmonary hypertension. Br J Radiol. 2022; 95(1139): 20210722, doi: 10.1259/bjr.20210722, indexed in Pubmed: 36043477.

Figure legend

Figure 1. Pulmonary perfusion evaluation in CTEPH. **A, B:** Ventilation-perfusion scintigraphy (V/Q scan) in 55-year-old man diagnosed with CTEPH. A) After inhalation of gaseous radionuclides, scintigraphic images obtained in the posterior projection showing ventilation to lungs. B) After intravenous injection of Technetium-99m macroaggregated albumin, scintigraphic images were obtained, shown here in the posterior projection. This view shows perfusion defects in the apicoposterior segment of the left upper lobe and lingula (*blue arrows*) corresponding with normally ventilated areas (*yellow arrows*) on ventilation scan (A) - V/Q mismatch. **C, D:** Dual-energy computed tomography (DECT) in 65-year-old

woman with CTEPH. DECT left lung (C) and right lung (D) pulmonary angiography sagittal views showing the peripheral perfusion defects (*red arrows*)

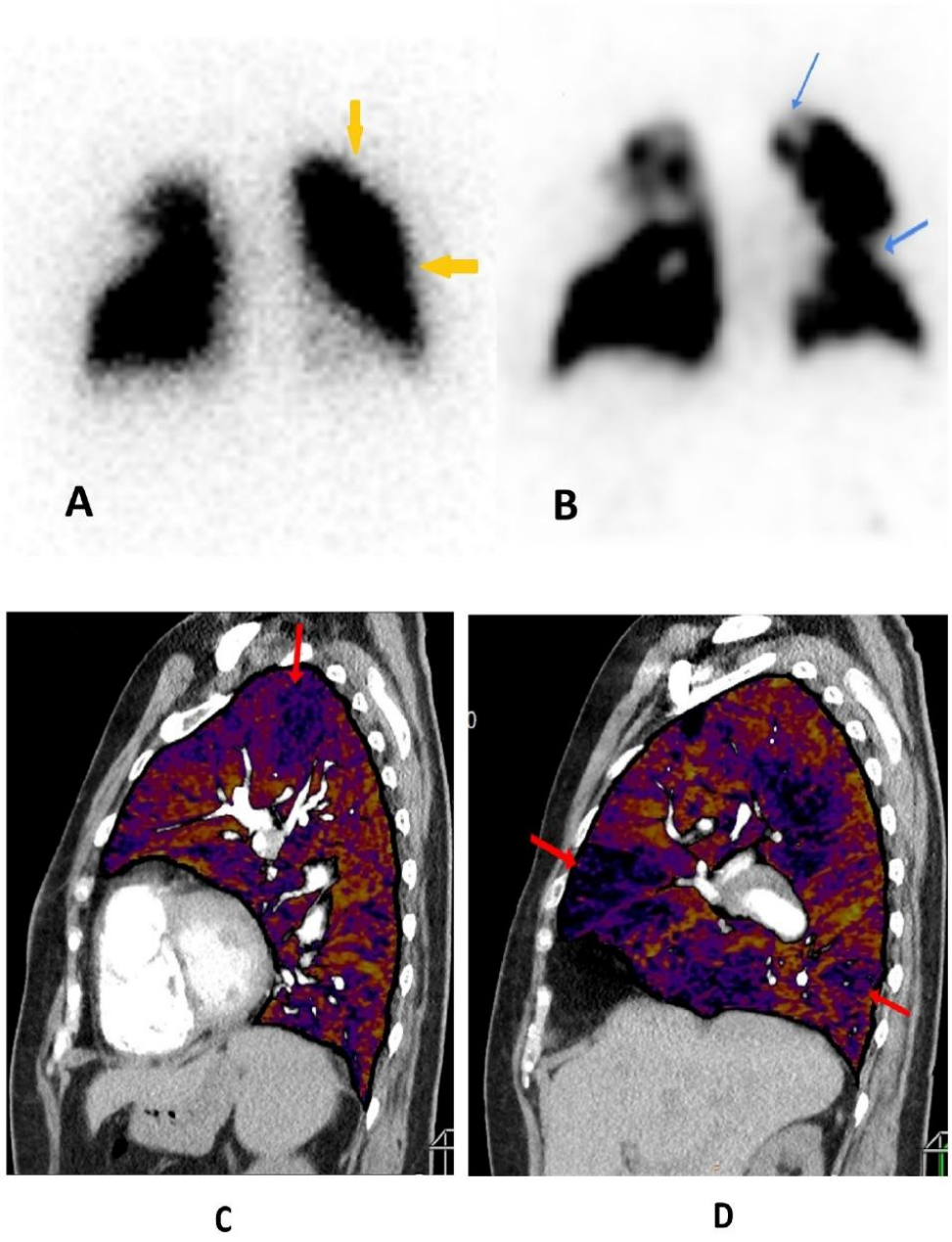


Figure 2. Conventional pulmonary angiography (CPA) in a 77-year-old woman with CTEPH.

Anteroposterior view showing post-contrast visualization of right lung pulmonary arteries (**A**). Lateral view showing post-contrast visualization of left lung pulmonary arteries (**B**). Both views showing stenoses (*white arrows*) with post-stenotic dilatations, dilatation of main pulmonary artery (*blue arrow*), and tortuosity of segmental-level vessels (*yellow arrow*)

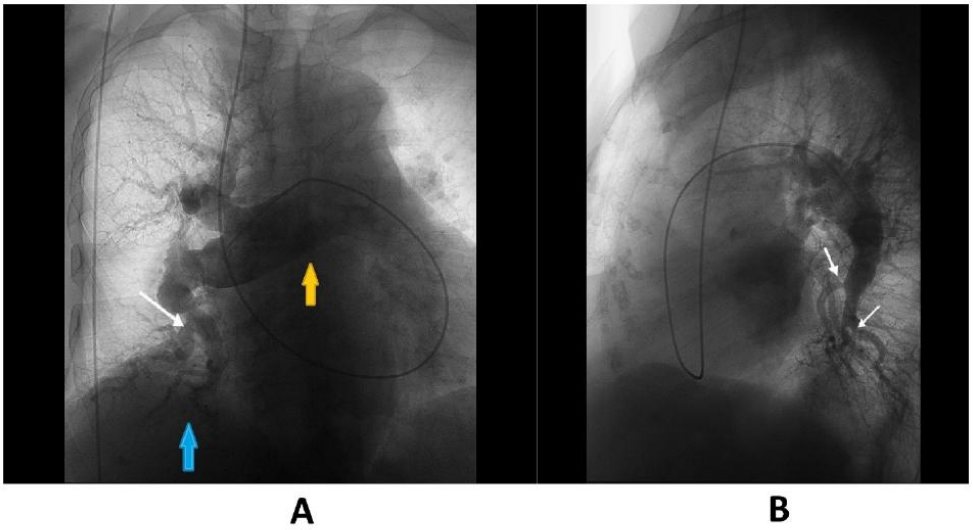


Figure 3. Computed tomography pulmonary angiography (CTPA) in an 83-year-old woman with CTEPH. **A.** CTPA axial plane image showing dilated lower lobes arteries with narrowing of its lumen due to eccentric emboli (*blue arrows*); **B.** CTPA sagittal plane left pulmonary arteries image showing variability in the size of lower lobe and segmental-level vessels,

tortuosity, vessel narrowing, and intimal irregularities (*red arrow*)

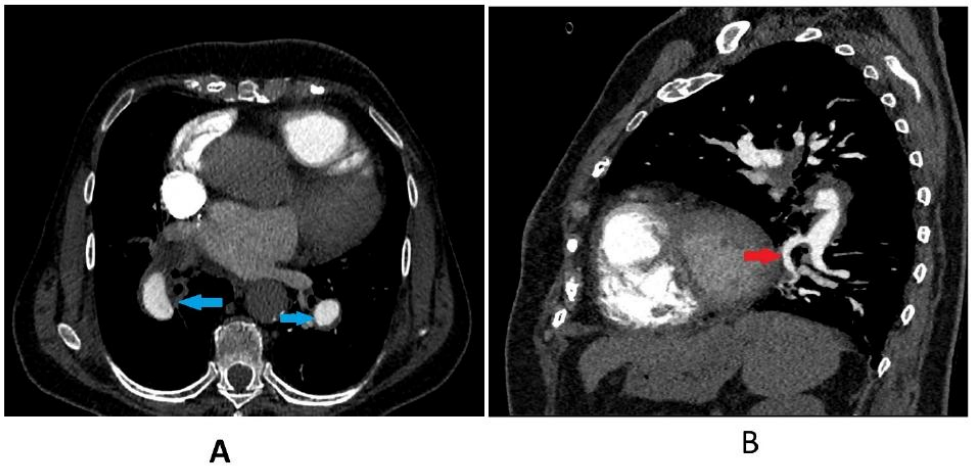
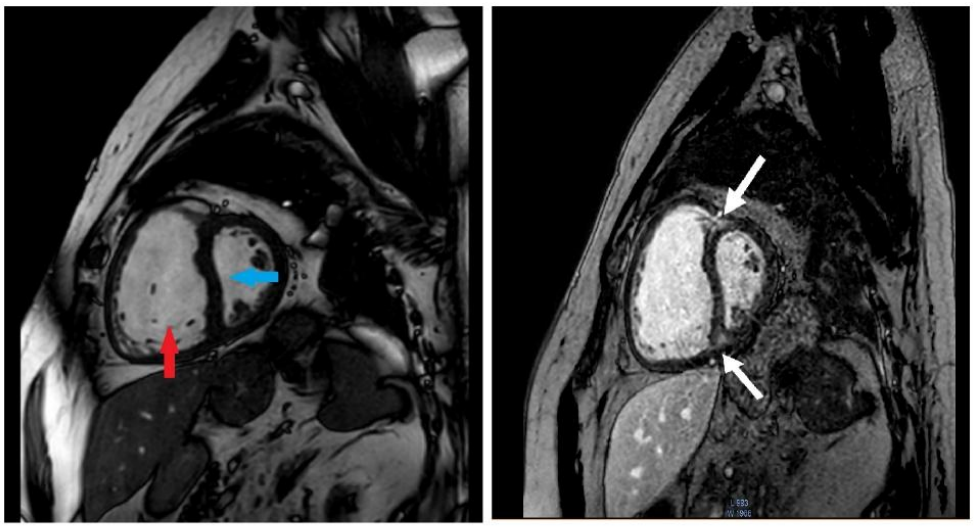
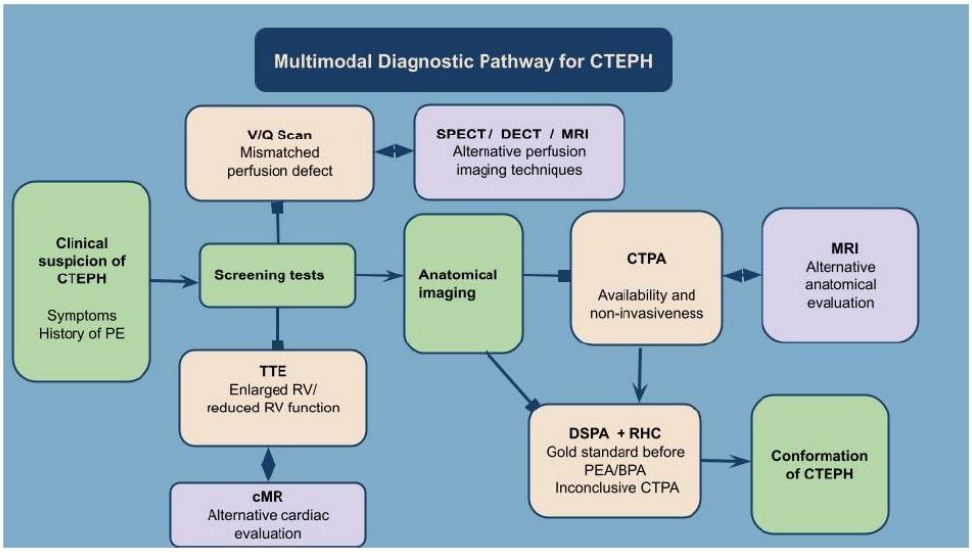


Figure 4. Cardiac magnetic resonance (cMR) in a 58-year-old man with CTEPH. **A.** Cine cMR image in the short-axis view showing the dilated right heart (*red arrow*) and leftward bowing of the interventricular septum (*blue arrow*); **B.** Gradient echo (GRE) inversion recovery image showing delayed enhancement at right ventricular septal insertions (*white arrows*) consistent with chronic pulmonary hypertension



A B

Central illustration



Multimodal diagnostic pathway for CTEPH

CTEPH — chronic thromboembolic pulmonary hypertension; BPA — balloon pulmonary angioplasty; cMR — cardiac magnetic resonance; CTPA — computed tomography pulmonary angiography; DECT — dual-energy computed tomography; DSPA — digital subtraction pulmonary angiography; MRI — magnetic resonance imaging; PEA — pulmonary endarterectomy; RHC — right heart catheterization; RV — right ventricle; SPECT — single-photon emission computed tomography; TTE — transthoracic echocardiography; V/Q scan — ventilation/perfusion scan

Table 1. Multimodal imaging in CTEPH diagnosis

Modality	Pros	Cons	Special use	Patient-specific considerations	
TTE	Non-invasive, widely available; useful for initial detection of PH and RV overload; evaluates cardiac function and anatomy	Suggestive but not diagnostic; limited by operator dependency; limited by poor acoustic windows	Initial screening for PH; helps guide further diagnostics.	May be less reliable in patients with obesity, lung disease.	
V/Q scan	Recommended first-line screening tool; high sensitivity for perfusion defects; negative result effectively rules out CTEPH; no contrast needed.	Cannot confirm CTEPH diagnosis; non-specific; underestimates severity.	First-line screening in symptomatic patients; useful for ruling out CTEPH.	Safe in patients with renal insufficiency.	
SPECT	Provides 3D visualization of perfusion defects; higher sensitivity and spatial resolution than planar V/Q scan.	Limited availability; higher radiation dose than planar V/Q scan; longer acquisition time than planar V/Q scan; may require additional expertise.	Precise localization of perfusion abnormalities.	Same as V/Q scan.	

CTPA	Widely available; reveals characteristic signs of chronic thromboembolism, PH and RV overload; high spatial and contrast resolution; allows differential diagnosis.	Lower sensitivity for peripheral lesions; requires expert interpretation; uses iodinated contrast.	Initial imaging for APE; differentiates CTEPH from mimics; assesses chronic vs. acute thrombi.	Use caution in patients with renal impairment or contrast allergy.	
DECT	Combines anatomical and functional imaging; enhanced vascular imaging with iodine perfusion maps; correlates with disease severity; high diagnostic accuracy.	Limited availability; requires advanced equipment and experience; uses iodinated contrast; expensive; artifact-prone.	Quantitative perfusion mapping; useful for visualizing distal perfusion mismatch.	Avoid in patients with renal dysfunction or iodine allergy.	
MRI	No radiation; effective for evaluating RV function; detects perfusion defects; provides soft tissue detail; suitable for follow-up.	Requires specialized software and expertise; long scan times; limited availability; motion and reconstruction challenges.	Monitoring of CTEP; alternative for patients with renal dysfunction or contrast contraindication; useful in patients where radiation is contraindicated; useful for	Avoid in patients with non-compatible implants or severe claustrophobia.	

			fibrosis evaluation.		
Pulmonary angiography	Gold standard for evaluating pulmonary vascular anatomy essential for surgical /interventional planning.	Invasive; not suitable in unstable patients; may underestimate peripheral disease requires specialized expertise	Final anatomical confirmation before PEA or BPA;	Requires stable clinical condition; performed in expert centers.	

APE — Acute pulmonary embolism; BPA — balloon pulmonary angioplasty; CTEPH — chronic thromboembolic pulmonary hypertension; CTPA — computed tomography pulmonary angiography; DECT — dual-energy computed tomography; MRI — magnetic resonance imaging; PEA — pulmonary endarterectomy; PH — pulmonary hypertension; RV — right ventricle; TTE — transthoracic echocardiography; V/Q Scan — ventilation/perfusion scan

7.2. Chronic thromboembolic hypertension predictors in computer tomography angiography . One center study

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Original paper

Chronic thromboembolic hypertension predictors in computed tomography angiography. Single-centre study

Konstantin Szewczuk[1,A,B,C,D,E,F], Olga Dzikowska-Diduch[2,B], Marek Roik[2,B], Piotr Pruszczyk[2,B,E], Dorota Piotrowska-Kownacka[1,F], Marek Gołębiowski[1,A,D,E,F]

[1]1st Department of Clinical Radiology, Medical University of Warsaw, Poland
[2]Department of Internal Medicine and Cardiology with the Centre for Diagnosis and Treatment of Venous Thromboembolism, Medical University of Warsaw, Poland

Abstract

Purpose: Chronic thromboembolic pulmonary hypertension (CTEPH) is a life-threatening but curable form of pulmonary hypertension. Early diagnosis is crucial for effective management and improved outcomes. Computed tomography pulmonary angiography (CTPA), characterised by high sensitivity and specificity, is integral to diagnosing CTEPH by identifying thrombi and associated pulmonary and mediastinal abnormalities. However, radiological features often overlap with other diseases, and their detection depends on radiologist expertise. This study aims to assess the frequency of characteristic radiological features in CTEPH, compare their prevalence with chronic thromboembolic disease (CTED), pulmonary arterial hypertension (PAH), and acute pulmonary embolism (APE), and evaluate their diagnostic predictive value.

Material and methods: This retrospective study analysed 115 patients divided into CTEPH (n = 35), CTED (n = 20), PAH (n = 24), and APE (n = 36) groups, matched by age and sex. CTPA scans were reviewed for signs of chronic embolism, pulmonary hypertension, and right heart overload. Sensitivity, specificity, accuracy, and predictive values were assessed using ROC analysis, expressed as the area under the curve (AUC).

Results: CTEPH patients exhibited vessel narrowing, intimal irregularities, bands, and webs in all cases (100%), with the highest diagnostic value at the segmental level (AUC = 0.906). Mosaic perfusion and variability in vessel size demonstrated moderate predictive value (AUC = 0.740 and AUC = 0.788, respectively).

Conclusions: CTPA is essential for differentiating CTEPH from other pulmonary vascular conditions. While no single feature achieves 100% predictive value, a comprehensive approach integrating vascular, parenchymal, and cardiac findings is critical for accurate diagnosis.

Key words: chronic thromboembolic pulmonary hypertension, tomography pulmonary angiography, pulmonary arteries, chronic thromboembolic disease, acute pulmonary embolism.

Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is a potentially life-threatening condition and a rare complication of acute pulmonary embolism (APE), affecting an estimated 0.5-9% of patients following an embolic event [1]. Categorised as group 4 WHO pulmonary hypertension (PH), CTEPH is the only potentially curable form of PH [2]. The pathogenesis of CTEPH remains poorly understood. In affected patients, pulmonary emboli fail to resolve completely, leading to increased pulmonary vascular resistance,

Correspondence address:
Konstantin Szewczuk, 1st Department of Clinical Radiology, Medical University of Warsaw, Warsaw, Poland, e-mail: konstantin.szewczuk@uckwum.pl

Authors' contribution:
A Study design · B Data collection · C Statistical analysis · D Data interpretation · E Manuscript preparation · F Literature search · G Funds collection

pulmonary hypertension, and subsequent right heart failure [2,3].

Early diagnosis is challenging because CTEPH often presents with nonspecific symptoms such as dyspnoea, fatigue, and chest pain [2]. Furthermore, a variety of diagnostic approaches, delays in referring patients to specialist centres, and insufficient awareness of this condition among radiologists contribute to diagnostic downtime [4]. On average, it takes 14-24 months to establish a correct diagnosis [5]. Imaging plays a central role in the multidisciplinary management of CTEPH. It is crucial for diagnosis, assessing the extent of the disease, planning treatment, and monitoring post-treatment outcomes. Computed tomography pulmonary angiography (CTPA) imaging is a key component of the diagnostic workup for CTEPH, with a sensitivity and specificity of 94-95% [6]. Although a normal CTPA result does not exclude CTEPH, because distal disease can be missed, CTPA provides vital information on the location and morphology of thrombi, which is critical for surgical or interventional planning [7]. Additionally, computed tomography (CT) scanning identifies underlying parenchymal lung and mediastinal diseases and aids in detecting other pulmonary vessel disorders [2].

Typical CTPA features of CTEPH include vascular signs of chronic embolism (such as partial obstruction, eccentric thrombus, calcified thrombus, bands, slits, and webs) and signs of pulmonary hypertension (such as enlargement of the main pulmonary arteries and enlargement of bronchial arteries) [8,9]. Furthermore, CTPA can assess parenchymal signs, such as scars, mosaic perfusion patterns, and bronchial anomalies, as well as signs of right heart overload, including right ventricular enlargement and hypertrophy [8,9]. CT findings in patients with CTEPH can differ according to the disease's severity, the extent of vascular blockage, and the degree of PH [10].

However, imaging features are not exclusive only to CTEPH and overlap with other disease entities. Moreover, studies suggest that the sensitivity of CTPA for detecting CTEPH depends on the experience of the readers and differs between non-specialist centres and high-expertise institutions [11]. Therefore, expertise in interpreting CTPA imaging results and improving the sensitivity of CTEPH detection with CTPA is crucial because it could reduce the need for additional diagnostic tests, accelerate diagnosis, and improve therapeutic outcomes.

The CTPA imaging features in patients with CTEPH have been described in several previous reviews [4,6,8,9,12,13]. However, there are currently few publications investigating the frequencies of CTEPH-related signs and abnormalities on CTPA, as well as their predictive value [3,14,15].

The aims of our study are as follows: firstly, to assess the frequency of characteristic radiological features in CTEPH, categorised as signs of chronic pulmonary embolism (PE), pulmonary hypertension, and right heart overload; and secondly, to compare the prevalence of these features with other pulmonary vascular conditions, such as chronic thromboembolic disease (CTED), APE, and pulmonary arterial hypertension (PAH), which share many imaging similarities with CTEPH and must be considered in the differential diagnosis in clinical practice [2]. These conditions are frequently evaluated using CTPA as the first-line diagnostic test.

Finally, based on our findings, we aim to determine the sensitivity, specificity, and predictive value of these radiological features in diagnosing CTEPH. This approach could significantly contribute to achieving earlier and more accurate diagnoses of CTEPH.

To the best of our knowledge, this is one of the first studies to comprehensively evaluate the predictive value of radiological features in CTEPH compared with selected pulmonary vascular conditions.

Material and methods

The present study is a retrospective cross-sectional study, conducted at the referral centre of the Medical University of Warsaw. The local Bioethics Committee approved the study protocol (approval number: AKBE/290/2024). All investigations were carried out in accordance with the principles of the Helsinki Declaration. Informed consent from the patients was not required for this study.

Patients

Thirty-five patients with a diagnosis of CTEPH, established according to current guidelines [2], confirmed by right heart catheterisation (RHC) and a corresponding CTPA, were recruited for the study.

Three control groups were matched by age and sex to the CTEPH cohort with diagnoses made in accordance with current guidelines [2]. The first group ($n = 20$) included patients with CTED, while the second group ($n = 26$) comprised individuals with PAH.

For these groups, the most recent CTPA examination closest in time to the RHC was selected for the analysis. Relevant RHC data, including mean pulmonary arterial pressure (mPAP) and pulmonary vascular resistance (PVR), were extracted from medical records.

The third control group consisted of 36 consecutive patients with APE, diagnosed in accordance with current guidelines and undergoing CTPA.

CT protocols

Computed tomography scans were obtained using a 64-slice multidetector computed tomography (64-MDCT) scanner with electrocardiographic gating, with a slice thickness of 0.625 mm and rotation time of 0.5 sec. The injection protocol included administering 80 ml of a nonionic contrast agent (Iohexol, Omnipaque 350, GE Healthcare), followed by 100 ml of 0.9% NaCl solution. Automatic bolus tracking

was applied, with the ROI positioned at the level of the pulmonary trunk and the threshold for triggering data acquisition set at 100 HU. The whole chest was scanned during a single breath-hold.

Image analysis

The anonymised CTPA images were assessed by consensus statement of chest radiologists in a random order for the presence of CTEPH features, which were categorised into signs of chronic PE, signs of PH, and signs of right heart overload. Signs of chronic PE included vessel narrowing, intimal irregularities, bands, and webs (Figure 1), which were analysed at the central, lobar, and segmental levels; variability in the size of lobar and segmental arteries (Figure 2), defined by a vessel size ratio exceeding 1, determined by comparing segmental diameters of pulmonary arteries at corresponding levels in the right and left lobes; mosaic perfusion (Figure 3); complete vessel obstruction (Figure 4), analysed at the central, lobar, and

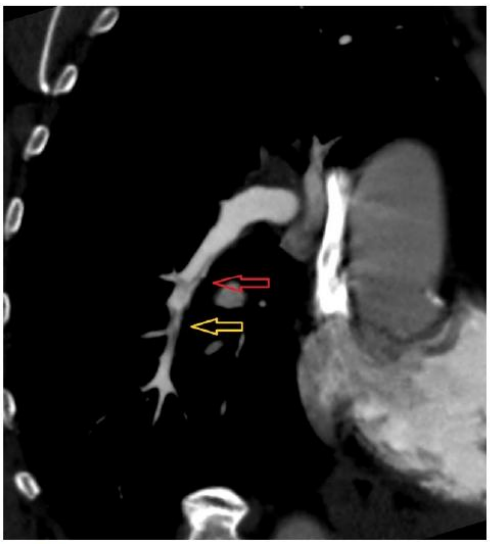


Figure 1. Electrocardiographically-gated computer tomography pulmonary angiography in a 65-year-old female patient diagnosed with chronic thromboembolic pulmonary hypertension. Multiplanar reconstruction view shows right lower lobe pulmonary artery with band-like filling defects (red arrow) and eccentric vessel narrowing (yellow arrow)

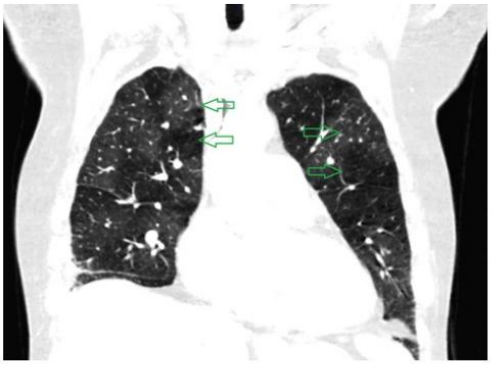


Figure 3. Electrocardiographically-gated computer tomography pulmonary angiography in a 67-year-old female patient diagnosed with chronic thromboembolic pulmonary hypertension. Multiplanar reconstruction coronal view shows areas of lower and higher lung attenuation (green arrows) corresponding to mosaic attenuation of the lung parenchyma

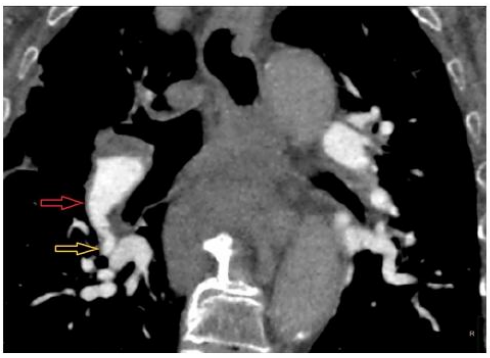


Figure 2. Electrocardiographically-gated computer tomography pulmonary angiography in a 57-year-old male patient diagnosed with chronic thromboembolic pulmonary hypertension. Multiplanar reconstruction coronal view shows prominent variability in the size of the right lower lobe (red arrow) and segmental-level artery (yellow arrow)

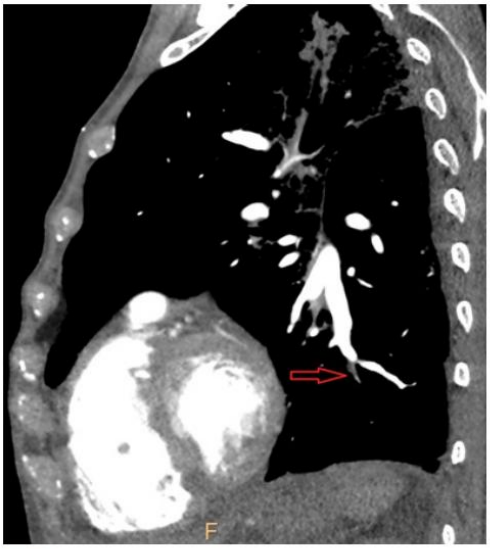


Figure 4. Electrocardiographically-gated computer tomography pulmonary angiography in a 69-year-old male patient diagnosed with chronic thromboembolic pulmonary hypertension. Multiplanar reconstruction sagittal view shows chronic occlusion of the left lower lobe basal segment artery with vessel retraction (red arrow)

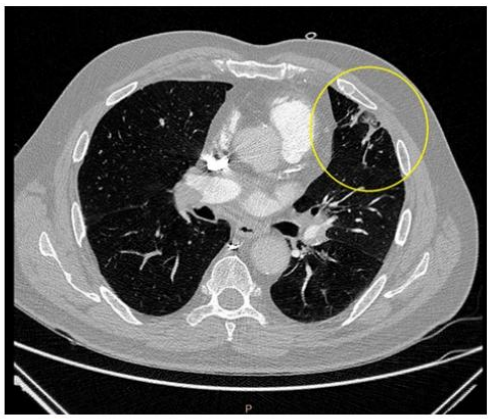


Figure 5. Electrocardiographically-gated computer tomography pulmonary angiography in a 62-year-old male patient diagnosed with chronic thromboembolic pulmonary hypertension. Pulmonary window axial view shows pulmonary scars and infarction on the periphery of the left upper lobe (yellow marking)

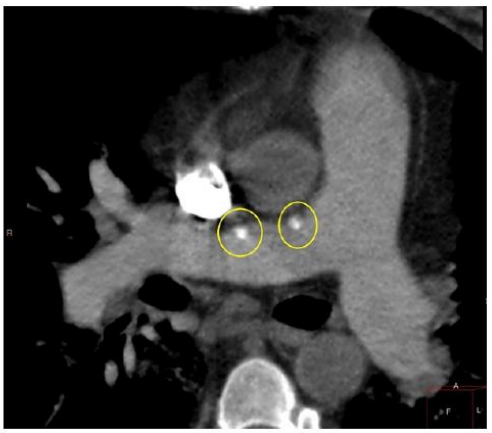


Figure 6. Computer tomography pulmonary angiography in a 57-year-old male patient diagnosed with chronic thromboembolic pulmonary hypertension. Axial plane view shows calcifications in the wall of the right pulmonary artery (yellow markings)

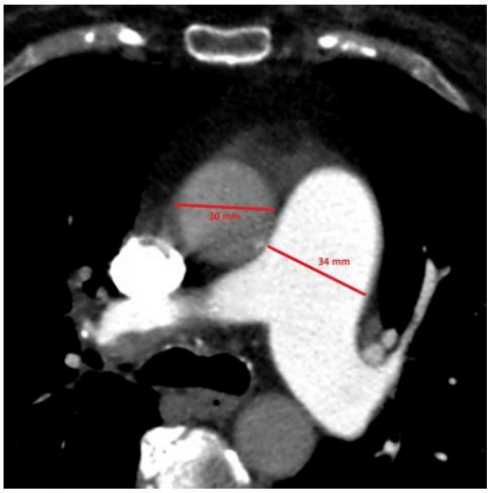


Figure 7. Electrocardiographically-gated computer tomography pulmonary angiography in a 55-year-old female patient diagnosed with chronic thromboembolic pulmonary hypertension. Axial plane view shows pulmonary trunk/aorta diameter index > 1. Dilated pulmonary trunk and left pulmonary artery

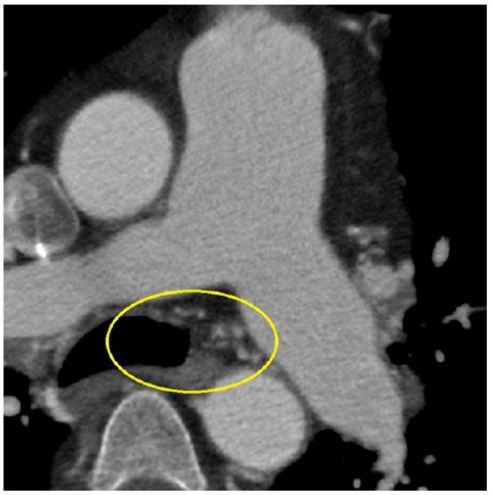


Figure 8. Electrocardiographically-gated computer tomography coronary arteries angiography in a 59-year-old female patient diagnosed with chronic thromboembolic pulmonary hypertension. Axial plane view shows dilated, tortuous right bronchial artery (yellow marking)

segmental levels; scars and pulmonary infarctions(Figure 5); and pulmonary artery calcifications (Figure 6). Signs of PH included a pulmonary trunk to aorta diameter ratio above 1 (PT/AO index > 1) (Figure 7); enlarged bronchial arteries (Figure 8), measured as a diameter > 2 mm; enlarged or calcified lymph nodes, measured as 10 mm or more in the short axis; and pericardial effusion or pericardial thickening, measured as > 4 mm. Signs of right heart overload included a right ventricular to left ventricular diameter ratio above 1 (RV/LV ratio > 1) (Figure 9); reflux of contrast material into the inferior vena cava or hepatic veins (Figure 10); flattening or bowing of the interventricular septum (Figure 9); and right ventricular wall hypertrophy (Figure 9), measured as free wall thickness > 5 mm.

Statistical analysis

Numeric variables are presented as mean ± standard deviation due to normal distributions. Categorical variables are presented as *n* (%). Distribution normality was assessed with the Shapiro-Wilk test, skewness, and kurtosis. Variance homogeneity was assessed with Levene's test.

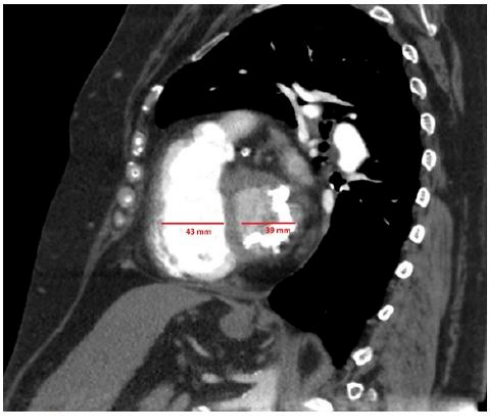


Figure 9. Electrocardiographically-gated computer tomography pulmonary angiography in a 73-year-old male patient diagnosed with chronic thromboembolic pulmonary hypertension. Multiplanar reconstruction 4-chamber sagittal view shows enlargement of the right ventricle with increased right ventricle/left ventricle ratio > 1; leftward flap of the interventricular septum

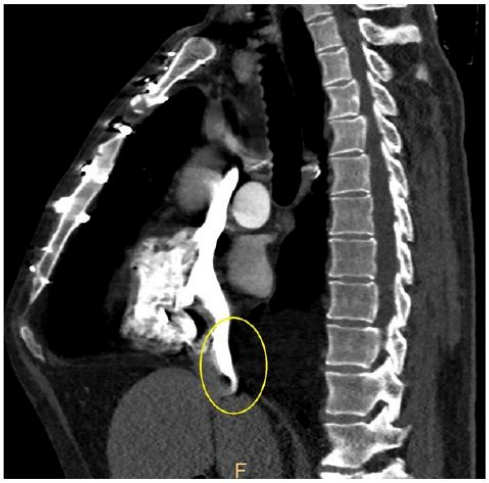


Figure 10. Electrocardiographically-gated computer tomography pulmonary angiography in a 61-year-old female patient diagnosed with chronic thromboembolic pulmonary hypertension. Multiplanar reconstruction sagittal view shows reflux of contrast to the inferior vena cava (yellow oval marking)

Comparisons of CTEPH group with other groups were performed with *t*-Student test, *t*-Welch test, Pearson's χ^2 test or Fisher's exact test, as appropriate. All *p*-values were further adjusted using Bonferroni correction to control for multiple comparisons. Predictive qualities of radiological parameters to classify patients between CTEPH and non-CTEPH were assessed with receiver operating characteristics (ROC) analysis. Area under the curve (AUC) was used as the primary measure of prognostic effectiveness, along with 95% confidence intervals (CI). High or very high effectiveness was considered if AUC > 0.8, moderate effectiveness was considered if AUC > 0.7. Positive likelihood ratio was calculated as sensitivity/(1-specificity). Negative likelihood ratio was calculated as (1-sensitivity)/specificity. All outcomes were considered significant if $p < 0.05$. Calculations were performed in R software (R 4.1.2).

Results

Demographics

In total, the study cohort comprised 115 patients, categorised into 4 groups: CTEPH (n = 35, 30.4%), CTED (n = 20, 17.4%), PAH (n = 24, 20.9%), and APE (n = 36, 31.3%). Table 1 provides an overview of the demographic characteristics for each group. No significant differences in age or sex distribution were observed across the groups. Right heart catheterisation was performed in all patients except those in the APE group. Patients with CTEPH demonstrated significantly elevated mPAP and PVR compared to those with CTED (mPAP: 38.00 ± 12.25 mmHg

Table 1. Comparison of demographic characteristics and catheterisation parameters between analysed groups

Variable	CTEPH (n = 35, 30.4%) Statistic	CTEPD (n = 20, 17.4%)		PAH (n = 24, 20.9%)		APE (n = 36, 31.3%)	
		Statistic	p_1	Statistic	p_2	Statistic	p_3
Age (years)	63.23 ± 15.99	64.12 ± 16.17	> 0.999	69.29 ± 11.98	0.602	71.44 ± 16.78	0.192
Sex, female	17 (48.6)	10 (50.0)	> 0.999	17 (70.8)	0.761	19 (52.8)	> 0.999
Catheterisation	35 (100.0)	20 (100.0)	> 0.999	24 (100.0)	0.999	0 (0.0)	< 0.001
mPAP (mmHg)	38.00 ± 12.25	16.91 ± 1.92	< 0.001	36.92 ± 10.13	> 0.999	–	–
PVR (WU)	5.13 ± 2.91	1.81 ± 0.63	0.001	6.67 ± 3.70	0.746	–	–

Data presented with mean ± standard deviation for continuous variables and n (%) for categorical variables.
CTEPH – chronic thromboembolic pulmonary hypertension, CTEPD – chronic thromboembolic pulmonary disease, PAH - pulmonary arterial hypertension, APE – acute pulmonary embolism, mPAP – mean pulmonary artery pressure, PVR – pulmonary vascular resistance
p_1 – comparison between CTEPH and CTED group; p_2 – comparison between CTEPH and PAH group; p_3 – comparison between CTEPH and APE group. Comparisons performed with *t*-Student test or *t*-Welch test for continuous variables and Pearson's χ^2 test or Fisher's exact test for categorical variables, as appropriate. Bonferroni correction was used for all *p* values.

vs. 16.91 ± 1.92 mmHg, $p < 0.001$; PVR: 5.13 ± 2.91 WU vs. 1.81 ± 0.63 WU, $p = 0.001$).

Radiological features of chronic thromboembolic pulmonary hypertension

Table 2 and Figure 11 summarise the radiological findings in patients with CTEPH.

Radiological signs of chronic pulmonary embolism

Among signs of chronic PE, vessel narrowing, intimal irregularities, bands, and webs were observed in all 35 patients (100.0%), with localisation at the central level in 35 patients (100.0%), at the lobar level in 23 patients (65.7%), and at the segmental level in 14 patients (40.0%). Variability in the size of lobar and segmental arteries was found

Table 2. Radiological findings in patients with chronic thromboembolic pulmonary hypertension (CTEPH) ($N = 35$)

Variable	Patients with CTEPH, *n* (%)
Vessel narrowing, intimal irregularities, bands, and webs	35 (100.0)
Segmental vessel narrowing, intimal irregularities, bands, and webs	35 (100.0)
RV/LV ratio ≥ 1	30 (85.7)
Variability in the size of lobar and segmental-level vessels	25 (71.4)
Lobar vessel narrowing, intimal irregularities, bands, and webs	23 (65.7)
Reflux of contrast to VCI	20 (57.1)
Pulmonary trunk/aorta index ≥ 1	19 (54.3)
Mosaic perfusion	19 (54.3)
Vessel occlusion	16 (45.7)
Pulmonary infarctions and scars	16 (45.7)
Flattening/flap of IV septum	15 (42.9)
Segmental vessel occlusion	14 (40.0)
Dilated bronchial arteries	13 (37.1)
Central vessel narrowing, intimal irregularities, bands, and webs	13 (37.1)
Enlarged/calcified mediastinal lymph nodes	10 (28.6)
Pericardial effusion /pericardial thickening	7 (20.0)
Pulmonary artery wall calcifications	6 (17.1)
RV wall hypertrophy	5 (14.3)
Lobar vessel occlusion	3 (8.6)
Central vessel occlusion	2 (5.7)

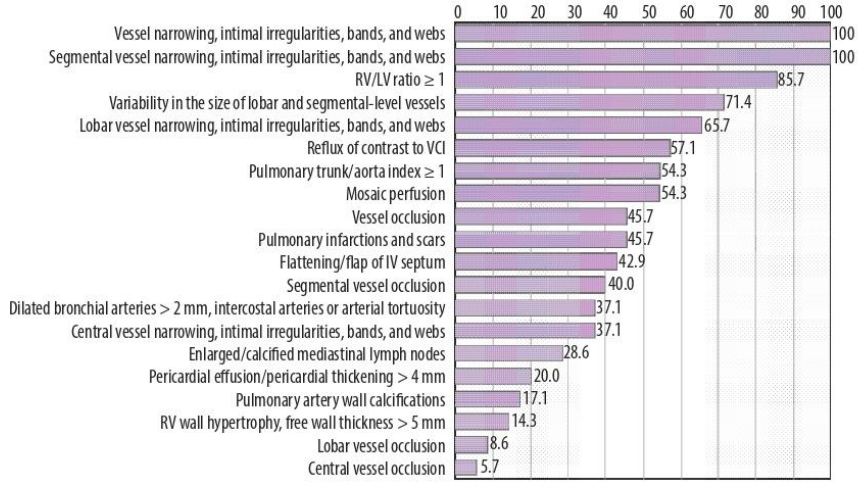


Figure 11. Incidence of radiological traits among patients with chronic thromboembolic pulmonary hypertension (%)

in 25 patients (71.4%). Mosaic perfusion was identified in 19 patients (54.3%). Complete vessel obstruction was documented in 16 patients (45.7%), including 2 patients (5.7%) at the central level, 3 patients (8.6%) at the lobar level, and 14 patients (40.0%) at the segmental level. Scars and pulmonary infarctions were seen in 16 patients (45.7%), while pulmonary artery calcifications were noted in 6 patients (17.1%).

Radiological signs of pulmonary hypertension

Indicators of pulmonary hypertension included a pulmonary trunk to aortic (PT/AO) ratio > 1 in 19 patients (54.3%). Dilated bronchial arteries were found in 13 patients (37.1%). Enlarged or calcified mediastinal lymph nodes were observed in 10 patients (28.6%). Pericardial effusion or pericardial thickening was identified in 7 patients (20.0%).

Radiological signs of right heart failure

Markers of right heart failure included an RV/LV ratio ≥ 1 in 30 patients (85.7%). Reflux of contrast material into the inferior vena cava or hepatic veins was present in 20 patients (57.1%). Flattening or bowing of the interventricular septum was observed in 15 patients (42.9%), and right ventricular wall hypertrophy was noted in 5 patients (14.3%).

Comparison of the occurrence of radiological features between the groups

Table 3 presents a comparison of the frequency of radiological features between the groups.

Comparison of radiological features between CTEPH and CTED

Pulmonary trunk to aorta index ≥ 1 was significantly more frequent in CTEPH compared to CTED (54.3% vs. 10.0%, $p = 0.015$). Flattening or bowing of the interventricular septum was also observed more often in CTEPH (42.9% vs. 5.0%, $p = 0.038$). Segmental vessel narrowing, intimal irregularities, bands, and webs occurred in 100.0% of CTEPH cases and 75.0% of CTED cases, with a significant difference ($p = 0.022$). Variability in the size of lobar and segmental

Table 3. Comparison of the frequency of radiological features between the groups

Variable	CTEPH	CTED		PAH		APE	
	Statistics	Statistics	*p*	Statistics	*p*	Statistics	*p*
Pulmonary trunk/aorta index ≥ 1	19 (54.3)	2 (10.0)	0.015	10 (41.7)	> 0.999	4 (11.1)	0.001
Dilated bronchial arteries > 2 mm, intercostal arteries or arterial tortuosity	13 (37.1)	2 (10.0)	0.315	1 (4.2)	0.045	1 (2.8)	0.004
Enlarged/calcified mediastinal lymph nodes	10 (28.6)	1 (5.0)	0.210	11 (45.8)	> 0.999	2 (5.6)	0.116
Pericardial effusion/pericardial thickening > 4 mm	7 (20.0)	1 (5.0)	> 0.999	4 (16.7)	> 0.999	3 (8.3)	> 0.999
Flattening/flap of IV septum	15 (42.9)	1 (5.0)	0.038	9 (37.5)	> 0.999	5 (13.9)	0.072
RV/LV ratio ≥ 1	30 (85.7)	11 (55.0)	0.141	18 (75.0)	> 0.999	17 (47.2)	0.007
RV wall hypertrophy, free wall thickness > 5 mm	5 (14.3)	0 (0.0)	0.733	4 (16.7)	> 0.999	0 (0.0)	0.125
Reflux of contrast to VCI	20 (57.1)	11 (55.0)	> 0.999	17 (70.8)	> 0.999	17 (47.2)	> 0.999
Vessel occlusion	16 (45.7)	6 (30.0)	> 0.999	0 (0.0)	0.002	36 (100.0)	< 0.001
Central vessel occlusion	2 (5.7)	1 (5.0)	> 0.999	0 (0.0)	> 0.999	10 (27.8)	0.153
Lobar vessel occlusion	3 (8.6)	1 (5.0)	> 0.999	0 (0.0)	> 0.999	21 (58.3)	< 0.001
Segmental vessel occlusion	14 (40.0)	4 (20.0)	> 0.999	0 (0.0)	0.006	36 (100.0)	< 0.001
Pulmonary arteries wall calcifications	6 (17.1)	1 (5.0)	> 0.999	0 (0.0)	0.360	0 (0.0)	0.057
Vessel narrowing, intimal irregularities, bands, and webs	35 (100.0)	17 (85.0)	0.217	0 (0.0)	< 0.001	0 (0.0)	< 0.001
Central vessel narrowing, intimal irregularities, bands, and webs	13 (37.1)	1 (5.0)	0.104	0 (0.0)	0.011	0 (0.0)	0.001
Lobar vessel narrowing, intimal irregularities, bands, and webs	23 (65.7)	7 (35.0)	0.275	0 (0.0)	< 0.001	0 (0.0)	< 0.001
Segmental vessel narrowing, intimal irregularities, bands, and webs	35 (100.0)	15 (75.0)	0.022	0 (0.0)	< 0.001	0 (0.0)	< 0.001
Variability in the size of lobar and segmental-level vessels	25 (71.4)	6 (30.0)	0.035	3 (12.5)	< 0.001	2 (5.6)	< 0.001
Mosaic perfusion	19 (54.3)	1 (5.0)	0.004	0 (0.0)	< 0.001	4 (11.1)	0.001
Scars and pulmonary infarctions	16 (45.7)	6 (30.0)	> 0.999	4 (16.7)	0.209	11 (30.6)	> 0.999

Data presented with *n* (%). *p* – comparison between CTEPH and respective control group. Comparisons performed with Pearson's χ^2 test or Fisher's exact test, as appropriate. Bonferroni correction was used for all *p*-values.

vessels was more frequent in CTEPH (71.4% vs. 30.0%, $p = 0.035$). Mosaic perfusion was observed more frequently in CTEPH than in CTED (54.3% vs. 5.0%, $p = 0.004$).

Comparison of radiological features between CTEPH and PAH

Dilated bronchial arteries were more common in CTEPH than in PAH (37.1% vs. 4.2%, $p = 0.045$). Both general and segmental vessel occlusions were observed exclusively in CTEPH (45.7% and 40.0%, respectively) and were absent in PAH, with significant differences ($p = 0.002$ and $p = 0.006$). Vessel narrowing, intimal irregularities, bands, and webs were universally present in CTEPH but absent in PAH, with significant differences ($p < 0.001$ for general, lobar, and segmental locations; $p = 0.011$ for central). Variability in the size of lobar and segmental vessels was significantly more frequent in CTEPH (71.4% vs. 12.5%, $p < 0.001$). Mosaic perfusion was exclusive to CTEPH (54.3%, $p < 0.001$).

Comparison of radiological features between CTEPH and APE

The PT/AO index ≥ 1 was more frequent in CTEPH compared to APE (54.3% vs. 11.1%, $p = 0.001$). Dilated bronchial arteries were also more common in CTEPH (37.1% vs. 2.8%, $p = 0.004$). RV/LV ratio ≥ 1 was significantly more frequent in CTEPH (85.7% vs. 47.2%, $p = 0.007$). General, lobar, and segmental vessel occlusions were significantly less frequent in CTEPH than in APE (45.7% vs. 100.0%, 8.6% vs. 58.3%, and 40.0% vs. 100.0%, respectively; $p < 0.001$ for all). Vessel narrowing, intimal irregularities, bands, and webs occurred universally in CTEPH but were absent in APE, with significant differences ($p \leq 0.001$). Variability in the size of lobar and segmental vessels was significantly more frequent in CTEPH (71.4% vs. 5.6%, $p < 0.001$). Mosaic perfusion was significantly more frequent in CTEPH (54.3% vs. 11.1%, $p = 0.001$).

Table 4. Radiological parameters as diagnostic tests for chronic thromboembolic pulmonary hypertension (CTEPH) vs. non-CTEPH

Variable	AUC (95% CI)	Sensitivity	Specificity	PPV	NPV	Accuracy	LR+	LR–	*p*
Segmental vessel narrowing, intimal irregularities, bands, and webs	0.906 (0.863-0.950)	1.00	0.81	0.70	1.00	0.87	5.26	0.00	< 0.001
Vessel narrowing, intimal irregularities, bands, and webs	0.894 (0.850-0.938)	1.00	0.79	0.67	1.00	0.85	4.76	0.00	< 0.001
Variability in the size of lobar and segmental-level vessels	0.788 (0.703-0.871)	0.71	0.86	0.69	0.87	0.82	05.07	0.34	< 0.001
Lobar vessel narrowing, intimal irregularities, bands, and webs	0.785 (0.699-0.864)	0.66	0.91	0.77	0.86	0.83	7.33	0.37	< 0.001
Mosaic perfusion	0.740 (0.654-0.824)	0.54	0.94	0.79	0.82	0.82	9.00	0.49	< 0.001
Central vessel narrowing, intimal irregularities, bands, and webs	0.679 (0.600-0.759)	0.37	0.99	0.93	0.78	0.80	37.00	0.64	< 0.001
Pulmonary trunk/aorta index ≥ 1	0.671 (0.575-0.762)	0.54	0.80	0.54	0.80	0.72	2.70	0.58	< 0.001
Dilated bronchial arteries	0.661 (0.580-0.746)	0.37	0.95	0.76	0.78	0.77	7.40	0.66	< 0.001
RV/LV ratio ≥ 1	0.641 (0.559-0.720)	0.86	0.42	0.39	0.87	0.56	1.48	0.33	0.002
Flattening/flap of IV septum	0.621 (0.526-0.715)	0.43	0.81	0.50	0.76	0.70	2.26	0.70	0.008
Pulmonary infarctions and scars	0.597 (0.499-0.689)	0.46	0.74	0.43	0.76	0.65	1.77	0.73	0.043
Paa wall calcifications	0.579 (0.518-0.645)	0.17	0.99	0.86	0.73	0.74	17.00	0.84	0.002
Enlarged/calcified mediastinal lymph nodes	0.555 (0.471-0.637)	0.29	0.82	0.42	0.73	0.66	1.61	0.87	0.188
Pericardial effusion/pericardial thickening	0.550 (0.479-0.626)	0.20	0.90	0.47	0.72	0.69	2.00	0.89	0.156
Segmental vessel occlusion	0.550 (0.451-0.646)	0.60	0.50	0.34	0.74	0.53	1.20	0.80	0.321
RV wall hypertrophy	0.546 (0.491-0.610)	0.14	0.95	0.56	0.72	0.70	2.80	0.91	0.103
Vessel occlusion	0.534 (0.433-0.632)	0.54	0.52	0.33	0.72	0.53	1.13	0.88	0.503
Dilated pulmonary trunk > 29 mm	0.528 (0.428-0.627)	0.54	0.51	0.33	0.72	0.52	1.10	0.90	0.585
Reflux of contrast to VCI	0.504 (0.408-0.605)	0.57	0.44	0.31	0.70	0.48	01.02	0.98	0.929
Central vessel occlusion*	–	–	–	–	–	–	–	–	–
Lobar vessel occlusion*	–	–	–	–	–	–	–	–	–

p – significance of difference between AUC for given parameters and AUC = 0.5 (equal to random classifier).
*AUC < 0.5.
AUC – area under curve, CI – confidence interval, LR+ – positive likelihood ratio, LR– – negative likelihood ratio, NPV – negative predictive value, PPV – positive predictive value

Radiological parameters as diagnostic tests for CTEPH vs. non-CTEPH conditions

Table 4 summarizes the predictive value of radiological features in ROC analysis, expressed as AUC, sensitivity, specificity, accuracy, PPV, and NPV.

Segmental and general vessel narrowing, intimal irregularities, bands, and webs demonstrated high prognostic properties for predicting CTEPH, with AUC values of 0.906 (95% CI: 0.863-0.950, $p < 0.001$) and 0.894 (95% CI: 0.850-0.938, $p < 0.001$), respectively (Figure 12). Moderate predictive value was observed for variability in the size of lobar and segmental vessels, lobar vessel narrowing, intimal irregularities, bands, and webs, as well as mosaic perfusion. These features showed AUC values of 0.788 (95% CI: 0.703-0.871, $p < 0.001$), 0.785 (95% CI: 0.699-0.864, $p < 0.001$), and 0.740 (95% CI: 0.654-0.824, $p < 0.001$), respectively (Figure 13). Other radiological parameters had either lower prognostic properties (AUC < 0.7) or yielded insignificant outcomes ($p > 0.05$).

The highest sensitivity was observed for segmental and general vessel narrowing, intimal irregularities, bands, and webs (1.00 for both) and for RV/LV ratio ≥ 1 (0.86). High specificity (> 0.90) was noted for central vessel narrowing, intimal irregularities, bands, and webs (0.99); pulmonary artery wall calcifications (0.99); dilated bronchial arteries, intercostal arteries, or arterial tortuosity (0.95); mosaic perfusion (0.94); and lobar vessel narrowing, intimal irregularities, bands, and webs (0.91).

Discussion

This retrospective study provides a comprehensive analysis of the frequency and diagnostic utility of CTPA signs in patients with documented CTEPH, compared with groups with confirmed CTED, APE, and PAH. By evaluating the sensitivity, specificity, and predictive value of these signs through ROC analysis, our findings highlight key imaging characteristics that may aid in differentiating CTEPH from other pulmonary vascular disorders.

The results of our study showed that the most common radiologic features, observed in all patients (100%) with CTEPH, were vessel narrowing, intimal irregularities, bands, and webs. These findings were most frequently located at the segmental level (100% of patients), where they were significantly less common in CTED, PAH, and APE, demonstrating the highest prognostic value in the ROC analysis for distinguishing CTEPH from these non-CTEPH conditions, with an AUC of 0.906. These features were less frequently observed at the lobar level (65.7%) and were rarest at the central level (37.1%), where they did not differ statistically from CTED. At the lobar and central levels, these features demonstrated moderate (AUC of 0.785) and low (AUC of 0.679) prognostic value in the ROC analysis, respectively. These findings align with the chronic nature of CTEPH, which results from partial filling defects caused by organized thrombus or recanalization within a large thrombus [9]. Our findings are consistent with those of Fathala *et al.* [3], who reported that

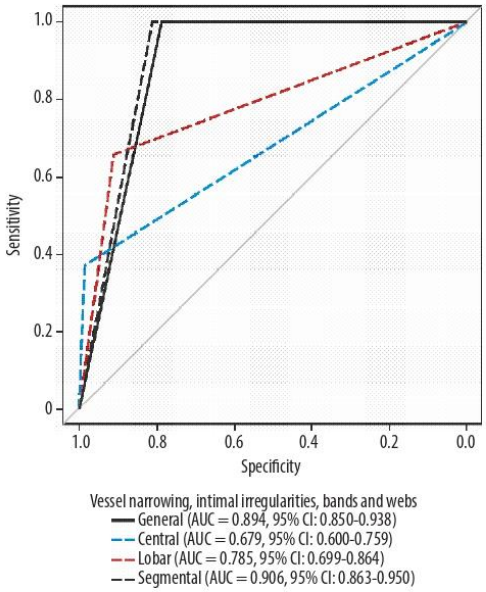


Figure 12. ROC curve of vessel narrowing, intimal irregularities, bands, and webs by location as predictors of chronic thromboembolic pulmonary hypertension

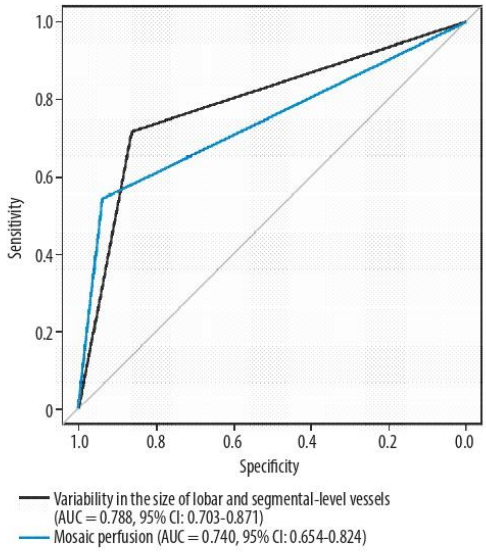


Figure 13. ROC curve of variability in the size of lobar and segmental-level vessels and mosaic perfusion as predictors of chronic thromboembolic pulmonary hypertension

the most frequent CTPA findings in central pulmonary arteries and peripheral arteries were thrombotic material and abnormal vessel narrowing. Additionally, our results confirm the observations by Grosse *et al.* [14], whose study identified direct vascular signs of chronic PE – including abrupt vessel cutoffs, wall-adherent thrombi, intraluminal webs or bands, stenoses, and wall irregularities – as significantly more common in patients with CTEPH than in those with non-thromboembolic PH. These features were critical for differentiating CTEPH from other causes of PH. Moreover, the InShape III study, which evaluated the diagnostic accuracy of dedicated CTPA readings in cases of suspected acute PE, demonstrated that the presence of intravascular webs serves as an independent predictor for a future diagnosis of CTEPH [16]. In our study, these signs were most frequently observed at the segmental and lobar levels, consistent with previous findings [8,17]. Identifying changes, particularly at the segmental level, is crucial for accurate pre-operative classification because this enables optimal surgical planning. Misdiagnosis in such cases can lead to challenging post-operative management due to residual PH [18].

A moderate prognostic ratio was established for variability in the size of lobar and segmental arteries and mosaic perfusion (AUC of 0.789 and 0.740, respectively) for predicting CTEPH. Both features were also significantly less common in the CTED, PAH, and APE groups. Although variability in the size of lobar and segmental arteries was observed more frequently (71.4) than mosaic perfusion (54.3) in patients with CTEPH, the latter had higher specificity (0.94 vs. 0.86). Both of these radiological features are indirect signs of chronic thromboembolism and serve as useful indicators for identifying the locations of direct vascular abnormalities [12] reflecting an irregular distribution of emboli within the pulmonary lobes [14] or indicating regional hypoperfusion [19]. Our findings point to similar conclusions as previous studies that highlighted the importance of these radiological features in differentiating CTEPH from other conditions. In the study by Capone *et al.* [15], mosaic attenuation was significantly less common in patients with CTED compared to those with CTEPH. Furthermore, patients with CTED exhibited significantly smaller perfusion defect extents on iodine maps, which, as the authors suggested, strongly indicates that the absence of peripheral disease (i.e. small vessel remodeling) may explain the lack of pulmonary hypertension in CTED patients compared to those with CTEPH. Moreover, similarly to the studies by Bergin *et al.* [20] and Grosse *et al.* [14], our study demonstrates equivalent results confirming that the combination of segmental vessel size variability and mosaic perfusion are highly specific for CTEPH [20] and occur at significantly higher frequencies in patients with CTEPH than in those with PAH and other forms of non-thromboembolic PH [14].

Another radiological sign demonstrating moderate diagnostic accuracy in our study was enlarged bronchial arteries, which were observed in 37.1% of patients with CTEPH, whereas they were significantly less frequent in patients with CTED, PAH, and APE, with a high specificity of 95% and an AUC of 0.661 (95% CI: 0.580-0.746). Bronchial arterial flow increases in response to chronic obstruction of the pulmonary arteries, compensating reduced pulmonary artery circulation [8]. Normally, bronchial arterial blood flow constitutes approximately 1-2% of cardiac output and primarily serves a nutritional function. However, in patients with CTEPH, bronchial arterial flow can account for up to 30% of systemic blood flow and contributes to oxygenation [21,22]. Although dilated bronchial arteries are not specific to CTEPH and can also occur in other forms of pulmonary hypertension [16], our findings showed a higher frequency of abnormally enlarged bronchial arteries in CTEPH compared with PAH, leading to similar results as seen in previous studies. For example, in the study by Grosse *et al.* [14], 69% of patients with CTEPH and 21% of those with PAH had enlarged bronchial arteries; moreover, the study by Remy-Jardin *et al.* [23] demonstrated a higher prevalence of abnormally enlarged bronchial arteries, as well as non-bronchial systemic arteries, in patients with CTEPH compared with those with primary pulmonary hypertension. Furthermore, unilateral or bilateral bronchial dilation without bronchial wall thickening was identified as the most specific finding to distinguish CTEPH from non-thromboembolic pulmonary hypertension, with a specificity of 97.1%.

Complete vessel obstruction was observed in 45.7% of CTEPH cases, predominantly at the segmental level (40%), and significantly less frequently at the lobar (8.6%) and central (5.7%) levels. Although this sign was absent in PAH, it is common in both CTEPH and APE, showing moderate specificity (50%) and limited effectiveness (AUC 0.550) as an isolated predictor of CTEPH. However, it gains diagnostic value when evaluated alongside other radiologic signs. A key distinguishing feature is the shape of the obstruction. In APE, complete obstruction typically shows a concave contour within the contrast material due to the trailing edge of the thrombus. Conversely, chronic PE (as seen in CTEPH) is characterised by a convex margin relative to the contrast material, creating a 'pouch' defect. This difference arises from thrombus contraction in chronic PE. Additionally, a decrease in the diameter of the vessel distal to the complete obstruction is often visible on CTPA [24,25]. Our findings align with those of Capone *et al.* [15], who demonstrated that the vascular obstruction burden in CTED was similar to that in CTEPH. However, unlike our study, Capone *et al.* reported that proximal arterial obstruction was more frequently observed in CTED patients compared to those with CTEPH. This discrepancy warrants further investigation to better understand its implications.

Signs of right heart overload are commonly observed in CTEPH, resulting from increased pulmonary artery

pressure [8,9]. In our study, cardiac radiological signs – including RV/LV ratio > 1, septal flattening, contrast reflux into the inferior vena cava, and RV hypertrophy – demonstrated low predictive value in ROC analysis, with AUC values of 0.641, 0.621, 0.504, and 0.546, respectively. These findings reflect the general manifestation of elevated right ventricular afterload rather than disease specificity [8]. The most frequent cardiac sign, and the second most common feature identified in CTEPH cases, was an RV/LV ratio > 1 (observed in 85.7%), indicative of right heart chamber enlargement. This feature is a marker of advanced disease and is suggestive of CTEPH [3,26]. Our results overlap with those of Fathala's study, which also identified an RV/LV ratio > 1 as the most common cardiac feature (69%) in patients with CTEPH [2]. Although not exclusive to CTEPH, this feature – when combined with evidence of right ventricular hypertrophy (14.3%) and septal flattening (42.9%) – enhances the diagnostic specificity of CTEPH, aiding in its differentiation from CTED [15]. Despite the fact that in cases of APE, CTPA signs of right ventricular overload are frequently present [24], these findings in some cases may indicate that CTEPH was already present at the time of the initial PE diagnosis and remained unrecognised due to a lack of targeted evaluation. Which supports the concept of an "acute-on-chronic" diagnosis [16]. Furthermore, these parameters may serve as potential indicators of an increased risk of developing CTEPH in the future, emphasising the need for careful follow-up in such patients [16].

Pulmonary scars and infarctions, detected in 45.7% of CTEPH cases, were less common across CTED (30.0%; $p > 0.999$), PAH (16.7%; $p = 0.209$), and APE (26.2%; $p = 0.330$), but these differences were not statistically significant. Although less specific than other features, and demonstrating low predictive value (AUC = 0.597), these findings likely reflect a history of prior pulmonary ischaemic events, consistent with the chronic nature of CTEPH [8]. Pulmonary scars are commonly found in areas of reduced lung attenuation. They are typically multiple, predominantly located in the lower lung lobes, and often associated with pleural thickening [23].

Pulmonary artery calcifications are a rare finding associated with chronic organising thrombi [27]. We obtained got similar results in our study, where calcifications were observed only in 17.1% of CTEPH cases and 5% of CTED cases, and they were absent in the APE and PAH groups. Although their presence markedly enhances diagnostic specificity (specificity in CTEPH of 99%), indicating a chronic embolic process, they do not allow differentiation between CTEPH and CTED, resulting in a low predictive value (AUC = 0.579).

Pulmonary trunk enlargement and PT/AO diameter ratio > 1 were present in 54.3% of CTEPH cases. While these features serve as general markers of pulmonary hypertension [19], they lacked specificity for CTEPH, with AUC values of 0.528 and 0.671, respectively. However, the higher prevalence of the PT/AO ratio in CTEPH compared to APE (11.1%) and CTED (10%) may aid in differential diagnosis, particularly when other CTEPH-specific changes are identified. Additionally, central pulmonary arteries in patients with CTEPH are often asymmetric in size, in contrast to the symmetric pulmonary artery enlargement observed in non-thromboembolic pulmonary artery hypertension [25,28].

Other features, such as enlarged or calcified mediastinal lymph nodes (28.6% of CTEPH cases) and pericardial effusion or thickening (20%) showed no significant differences compared to CTED, PH, and APE. Individually, these features demonstrated lower specificity, with AUC values of 0.555 and 0.550, respectively. However, the presence of pericardial effusion may indicate severe pulmonary hypertension [29] and is associated with a worse prognosis [30].

Conclusions

Our retrospective study showed the utility of CTPA as a comprehensive diagnostic tool for identifying CTEPH and differentiating it from other conditions affecting pulmonary arteries. Among the most significant findings observed in patients with CTEPH were vessel narrowing, intimal irregularities, bands, and webs demonstrating the highest predictive value for CTEPH, particularly at the segmental level. Variability in the size of lobar and segmental arteries, mosaic perfusion, and complete vessel obstruction also exhibited moderate predictive value. Notably, no single finding provided 100% predictive value, underscoring the importance of a multifaceted approach to diagnosis. Radiologists must be familiar with this limitation and recognise that the most reliable way to diagnose CTEPH is by integrating multiple vascular, parenchymal, and cardiac findings.

Disclosures

1. Institutional review board statement: The study was approved by the Bioethics Committee. Approval number: AKBE/290/2024.
2. Assistance with the article: None.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

References

1. Ruaro B, Baratella E, Caforio G, Confalonieri P, Wade B, Marrocchio C, et al. Chronic thromboembolic pulmonary hypertension: an update. Diagnostics (Basel) 2022; 12: 235. DOI: 10.3390/diagnostics12020235.
2. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, et al.; ESC/ERS Scientific Document Group. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Respir J 2023; 61: 2200879. DOI: 10.1183/13993003.00879-2022.
3. Fathala A, Aldurabi A. Frequency of computed tomography abnormalities in patients with chronic thromboembolic pulmonary hypertension: a comparative study between lung perfusion scan and computed tomography pulmonary angiography. Multidiscip Respir Med 2021; 16: 753. DOI: 10.4081/mrm.2021.753.
4. Gopalan D, Delcroix M, Held M. Diagnosis of chronic thromboembolic pulmonary hypertension. Eur Respir Rev 2017; 26: 160108. DOI: 10.1183/16000617.0108-2016.
5. Zhang Y, Yu X, Jin Q, Luo Q, Zhao Z, Zhao Q, et al. Advances in targeted therapy for chronic thromboembolic pulmonary hypertension. Heart Fail Rev 2019; 24: 949-965.
6. Gopalan D, Blanchard D, Auger WR. Diagnostic evaluation of chronic thromboembolic pulmonary hypertension. Ann Am Thorac Soc 2016; 13 Suppl 3: S222-S239. DOI: 10.1513/AnnalsATS.201509-623AS.
7. Ciurzyński M, Kurzyna M, Kopeć G, Błaszczak P, Chrzanowski Ł, Kamiński K, et al. An expert opinion of the Polish Cardiac Society Working Group on Pulmonary Circulation on screening for chronic thromboembolic pulmonary hypertension patients after acute pulmonary embolism: update. Kardiol Pol 2022; 80: 723-732.
8. Castañer E, Gallardo X, Ballesteros E, Andreu M, Pallardó Y, Mata JM, et al. CT diagnosis of chronic pulmonary thromboembolism. Radiographics 2009; 29: 31-50; discussion 50-53.
9. Willemink MJ, van Es HW, Koobs L, Morshuis WJ, Snijder RJ, van Heesewijk JP. CT evaluation of chronic thromboembolic pulmonary hypertension. Clin Radiol 2012; 67: 277-285.
10. Nishiyama KH, Saboo SS, Tanabe Y, Jasinowodolinski D, Landay MJ, Kay FU. Chronic pulmonary embolism: diagnosis. Cardiovasc Diagn Ther 2018; 8: 253-271.
11. Rogberg AN, Gopalan D, Westerlund E, Lindholm P. Do radiologists detect chronic thromboembolic disease on computed tomography? Acta Radiol 2019; 60: 1576-1583.
12. Wittram C, Kalra MK, Maher MM, Greenfield A, McLoud TC, Shepard JA. Acute and chronic pulmonary emboli: angiography-CT correlation. AJR Am J Roentgenol 2006; 186 (6 Suppl 2): S421-S429. DOI: 10.2214/AJR.04.1955.
13. Lambert L, Michalek P, Burgetova A. The diagnostic performance of CT pulmonary angiography in the detection of chronic thromboembolic pulmonary hypertension-systematic review and meta-analysis. Eur Radiol 2022; 32: 7927-7935.
14. Grosse A, Grosse C, Lang IM. Distinguishing chronic thromboembolic pulmonary hypertension from other causes of pulmonary hypertension using CT. AJR Am J Roentgenol 2017; 209: 1228-1238.
15. Capone C, Valentini A, Spinillo SL, Klersy C, Celentano A, Pin M, et al. Radiological differences between chronic thromboembolic pulmonary disease (CTEPD) and chronic thromboembolic pulmonary hypertension (CTEPH). Eur Radiol 2021; 31: 6230-6238.
16. Ende-Verhaar YM, Meijboom LJ, Kroft LJM, Beenen LFM, Boon GJAM, Middeldorp S, et al. Usefulness of standard computed tomography pulmonary angiography performed for acute pulmonary embolism for identification of chronic thromboembolic pulmonary hypertension: results of the InShape III study. J Heart Lung Transplant 2019; 38: 731-738.
17. Auger WR, Fedullo PF, Moser KM, Buchbinder M, Peterson KL. Chronic major-vessel thromboembolic pulmonary artery obstruction: appearance at angiography. Radiology 1992; 182: 393-398.
18. McInnis MC, Wang D, Donahoe L, Granton J, Thenganatt J, Tan K, et al. Importance of computed tomography in defining segmental disease in chronic thromboembolic pulmonary hypertension. ERJ Open Res 2020; 6: 00461-2020. DOI: 10.1183/23120541.00461-2020.
19. King MA, Bergin CJ, Yeung DW, Belezzouli EE, Olson LK, Ashburn WL, et al. Chronic pulmonary thromboembolism: detection of regional hypoperfusion with CT. Radiology 1994; 191: 359-363.
20. Bergin CJ, Rios G, King MA, Belezzuoli E, Luna J, Auger WR. Accuracy of high-resolution CT in identifying chronic pulmonary thromboembolic disease. AJR Am J Roentgenol 1996; 166: 1371-1377.
21. Endrys J, Hayat N, Cherian G. Comparison of bronchopulmonary collaterals and collateral blood flow in patients with chronic thromboembolic and primary pulmonary hypertension. Heart 1997; 78: 171-176.
22. Ley S, Kreitner KF, Morgenstern I, Thelen M, Kauczor HU. Bronchopulmonary shunts in patients with chronic thromboembolic pulmonary hypertension: evaluation with helical CT and MR imaging. AJR Am J Roentgenol 2002; 179: 1209-1215.
23. Remy-Jardin M, Duhamel A, Deken V, Bouaziz N, Dumont P, Remy J. Systemic collateral supply in patients with chronic thromboembolic and primary pulmonary hypertension: assessment with multi-detector row helical CT angiography. Radiology 2005; 235: 274-281.
24. van der Bijl N, Klok FA, Huisman MV, van Rooden JK, Mertens BJA, de Roos A, et al. Measurement of right and left ventricular function by ECG-synchronized CT scanning in patients with acute pulmonary embolism: usefulness for predicting short-term outcome. Chest 2011; 140: 1008-1015.
25. Ng CS, Wells AU, Padley SP. A CT sign of chronic pulmonary arterial hypertension: the ratio of main pulmonary artery to aortic diameter. J Thorac Imaging 1999; 14: 270-278.
26. Chan AL, Juarez MM, Shelton DK, MacDonald T, Li CS, Lin TC, et al. Novel computed tomographic chest metrics to detect pulmonary hypertension. BMC Med Imaging 2011; 11: 7. DOI: 10.1186/1471-2342-11-7.
27. Cummings KW, Bhalla S. Multidetector computed tomographic pulmonary angiography: beyond acute pulmonary embolism. Radiol Clin North Am 2010; 48: 51-65.
28. King MA, Ysrael M, Bergin CJ. Chronic thromboembolic pulmonary hypertension: CT findings. AJR Am J Roentgenol 1998; 170: 955-960.
29. Baque-Juston MC, Wells AU, Hansell DM. Pericardial thickening or effusion in patients with pulmonary artery hypertension: a CT study. AJR Am J Roentgenol 1999; 172: 361-364.
30. Raymond RJ, Hinderliter AL, Willis PW, Ralph D, Caldwell EJ, Williams W, et al. Echocardiographic predictors of adverse outcomes in primary pulmonary hypertension. J Am Coll Cardiol 2002; 39: 1214-1219.

8. PODSUMOWANIE I WNIOSKI

W niniejszej pracy dokonano kompleksowego przeglądu aktualnych danych dotyczących zastosowania technik obrazowych w diagnostyce, leczeniu oraz monitorowaniu CTEPH. Analiza dostępnej literatury podkreśliła istotną rolę badania CTPA w praktyce klinicznej jako szeroko dostępnego, często wykonywanego i nieinwazyjnego narzędzia diagnostycznego, które umożliwia jednoczesną ocenę wielu parametrów morfologicznych, a także skuteczne różnicowanie CTEPH z innymi jednostkami chorobowymi. Charakteryzuje się wysoką czułością i swoistością, jednak nie pozwala na wykluczenie CTEPH. Jego skuteczność w dużym stopniu zależy od jakości i techniki badania oraz doświadczenia i kompetencji oceniającego radiologa.

W celu poprawy rozpoznawalności CTEPH oraz określenia wartości diagnostycznej wybranych cech radiologicznych w CTPA, przeprowadzono retrospektywne badanie obserwacyjne w wyspecjalizowanym ośrodku referencyjnym w Warszawie. Do analizy włączono 35 pacjentów z rozpoznanym CTEPH, potwierdzonym zgodnie z aktualnymi wytycznymi za RHC, u których wykonano również badanie CTPA.

W ramach badania przeprowadzono jakościową analizę obecności cech radiologicznych typowych dla CTEPH, sklasyfikowanych w trzech kategoriach:

1. Cechy przewlekłej zatorowości płucnej:
    - Zwężenie naczyń, nieregularności błony wewnętrznej oraz obecność pasm i przegród naczyniowych (bands and webs) – analizowane na poziomie centralnym, płatowym i segmentalnym.
    - Zmienność średnicy naczyń płatowych i segmentalnych.
    - Mozaikowa perfuzja miąższu płucnego.
    - Całkowita niedrożność naczynia.
    - Obecność zawałów i blizn płucnych.
    - Zwapnienia ścian tętnic płucnych.
2. Cechy nadciśnienia płucnego:
    - Stosunek średnicy pnia płucnego do aorty (PT/Ao) ≥ 1.
    - Poszerzenie naczyń oskrzelowych (średnica > 2 mm).
    - Powiększone lub zwapniałe węzły chłonne śródpiersia (≥ 10 mm w osi krótkiej).
    - Obecność płynu osierdziowego lub pogrubienie osierdzia (> 4 mm).
3. Cechy przeciążenia prawej komory serca:
    - Stosunek RV/LV ≥ 1.
    - Refluks środka kontrastowego do żyły głównej dolnej lub żył wątrobowych.
    - Spłaszczenie lub uwypuklenie przegrody międzdwóchykomorowej.

- Przerost ściany prawej komory (grubość > 5 mm).

Badania obrazowe przeprowadzono z wykorzystaniem 64-MDCT z bramkowaniem EKG, przy grubości warstwy 0,625 mm i czasie obrotu 0,5 sekundy. Obrazy CTPA oceniano anonimowo, w losowej kolejności, na podstawie konsensusu dwóch specjalistów radiologów. Każda cecha była oceniana jakościowo jako obecna lub nieobecna, zgodnie z wcześniej zdefiniowanymi kryteriami.
Oceniane cechy porównano z trzema grupami pacjentów: z CTED (n = 20), z PAH (n = 26) oraz z APE (n = 36). Diagnozy w każdej z grup kontrolnych ustalano zgodnie z obowiązującymi wytycznymi klinicznymi. W przypadku grupy CTEPH, CTED oraz PAH do analizy włączono te badania CTPA, które wykonano najbliżej czasowo w stosunku do RHC. Z dokumentacji medycznej pozyskano dane hemodynamiczne, w tym mPAP oraz PVR. Wszystkie grupy nie wykazywały istotnych różnic pod względem wieku i płci.
Na podstawie uzyskanych wyników przeprowadzono analizę statystyczną, obejmującą ocenę czułości, swoistości, wartości predykcyjnej dodatniej (PPV) i ujemnej (NPV), a także wartości prognostycznej badanych cech, wyrażonej jako pole pod krzywą ROC (AUC) wraz z 95% przedziałem ufności (CI).
W analizowanej grupie pacjentów z CTEPH najczęściej obserwowanymi zmianami były zwężenia naczyń, nieregularności błony wewnętrznej oraz pasma i przegrody naczyniowe, obecne u wszystkich badanych (100%). Zmiany te najczęściej występowały na poziomie segmentalnym, gdzie cechowały się najwyższą wartością diagnostyczną (AUC = 0,906). Na poziomie płatowym i centralnym skuteczność diagnostyczna była odpowiednio umiarkowana (AUC = 0,785) i niska (AUC = 0,679). Opisane zmiany są zgodne z przewlekłym charakterem CTEPH, wynikającym z obecności zorganizowanych skrzeplin lub rekanaalizacji w obrębie skrzeplin. Nasze wyniki są zgodne z wcześniejszymi doniesieniami, które również identyfikują te cechy jako najczęściej występujące oraz skuteczne w różnicowaniu CTEPH od innych typów nadciśnienia płucnego [64,65]. Ponadto, obecność tych zmian może mieć znaczenie prognostyczne dla rozwoju CTEPH po APE [66]. Identyfikacja tych zmian, szczególnie na poziomie segmentalnym, jest kluczowa dla dokładnej przedoperacyjnej klasyfikacji. Pominięcie takich zmian może skutkować utrzymywaniem się resztkowego nadciśnienia płucnego po operacji [67].
Umiarkowaną wartość predykcyjną wykazały również zmienność średnicy naczyń płatowych i segmentalnych (AUC = 0,788) oraz mozaikowy wzór perfuzji (AUC = 0,740), które istotnie częściej występowały w grupie pacjentów z CTEPH niż w grupach kontrolnych. Chociaż zmienność średnicy naczyń płatowych i segmentalnych była obserwowana częściej (71,4%) niż mozaikowy wzór perfuzji (54,3%) u pacjentów z CTEPH, to jednak mozaikowy wzór perfuzji charakteryzował się wyższą swoistością diagnostyczną (0,94 vs. 0,86). Obie te cechy radiologiczne są uznawane za pośrednie wskaźniki przewlekłej zatorowości płucnej i mogą być

pomocne w identyfikacji lokalizacji bezpośrednich nieprawidłowości naczyniowych, odzwierciedlając nieregularną dystrybucję zatorów w obrębie płatów płucnych lub wskazując na regionalną hipoperfuzję [65,68].

Całkowita niedrożność naczynia zaobserwowana została u 45,7% pacjentów z CTEPH, głównie na poziomie segmentalnym (40%), rzadziej na poziomie płatowym (8,6%) i centralnym (5,7%). Ze względu na obecność tego objawu zarówno w CTEPH, jak i APE, izolowana wartość diagnostyczna tego parametru była ograniczona (AUC = 0,550).

Zwapnienia tętnic płucnych, będące rzadkim objawem związanym z przewlekle organizującymi się skrzeplinami (AUC = 0,579), mimo wysokiej swoistości (99%), również nie osiągnęły istotnej wartości diagnostycznej, ponieważ nie pozwalają na skuteczne różnicowanie CTEPH od CTED.

Blizny i zawały płucne, mimo że stwierdzane u 45,7% pacjentów z CTEPH, wykazują ograniczoną wartość różnicującą (AUC = 0,597). Ich obecność była rzadsza w grupach CTED (30,0%), PAH (16,7%) oraz APE (26,2%), jednak różnice te nie osiągnęły istotności statystycznej. Zmiany te odzwierciedlają przebyty epizod niedokrwienia płucnego, zgodny z przewlekłym charakterem CTEPH.

Kolejną analizowaną grupą stanowiły wskaźniki przeciążenia prawej komory serca, takie jak stosunek RV/LV ≥ 1 (AUC = 0,641), spłaszczenie przegrody międzykomorowej (AUC = 0,621), refluks kontrastu do żyły głównej dolnej (AUC = 0,504) oraz przerost ściany prawej komory (AUC = 0,546). Pomimo stosunkowo częstego występowania, na przykład stosunku RV/LV ≥ 1 odnotowanego u 85,7% pacjentów z CTEPH, wskaźniki te cechowały się ograniczoną swoistością oraz niską wartością różnicującą. Ograniczona przydatność diagnostyczna tych parametrów wynika z ich niespecyficzności – są one obserwowane w różnych postaciach nadciśnienia płucnego, co odzwierciedla ogólne zwiększenie obciążenia następczego prawej komory.

Podobnie, wskaźniki sugerujące obecność nadciśnienia płucnego, takie jak stosunek średnicy pnia płucnego do aorty (PT/Ao ≥ 1; AUC = 0,671), powiększone węzły chłonne śródpiersia (AUC = 0,555) oraz obecność płynu osierdziowego (AUC = 0,550), wykazywały ograniczoną wartość diagnostyczną w różnicowaniu CTEPH od innych jednostek chorobowych. Choć zmiany te nie są specyficzne, ich obecność może wskazywać na zaawansowane stadium choroby oraz przewlekły charakter procesu patologicznego [69].

Wśród analizowanych cech na szczególną uwagę zasługuje poszerzenie naczyń oskrzelowych, które stwierdzono u 37,1% pacjentów z CTEPH. Pomimo umiarkowanej wartości diagnostycznej (AUC = 0,661), cecha ta charakteryzowała się wysoką swoistością (95%). Zmiany te występowały istotnie rzadziej w grupach kontrolnych – CTED, PAH i APE – co sugeruje ich większą przydatność diagnostyczną w kontekście CTEPH. Poszerzenie naczyń oskrzelowych interpretowane jest jako mechanizm kompensacyjny rozwijający się w odpowiedzi na przewlekłe

zamknięcie tętnic płucnych i towarzyszące mu zmniejszenie przepływu w krążeniu płucnym. Choć zmiany te mogą występować również w innych postaciach nadciśnienia płucnego, w przeprowadzonym badaniu obserwowano ich wyraźnie wyższą częstość w CTEPH w porównaniu z PAH. Zgodnie z doniesieniami literaturowymi, jednostronne lub obustronne poszerzenie naczyń oskrzelowych bez pogrubienia ich ścian zostało uznane za cechę o najwyższej swoistości w odróżnianiu CTEPH od niezakrzepowych postaci nadciśnienia płucnego, osiągając wartość swoistości na poziomie 97,1% [70] .

Na podstawie wyników badania można sformułować następujące wnioski:

1. CTPA jest skuteczną metodą diagnostyczną w rozpoznawaniu CTEPH i różnicowaniu jej z innymi chorobami naczyń płucnych.

2. Zwężenia naczyń, nieregularności ich błony wewnętrznej, pasma oraz przegrody naczyniowe to cechy o najwyższej wartości predykcyjnej dla CTEPH w CTPA (AUC = 0,906; 95% CI: 0,863–0,950).

3. Żadna pojedyncza cecha CTEPH nie ma stuprocentowej wartości diagnostycznej - zawsze konieczna jest wieloparametryczna analiza obrazów CTPA.

4. Znajomość zalet i ograniczeń współczesnych metod obrazowania zarówno o klinicystów jak i radiologów ma kluczowe znaczenie dla trafnej diagnozy, wyboru odpowiedniego leczenia i poprawy rokowania.

9. PIŚMIENNICTWO

1. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, Carlsen J, Coats AJS, Escribano-Subias P, Ferrari P, Ferreira DS, Ghofrani HA, Giannakoulas G, Kiely DG, Mayer E, Meszaros G, Nagavci B, Olsson KM, Pepke-Zaba J, Quint JK, Rådegran G, Simonneau G, Sitbon O, Tonia T, Toshner M, Vachiery JL, Vonk Noordegraaf A, Delcroix M, Rosenkranz S; ESC/ERS Scientific Document Group. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Respir J. 2023 Jan 6;61(1):2200879. doi: 10.1183/13993003.00879-2022. PMID: 36028254.
2. Ruaro B, Baratella E, Caforio G, et al. Chronic Thromboembolic Pulmonary Hypertension: An Update. Diagnostics (Basel). 2022 Jan 19;12(2):235. doi: 10.3390/diagnostics12020235. PMID: 35204326; PMCID: PMC8871284
3. Ende-Verhaar YM, Cannegieter SC, Vonk Noordegraaf A, et al. Incidence of chronic thromboembolic pulmonary hypertension after acute pulmonary embolism: a contemporary view of the published literature. Eur Respir J. 2017 Feb 23;49(2):1601792. doi: 10.1183/13993003.01792-2016. PMID: 28232411.
4. Pengo V, Lensing AW, Prins MH, et al. Thromboembolic Pulmonary Hypertension Study Group. Incidence of chronic thromboembolic pulmonary hypertension after pulmonary embolism. N Engl J Med. 2004 May 27;350(22):2257-64. doi: 10.1056/NEJMoa032274. PMID: 15163775.
5. Valerio L, Mavromanoli AC, Barco S, et al. FOCUS Investigators. Chronic thromboembolic pulmonary hypertension and impairment after pulmonary embolism: the FOCUS study. Eur Heart J. 2022 Sep 21;43(36):3387-3398. doi: 10.1093/eurheartj/ehac206. PMID: 35484821; PMCID: PMC9492241
6. Verbelen T, Godinas L, Dorfmüller P, et al. Clinical-radiological-pathological correlation in chronic thromboembolic pulmonary hypertension. Eur Respir Rev. 2023 Dec 20;32(170):230149. doi: 10.1183/16000617.0149-2023. PMID: 38123236; PMCID: PMC10731457.
7. Gall H, Hoeper MM, Richter MJ, Cacheris W, Hinzmann B, Mayer E. An epidemiological analysis of the burden of chronic thromboembolic pulmonary hypertension in the USA, Europe and Japan. Eur Respir Rev. 2017 Mar 29;26(143):160121. doi: 10.1183/16000617.0121-2016. PMID: 28356407; PMCID: PMC9488926.
8. Darocha S. Epidemiologia CTEPH. Presented at: 13. Konferencja Sekcji Krążenia

Płucnego Polskiego Towarzystwa Kardiologicznego; 2023 Oct; Warsaw, Poland. Dane z Bazy BNP-PL.

9. Ruan W, Yap JJ, Quah KK, Cheah FK, Phua GC, Sewa DW, Ismail AB, Chia AX, Jenkins D, Tan JL, Chao VT, Lim ST. Clinical Updates on the Diagnosis and Management of Chronic Thromboembolic Pulmonary Hypertension. Ann Acad Med Singap. 2020 May;49(5):320-330. PMID: 32582909.
10. Lang IM, Madani M. Update on chronic thromboembolic pulmonary hypertension. Circulation. 2014 Aug 5;130(6):508-18. doi: 10.1161/CIRCULATIONAHA.114.009309. PMID: 25092279
11. Pepke-Zaba J, Hoeper MM, Humbert M. Chronic thromboembolic pulmonary hypertension: advances from bench to patient management. Eur Respir J. 2013 Jan;41(1):8-9. doi: 10.1183/09031936.00181212. PMID: 23277517.
12. Ciurzyński M, Kurzyna M, Kopeć G, et al. An expert opinion of the Polish Cardiac Society Working Group on Pulmonary Circulation on screening for chronic thromboembolic pulmonary hypertension patients after acute pulmonary embolism: Update. Kardiol Pol. 2022;80(6):723-732. doi: 10.33963/KP.a2022.0141. Epub 2022 Jun 6. PMID: 35665906.
13. Higuchi S, Ota H, Yaoita N, et al. Update on the roles of imaging in the management of chronic thromboembolic pulmonary hypertension. J Cardiol. 2023 Mar;81(3):297-306. doi: 10.1016/j.jjcc.2022.03.001. Epub 2022 Apr 28. PMID: 35490106.
14. Blauwet LA, Edwards WD, Tazelaar HD, et al. Surgical pathology of pulmonary thromboendarterectomy: a study of 54 cases from 1990 to 2001. Hum Pathol. 2003 Dec;34(12):1290-8. doi: 10.1016/j.humpath.2003.07.003. PMID: 14691915.
15. Auger WR, Kerr KM, Kim NH, et al. Chronic thromboembolic pulmonary hypertension. Cardiol Clin. 2004 Aug;22(3):453-66, vii. doi: 10.1016/j.ccl.2004.04.006. PMID: 15302364.
16. Guérin L, Couturaud F, Parent F, et al. Prevalence of chronic thromboembolic pulmonary hypertension after acute pulmonary embolism. Prevalence of CTEPH after pulmonary embolism. Thromb Haemost. 2014 Sep 2;112(3):598-605. doi: 10.1160/TH13-07-0538. Epub 2014 Jun 5. PMID: 24898545.
17. Delcroix M, Kerr K, Fedullo P. Chronic Thromboembolic Pulmonary Hypertension. Epidemiology and Risk Factors. Ann Am Thorac Soc. 2016 Jul;13 Suppl 3:S201-6. doi: 10.1513/AnnalsATS.201509-621AS. PMID: 27571001.
18. Lang IM, Pesavento R, Bonderman D, et al. Risk factors and basic mechanisms of chronic thromboembolic pulmonary hypertension: a current understanding. Eur Respir J.2013 Feb;41(2):462-8. doi: 10.1183/09031936.00049312. Epub 2012 Jun 14. PMID: 22700839.
19. Otani N, Watanabe R, Tomoe T, et al. Pathophysiology and Treatment of Chronic

Thromboembolic Pulmonary Hypertension. Int J Mol Sci. 2023 Feb 16;24(4):3979. doi: 10.3390/ijms24043979. PMID: 36835383; PMCID: PMC9968103.

20. Yang J, Madani MM, Mahmud E, et al. Evaluation and Management of Chronic Thromboembolic Pulmonary Hypertension. Chest. 2023 Aug;164(2):490-502. doi: 10.1016/j.chest.2023.03.029. Epub 2023 Mar 28. PMID: 36990148; PMCID: PMC10410247.
21. Simonneau G, Dorfmüller P, Guignabert C, Mercier O, Humbert M. Chronic thromboembolic pulmonary hypertension: the magic of pathophysiology. Ann Cardiothorac Surg. 2022 Mar;11(2):106-119. doi: 10.21037/acs-2021-pte-10. PMID: 35433354; PMCID: PMC9012195.
22. Boulate D, Perros F, Dorfmuller P, Arthur-Ataam J, Guihaire J, Lamrani L, Decante B, Humbert M, Eddahibi S, Dartevelle P, Fadel E, Mercier O. Pulmonary microvascular lesions regress in reperfused chronic thromboembolic pulmonary hypertension. J Heart Lung Transplant. 2015 Mar;34(3):457-67. doi: 10.1016/j.healun.2014.07.005. Epub 2014 Jul 16. PMID: 25123056.
23. Fedullo P, Kerr KM, Kim NH, et al. Chronic thromboembolic pulmonary hypertension. Am J Respir Crit Care Med. 2011 Jun 15;183(12):1605-13. doi: 10.1164/rccm.201011-1854CI. Epub 2011 Feb 17. PMID: 21330453.
24. Verbelen T, Godinas L, Maleux G, et al. Chronic thromboembolic pulmonary hypertension: diagnosis, operability assessment and patient selection for pulmonary endarterectomy. Ann Cardiothorac Surg. 2022 Mar;11(2):82-97. doi: 10.21037/acs-2021-pte-12. PMID: 35433370; PMCID: PMC9012197.
25. Pepke-Zaba J, Delcroix M, Lang I, Mayer E, Jansa P, Ambroz D, Treacy C, D'Armini AM, Morsolini M, Snijder R, Bresser P, Torbicki A, Kristensen B, Lewczuk J, Simkova I, Barberà JA, de Perrot M, Hoeper MM, Gaine S, Speich R, Gomez-Sanchez MA, Kovacs G, Hamid AM, Jaïs X, Simonneau G. Chronic thromboembolic pulmonary hypertension (CTEPH): results from an international prospective registry. Circulation. 2011 Nov 1;124(18):1973-81. doi: 10.1161/CIRCULATIONAHA.110.015008. Epub 2011 Oct 3. PMID: 21969018.
26. Zhang Y, Yu X, Jin Q, et al. Advances in targeted therapy for chronic thromboembolic pulmonary hypertension. Heart Fail Rev. 2019 Nov;24(6):949-965. doi: 10.1007/s10741-019-09798-x. PMID: 31044326
27. Simeone B, Maggio E, Schirone L, Rocco E, Sarto G, Spadafora L, Bernardi M, Ambrosio L, Forte M, Vecchio D, Valenti V, Sciarretta S, Vizza CD. Chronic thromboembolic pulmonary hypertension: the diagnostic assessment. Front Cardiovasc Med. 2024 Sep 6;11:1439402. doi: 10.3389/fcvm.2024.1439402. PMID: 39309600; PMCID: PMC11412851.

28. Luijten D, Meijer FMM, Boon GJAM, Ende-Verhaar YM, Bavalia R, ElBouazzaoui LH, et al. Diagnostic efficacy of ECG-derived ventricular gradient forthe detection of chronic thromboembolic pulmonary hypertension in patients with acute pulmonary embolism. J Electrocardiol. (2022) 74:94–100. doi: 10.1016/j.jelectrocard.2022.08.007
29. Boon GJAM, Ende-Verhaar YM, Bavalia R, El Bouazzaoui LH, Delcroix M, Dzikowska-Diduch O, et al. Non-invasive early exclusion of chronic thromboembolic pulmonary hypertension after acute pulmonary embolism: the InShape II study. Thorax. (2021) 76(10):1002–9. doi: 10.1136/thoraxjnl-2020-216324
30. Kligerman S, Hsiao A. Optimizing the diagnosis and assessment of chronic thromboembolic pulmonary hypertension with advancing imaging modalities. Pulm Circ. 2021 May 24;11(2):20458940211007375. doi: 10.1177/20458940211007375. PMID: 34104420; PMCID: PMC8150458.
31. Tunariu N, Gibbs SJ, Win Z, et al. Ventilation-perfusion scintigraphy is more sensitive than multidetector CTPA in detecting chronic thromboembolic pulmonary disease as a treatable cause of pulmonary hypertension. J Nucl Med. 2007 May;48(5):680-4. doi: 10.2967/jnumed.106.039438. PMID: 17475953
32. Kim NH, D'Armini AM, Delcroix M, et al. Chronic thromboembolic pulmonary disease. Eur Respir J. 2024 Oct 31;64(4):2401294. doi: 10.1183/13993003.01294-2024. PMID: 39209473; PMCID: PMC11525345
33. Ribas Sola J, Sánchez-Corral Mena MÁ, Riera-Mestre A. Update in the management of chronic thrombo-embolic pulmonary hypertension. Med Clin (Barc). 2024 Feb9;162(3):126-133. English, Spanish. doi: 10.1016/j.medcli.2023.08.006. Epub 2023 Nov 2. PMID: 37925273.
34. Soler X, Hoh CK, Test VJ, et al. Single photon emission computed tomography in chronic thromboembolic pulmonary hypertension. Respirology. 2011 Jan;16(1):131-7. doi: 10.1111/j.1440-1843.2010.01867.x. PMID: 20920137.
35. 35. Frost A, Badesch D, Gibbs JSR, et al. Diagnosis of pulmonary hypertension. Eur Respir J. 2019 Jan 24;53(1):1801904. doi: 10.1183/13993003.01904-2018. PMID: 30545972; PMCID: PMC6351333
36. Masy M, Giordano J, Petyt G, et al. Dual-energy CT (DECT) lung perfusion in pulmonary hypertension: concordance rate with V/Q scintigraphy in diagnosing chronic thromboembolic pulmonary hypertension (CTEPH). Eur Radiol. 2018 Dec;28(12):5100-5110. doi: 10.1007/s00330-018-5467-2. Epub 2018 May 30. PMID: 29846802.
37. Dournes G, Verdier D, Montaudon M, et al. Dual-energy CT perfusion and angiography in chronic thromboembolic pulmonary hypertension: diagnostic accuracy and concordance with radionuclide scintigraphy. Eur Radiol. 2014 Jan;24(1):42-51. doi: 10.1007/s00330-013-2975-y. Epub 2013 Aug 28. PMID: 23982287.

38. Miwa K, Taniguchi Y, Fujii H, et al. Microvasculopathy Evaluated by Dual-Energy Computed Tomography in Patients with Chronic Thromboembolic Pulmonary Hypertension and Pulmonary Arterial Hypertension. Life (Basel). 2022 Aug 15;12(8):1232. doi:10.3390/life12081232. PMID: 36013412; PMCID: PMC9410450.
39. Onishi H, Taniguchi Y, Matsuoka Y, et al. Evaluation of microvasculopathy using dual-energy computed tomography in patients with chronic thromboembolic pulmonary hypertension. Pulm Circ. 2021 Jan 20;11(1):2045894020983162. doi: 10.1177/2045894020983162. PMID: 33532057; PMCID: PMC7829531.
40. Kang MJ, Park CM, Lee CH, et al. Focal iodine defects on color-coded iodine perfusion maps of dual-energy pulmonary CT angiography images: a potential diagnostic pitfall. AJR Am J Roentgenol. 2010 Nov;195(5):W325-30. doi: 10.2214/AJR.09.3241. PMID: 20966296.
41. Lacharie M, Villa A, Milidonis X, et al. Role of pulmonary perfusion magnetic resonance imaging for the diagnosis of pulmonary hypertension: A review. World J Radiol. 2023 Sep 28;15(9):256-273. doi: 10.4329/wjr.v15.i9.256. PMID: 37823020; PMCID: PMC10563854.
42. Hatabu H, Ohno Y, Gefter WB, et al. Fleischner Society. Expanding Applications of Pulmonary MRI in the Clinical Evaluation of Lung Disorders: Fleischner Society Position Paper. Radiology. 2020 Nov;297(2):286-301. doi: 10.1148/radiol.2020201138. Epub 2020 Sep 1. PMID: 32870136.
43. Alsop DC, Hatabu H, Bonnet M, et al. Multi-slice, breathhold imaging of the lung with submillisecond echo times. Magn Reson Med. 1995 May;33(5):678-82. doi: 10.1002/mrm.1910330513. PMID: 7596272.
44. Mayo JR, MacKay A, Müller NL. MR imaging of the lungs: value of short TE spin-echo pulse sequences. AJR Am J Roentgenol. 1992 Nov;159(5):951-6. doi: 10.2214/ajr.159.5.1414805. PMID: 1414805.
45. Nazir MS, Neji R, Speier P, et al. Simultaneous multi slice (SMS) balanced steady state free precession first-pass myocardial perfusion cardiovascular magnetic resonance with iterative reconstruction at 1.5 T. J Cardiovasc Magn Reson. 2018 Dec 10;20(1):84. doi:10.1186/s12968-018-0502-7. PMID: 30526627; PMCID: PMC6287353.
46. Johns CS, Swift AJ, Hughes PJC, et al. Pulmonary MR angiography and perfusion imaging-A review of methods and applications. Eur J Radiol. 2017 Jan;86:361-370. doi: 10.1016/j.ejrad.2016.10.003. Epub 2016 Oct 4. PMID: 28341390.
47. Johns CS, Swift AJ, Rajaram S, et al. Lung perfusion: MRI vs. SPECT for screening in suspected chronic thromboembolic pulmonary hypertension. J Magn Reson Imaging. 2017 Dec;46(6):1693-1697. doi: 10.1002/jmri.25714. Epub 2017 Apr 4. PMID: 28376242; PMCID: PMC5697671.

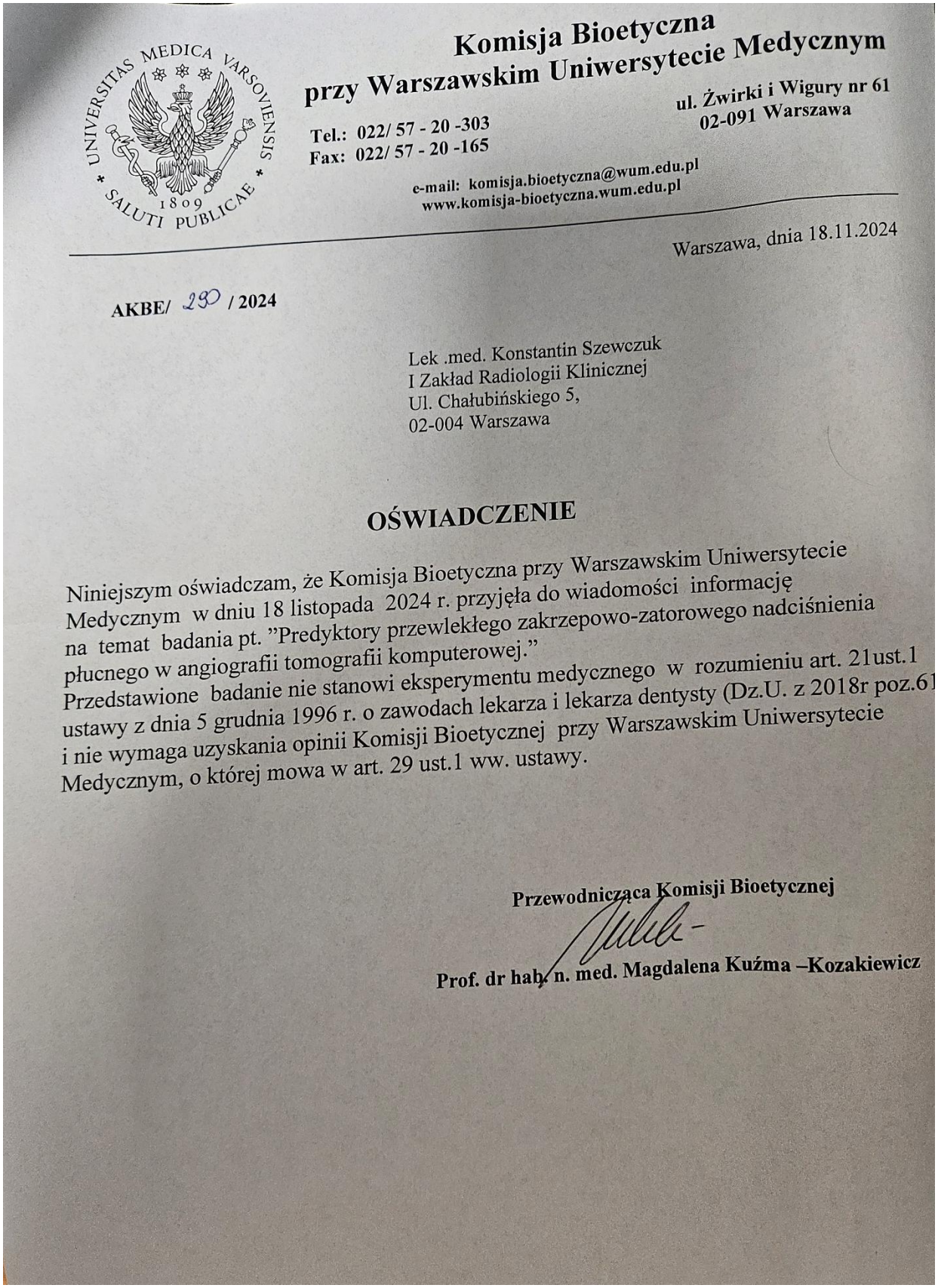
48. Rajaram S, Swift AJ, Telfer A, et al. 3D contrast-enhanced lung perfusion MRI is an effective screening tool for chronic thromboembolic pulmonary hypertension: results from the ASPIRE Registry. Thorax. 2013 Jul;68(7):677-8. doi: 10.1136/thoraxjnl-2012-203020. Epub 2013 Jan 24. PMID: 23349220.
49. Kopeć G, Dzikowska-Diduch O, Mroczek E, et.al Characteristics and outcomes of patients with chronic thromboembolic pulmonary hypertension in the era of modern therapeutic approaches: data from the Polish multicenter registry (BNP-PL). Ther Adv Chronic Dis. 2021 Mar 25;12:20406223211002961. doi: 10.1177/20406223211002961. PMID: 33854746; PMCID: PMC8010818.
50. Gopalan D, Blanchard D, Auger WR. Diagnostic Evaluation of Chronic Thromboembolic Pulmonary Hypertension. Ann Am Thorac Soc. 2016 Jul;13 Suppl 3:S222-39. doi: 10.1513/AnnalsATS.201509-623AS. PMID: 27571004.
51. Renapurkar RD, Shrikanthan S, Heresi GA, et al. Imaging in Chronic Thromboembolic Pulmonary Hypertension. J Thorac Imaging. 2017 Mar;32(2):71-88. doi: 10.1097/RTI.0000000000000256. PMID: 28060193.
52. Ley S, Grünig E, Kiely DG, et al. Computed tomography and magnetic resonance imaging of pulmonary hypertension: Pulmonary vessels and right ventricle. J Magn Reson Imaging. 2010 Dec;32(6):1313-24. doi: 10.1002/jmri.22373. PMID: 21105137.
53. Kreitner KF, Kunz RP, Ley S, et al. Chronic thromboembolic pulmonary hypertension - assessment by magnetic resonance imaging. Eur Radiol. 2007 Jan;17(1):11-21. doi: 10.1007/s00330-006-0327-x. Epub 2006 Jul 13. PMID: 16838142.
54. Ley S, Kauczor HU, Heussel CP, et al. Value of contrast-enhanced MR angiography and helical CT angiography in chronic thromboembolic pulmonary hypertension. Eur Radiol. 2003 Oct;13(10):2365-71. doi: 10.1007/s00330-003-1878-8. Epub 2003 Apr 24. PMID: 12712256.
55. Ley S, Ley-Zaporozhan J, Pitton MB, et al. Diagnostic performance of state-of-the-art imaging techniques for morphological assessment of vascular abnormalities in patients with chronic thromboembolic pulmonary hypertension (CTEPH). Eur Radiol. 2012 Mar;22(3):607-16. doi: 10.1007/s00330-011-2290-4. Epub 2011 Sep 27. PMID: 21947513.
56. Hahn LD, Papamatheakis DG, Fernandes TM, et al. Multidisciplinary Approach to Chronic Thromboembolic Pulmonary Hypertension: Role of Radiologists. Radiographics. 2023 Feb;43(2):e220078. doi: 10.1148/rg.220078. PMID: 36525366.
57. Reichelt A, Hoeper MM, Galanski M, et al. Chronic thromboembolic pulmonary hypertension: evaluation with 64-detector row CT versus digital substraction angiography. Eur J Radiol. 2009 Jul;71(1):49-54. doi: 10.1016/j.ejrad.2008.03.016. Epub 2008 May 6.PMID: 18462902.

58. Ley S, Ley-Zaporozhan J, Pitton MB, et al. Diagnostic performance of state-of-the-art imaging techniques for morphological assessment of vascular abnormalities in patients with chronic thromboembolic pulmonary hypertension (CTEPH). Eur Radiol. 2012 Mar;22(3):607-16. doi: 10.1007/s00330-011-2290-4. Epub 2011 Sep 27. PMID: 21947513.
59. Sugiura T, Tanabe N, Matsuura Y, et al. Role of 320-slice CT imaging in the diagnostic workup of patients with chronic thromboembolic pulmonary hypertension. Chest. 2013 Apr;143(4):1070-1077. doi: 10.1378/chest.12-0407. PMID: 23100061.
60. Humbert M, Kovacs G, Hoeper MM, et al. ESC/ERS Scientific Document Group. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Respir J. 2023 Jan 6;61(1):2200879. doi: 10.1183/13993003.00879-2022. PMID: 36028254
61. Castañer E, Gallardo X, Ballesteros E, Andreu M, Pallardó Y, Mata JM, Riera L. CT diagnosis of chronic pulmonary thromboembolism. Radiographics. 2009 Jan-Feb;29(1):31-50; discussion 50-3. doi: 10.1148/rg.291085061. PMID: 19168835.
62. Willemink MJ, van Es HW, Koobs L, Morshuis WJ, Snijder RJ, van Heesewijk JP. CT evaluation of chronic thromboembolic pulmonary hypertension. Clin Radiol. 2012 Mar;67(3):277-85. doi: 10.1016/j.crad.2011.09.012. Epub 2011 Nov 25. PMID: 22119298.
63. Nishiyama KH, Saboo SS, Tanabe Y, Jasinowodolinski D, Landay MJ, Kay FU. Chronic pulmonary embolism: diagnosis. Cardiovasc Diagn Ther. 2018 Jun;8(3):253-271. doi: 10.21037/cdt.2018.01.09. PMID: 30057874; PMCID: PMC6039808.
64. Fathala A, Aldurabi A. Frequency of computed tomography abnormalities in patients with chronic thromboembolic pulmonary hypertension: a comparative study between lung perfusion scan and computed tomography pulmonary angiography. Multidiscip Respir Med 2021; 16: 753. DOI: 10.4081/mrm.2021.753
65. Grosse A, Grosse C, Lang IM. Distinguishing chronic thromboembolic pulmonary hypertension from other causes of pulmonary hypertension using CT. AJR Am J Roentgenol 2017; 209: 1228-1238.
66. Ende-Verhaar YM, Meijboom LJ, Kroft LJM, Beenen LFM, Boon GJAM, Middeldorp S, et al. Usefulness of standard computed tomography pulmonary angiography performed for acute pulmonary embolism for identification of chronic thromboembolic pulmonary hypertension: results of the InShape III study. J Heart Lung Transplant 2019; 38: 731-738.
67. McInnis MC, Wang D, Donahoe L, Granton J, Thenganatt J, Tan K, et al. Importance of computed tomography in defining segmental disease in chronic thromboembolic

pulmonary hypertension. ERJ Open Res 2020; 6: 00461-2020. DOI: 10.1183/23120541.00461-2020.

68. Wittram C, Kalra MK, Maher MM, Greenfield A, McLoud TC, Shepard JA. Acute and chronic pulmonary emboli: angiography-CT correlation. AJR Am J Roentgenol 2006; 186 (6 Suppl 2): S421-S429. DOI: 10.2214/AJR.04.1955.
69. Raymond RJ, Hinderliter AL, Willis PW, Ralph D, Caldwell EJ, Williams W, et al. Echocardiographic predictors of adverse outcomes in primary pulmonary hypertension. J Am Coll Cardiol 2002; 39: 1214-1219.
70. Remy-Jardin M, Duhamel A, Deken V, Bouaziz N, Dumont P, Remy J. Systemic collateral supply in patients with chronic thromboembolic and primary pulmonary hypertension: assessment with multi-detector row helical CT angiography. Radiology 2005; 235: 274-281.

10. OPINIA KOMISJI BIOETYCZNEJ



Komisja Bioetyczna
przy Warszawskim Uniwersytecie Medycznym

Tel.: 022/ 57 - 20 -303
Fax: 022/ 57 - 20 -165

ul. Żwirki i Wigury nr 61
02-091 Warszawa

e-mail: komisja.bioetyczna@wum.edu.pl
www.komisja-bioetyczna.wum.edu.pl

Warszawa, dnia 18.11.2024

AKBE/ 230 / 2024

Lek .med. Konstantin Szewczuk
I Zakład Radiologii Klinicznej
Ul. Chałubińskiego 5,
02-004 Warszawa

OŚWIADCZENIE

Niniejszym oświadczam, że Komisja Bioetyczna przy Warszawskim Uniwersytecie Medycznym w dniu 18 listopada 2024 r. przyjęła do wiadomości informację na temat badania pt. "Predyktory przewlekłego zakrzepowo-zatorowego nadciśnienia płucnego w angiografii tomografii komputerowej."
Przedstawione badanie nie stanowi eksperymentu medycznego w rozumieniu art. 21ust.1 ustawy z dnia 5 grudnia 1996 r. o zawodach lekarza i lekarza dentysty (Dz.U. z 2018r poz.61 i nie wymaga uzyskania opinii Komisji Bioetycznej przy Warszawskim Uniwersytecie Medycznym, o której mowa w art. 29 ust.1 ww. ustawy.

Przewodnicząca Komisji Bioetycznej

Prof. dr hab. n. med. Magdalena Kuźma –Kozakiewicz

11.OŚWIADCZENIA WSPÓŁAUTORÓW

Chronic thromboembolic hypertension predictors in computer tomography angiography . One center study

...Warszawa...27.05.2025...
(miejscowość, data)

Olga Dzikowska-Diduch

OŚWIADCZENIE

Jako współautor pracy pt. Chronic thromboembolic hypertension predictors in computer tomography angiography . One center study.

oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi:

Zbieranie i analiza danych

Wkład Konstantina Szewczuka w powstawanie publikacji obejmował:

Projekt badania, Zbieranie danych, Analiza statystyczna, Interpretacja danych, Przygotowanie manuskryptu, Przegląd literatury

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lek. Konstantina Szewczuka

dr hab. n. med. Olga Dzikowska-Diduch
KARDIOLOG
PWZ 2217796

.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

...Warszawa... 27/05/2025
(miejscowość, data)

Piotr Pruszczyk

OŚWIADCZENIE

Jako współautor pracy pt. Chronic thromboembolic hypertension predictors in computer tomography angiography . One center study.

oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi:

Analiza danych, Przygotowanie manuskryptu

Wkład Konstantina Szewczuka w powstawanie publikacji obejmował:

Projekt badania, Zbieranie danych, Analiza statystyczna, Interpretacja danych, Przygotowanie manuskryptu, Przegląd literatury

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lek. Konstantina Szewczuka

KIEROWNIK
Kliniki Chorób Nadciśnieniowych i Kardiologii
z Centrum Diagnostyki i Leczenia
Żylnej Choroby Zakrzepowo-Zatorowej
Prof. dr hab. med. Piotr Pruszczyk

.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

27/05/2025

...Warszawa.....
(miejscowość, data)

Marek Roik

OŚWIADCZENIE

Jako współautor pracy pt. Chronic thromboembolic hypertension predictors in computer tomography angiography . One center study.

oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi:

Analiza danych

Wkład Konstantina Szewczuka w powstawanie publikacji obejmował:

Projekt badania, Zbieranie danych, Analiza statystyczna, Interpretacja danych, Przygotowanie manuskryptu, Przegląd literatury

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lek. Konstantina Szewczuka

Marek Roik
.....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

...Warszawa..30.05.2025.....
(miejscowość, data)

Dorota Piotrowska-Kownacka

OŚWIADCZENIE

Jako współautor pracy pt. Chronic thromboembolic hypertension predictors in computer tomography angiography . One center study.

oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi:

Przegląd literatury

Wkład Konstantina Szewczuka w powstawanie publikacji obejmował:

Projekt badania, Zbieranie danych, Analiza statystyczna, Interpretacja danych, Przygotowanie manuskryptu, Przegląd literatury

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lek. Konstantina Szewczuka

.....

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa 24.05.2009

Marek Gołębiowski
I Zakład Radiologii Klinicznej WUM

OŚWIADCZENIE

Jako współautor pracy Chronic thromboembolic hypertension predictors in computer tomography angiography . One center study. oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi **projekt badania, interpretacja danych, przygotowanie manuskryptu oraz krytyczny przegląd literatury**

Wkład Konstantina Szewczuka w powstawanie publikacji był dominujący i obejmował **projekt badania, zbieranie danych, analizę statystyczną, interpretację wyników, przygotowanie manuskryptu oraz przegląd literatury**

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lek. Konstantina Szewczuka

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

The use of imaging in the diagnosis and treatment of thromboembolic pulmonary hypertension.

Warszawa.29.05.2025

Marek Gołębiowski
I Zakład Radiologii Klinicznej WUM

OŚWIADCZENIE

Jako współautor pracy *The use of imaging in the diagnosis and treatment of thromboembolic pulmonary hypertension* oświadczam, iż mój własny wkład merytoryczny w przygotowanie, wykonanie analizy oraz przedstawienie pracy w formie publikacji stanowi **merytoryczny nadzór nad tworzonym materiałem, krytyczna analiza piśmiennictwa, redakcja manuskryptu.**

Wkład Konstantina Szewczuka w powstawanie publikacji obejmował: **projekt badania, zbieranie materiału, analizę danych, tworzenie manuskryptu**

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lek. Konstantina Szewczuka

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

...Warszawa..27.05.2015.....
(miejscowość, data)

Olga Dzikowska-Diduch

OŚWIADCZENIE

Jako współautor pracy pt. The use of imaging in the diagnosis and treatment of thromboembolic pulmonary hypertension

oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi:

Interpretacja wyników, Redakcja manuskryptu.

Wkład Konstantina Szewczuka w powstawanie publikacji obejmował:

Projekt badania, Zbieranie materiału, Analiza danych, Tworzenie manuskryptu

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lek. Konstantina Szewczuka

dr hab. n. med. Olga Dzikowska-Diduch
KARDIOLOG
PWZ 2217796

.....

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników