UNIWERSYTET MEDYCZNY
IM. PIASTÓW ŚLĄSKICH WE WROCŁAWIU

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Radiologiczny wskaźnik sercowo-płucny jako predyktor wielkości serca ocenianej metodami echokardiografii, tomografii komputerowej i rezonansu magnetycznego.

ROZPRAWA DOKTORSKA

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WROCŁAW 2022

Niniejsza rozprawa doktorska powstała jako owoc pracy, zaangażowania i wsparcia wielu osób, w sposób szczególny chciałbym podziękować choć kilkorgu z nich.

Dziękuję zwłaszcza mojemu Promotorowi,
***dr. hab. Pawłowi Gać, prof. UMW**,*
za nieocenioną pomoc w realizacji cyklu publikacji, nadzór merytoryczny na każdym etapie ich tworzenia, cierpliwość, motywację oraz olbrzymi wkład w część organizacyjną projektu.

Znakomitemu gronu współautorów cyklu publikacji:
prof. dr hab. n. med. Rafałowi Porębie,
dr hab. n. med. Małgorzacie Porębie, prof. AWF,
lek. Piotrowi Mackowi
za poświęcony czas, nadzór merytoryczny i krytyczne spojrzenie na wielu etapach pracy.

Doktorowi **Bartłomiejowi Kędzierskiemu**
za wprowadzenie mnie w zawiłe meandra radiologii i diagnostyki obrazowej serca, nauczenie rozumienia obrazów radiologicznych serca, za zarażanie pasją i zaangażowaniem.

Kierownikom mojej specjalizacji:
lek. Adamowi Adamowiczowi,
lek. Annie Kuśmierskiej,
lek. Małgorzacie Szumarskiej – Czech
za ukształtowanie mojej wiedzy radiologicznej i poświęcony czas.

*Dziękuję mojej **Rodzinie i Przyjaciołom**, w sposób szczególny **D**. za cierpliwość, wsparcie, miłość.*

SPIS TREŚCI

WPROWADZENIE

Radiogram klatki piersiowej w projekcji PA oprócz swej przydatności w onkologii, pulmonologii, pediatrii, i in. wykorzystywany jest także jako badanie przesiewowe w ocenie wielkości sylwetki serca. Powszechnie używanym parametrem do jej oceny jest tzw. wskaźnik sercowo-płucny (CTR – cardiothoracic ratio), po raz pierwszy opisany w 1919 r. [1]. Wskaźnik sercowo-płucny określa się jako stosunek największego poprzecznego wymiaru serca do największego poprzecznego wymiaru klatki piersiowej mierzonego do wewnętrznych powierzchni żeber na radiogramie PA klatki piersiowej. Parametr ten jest bardzo łatwy do wyznaczenia i nie wydłuża istotnie interpretacji obrazów RTG, zwłaszcza przy możliwościach narzędziowych współczesnych przeglądarek obrazów DICOM. Wartości prawidłowe mieszczą się pomiędzy 0.42 a 0.50, wartość powyżej 0.50 jest uznawana za nieprawidłową i może sugerować kardiomegalię [2].

Podstawowymi zaletami CTR dla jednostek i personelu medycznego wykonującego badania RTG klatki piersiowej, oprócz wymienionej powyżej łatwości wyznaczania CTR są brak ponoszenia dodatkowych kosztów oraz w zasadzie brak wzrostu obciążenia czasowego przy jego wyznaczeniu. Ważne jest również, aby pamiętać o zaletach jego pomiaru, które dotyczą pacjenta. Do takowych należy zaliczyć krótki czas badania, niską dawkę promieniowania (ok. 80 - 100 razy mniejszego niż w przypadku badań tomografii komputerowej) i w zasadzie brak specjalnego przygotowania do takiego badania. Kolejną grupą beneficjentów z wyznaczenia CTR są klinicyści, którzy niejako przy okazji badania klatki piersiowej wykonywanego z określonych wskazań medycznych uzyskać mogą informację o wielkości sylwetki serca

Musimy pamiętać o podstawowych ograniczeniach związanych z wyznaczaniem CTR w różnych sytuacjach klinicznych [3]. Za podstawowe ograniczenie (wynikające z definicji CTR) uznaje się niecelowość jego wyznaczania w zgodzie z ogólną wartością normatywną w innych niż PA projekcjach radiogramów klatki piersiowej. W przypadku radiogramów AP, szerokość sylwetki serca znajdującego się w śródpiersiu bliżej przedniej ściany klatki piersiowej będzie większa w związku ze skierowaniem wiązki promieniowania X od przodu ku tyłowi. Po drugie odległość źródła promieniowania (lampy) od detektora (kasety) jest krótsza niż podczas wykonywania radiogramów PA (dla radiogramów PA ok. 180-200 cm), co skutkuje na uzyskanym radiogramie powiększeniem zarówno sylwetki serca jak i wymiaru poprzecznego klatki piersiowej. Po trzecie często stan kliniczny takich pacjentów nie pozwala im na wykonanie pełnego wdechu czy jego utrzymanie przez odpowiedni czas co skutkuje niemiarodajnymi pomiarami wymiaru poprzecznego klatki piersiowej [4]. Należy także pamiętać o dużej zmienności warunków wykonania radiogramów przyłóżkowych.

Kolejną zmienną z jaką należy się zmierzyć w wyznaczaniu CTR jest faza oddechu. CTR u tego samego Pacjenta mierzony w trakcie wydechu będzie większy niż mierzony podczas wdechu pomimo zmian oddechowych zarówno wielkości serca jak i szerokości klatki piersiowej [5]. Fakt ten wydaje się szczególnie istotny u pacjentów pediatrycznych, u których otrzymanie radiogramów w określonej (wdechowej) fazie oddechu może stanowić nie lada wyzwanie.

W związku z powyższymi problemami CTR doczekał się wielu modyfikacji opartych na modelach tomografii komputerowej, badaniach pośmiertnych, czy pomiarach planimetrycznych [4,6,7,8,9]. Większość z nich nie jest jednak szeroko stosowana w codziennej praktyce klinicznej. Część autorów sugeruje stosowanie innych niż typowo uznane wartości normatywnych CTR, np. wartość CTR > 0,55 i szerokość sylwetki serca >165 mm dla mężczyzn oraz >150 mm dla kobiet jako wartości wskazujące na powiększenie sylwetki serca [10].

W ostatnich dekadach obserwuje się intensywny rozwój medycyny i technologii medycznych. W związku z powyższym dostępność echokardiografii jest obecnie powszechna i większość pacjentów z podejrzeniem patologii serca rutynowo ma wykonywane badanie USG serca.

Podobnie coraz bardziej powszechny jest dostęp do tomografii komputerowej, która oferuje szerokie możliwości oceny zarówno morfologii, jak i funkcji serca. Najczęstszymi wskazaniami do badań tomografii komputerowej serca i dużych naczyń należą: ocena tętnic płucnych przy podejrzeniu zatorowości płucnej, ocena aorty w podejrzeniu np. ostrych zespołów aortalnych, ocena tętnic wieńcowych w celu wykluczenia istotnych zwężeń w tętnicach nasierdziowych, ocena tzw. Calcium Score (wskaźnika uwapnienia tętnic wieńcowych, zastawki aortalnej) i in. Powyższe badania realizowane są w trybie planowym jak i we wskazaniach ostrodyżurowych w trybie pilnym i ze wskazań życiowych.

Wspomnieć w tym miejscu należy również o rosnącej dostępności rezonansu magnetycznego, który zgodnie z wytycznymi towarzystw naukowych stanowi złoty standard w ocenie parametrów czynności skurczowej jam serca, a także morfologii miokardium. Do podstawowych wskazań do wykonania badania rezonansu magnetycznego serca należą: ocena funkcji lewej komory oraz pomiary planimetryczne jam serca, ocena morfologii oraz patologii miokardium, określenie przyczyn niewydolności serca, detekcja i monitorowanie włóknienia miokardium i in.

Wobec powyższego zgodnie z zasadami medycyny opartej na faktach celowe było ustalenie, czy powszechne stosowanie wskaźnika sercowo-płucnego jako predyktora powiększenia sylwetki serca w obecnych czasach wciąż ma uzasadnienie.

ZAŁOŻENIA I CELE PRACY

Zasadniczym celem rozprawy doktorskiej była weryfikacja przydatności klinicznej wskaźnika sercowo-płucnego jako predyktora wielkości jam serca ocenianej nowoczesnymi metodami diagnostyki obrazowej, a więc echokardiografią, tomografią komputerową i rezonansem magnetycznym. Celami drugorzędowymi było oznaczenie ograniczeń oraz przydatności pomiarów CTR w określonych sytuacji klinicznych.

Zasadnicze założenia metodologiczne badania stanowiły bezpieczeństwo radiologiczne Pacjentów oraz maksymalna standaryzacja ocenianej metody.

Projekt był badaniem nieingerującym w postępowanie kliniczne z Pacjentem i niepowodującym dodatkowego narażenia na promieniowanie jonizujące czy środki kontrastowe. Wszystkie badania użyte w badaniu wykonane były ze wskazań klinicznych.

Współczynnik CTR został wyznaczony dla każdego Pacjenta włączonego do grupy na podstawie klasycznej definicji CTR, a więc jako stosunek największego poprzecznego wymiaru serca do największego wymiaru klatki piersiowej mierzonego do wewnętrznych powierzchni żeber mierzonych na radiogramie klatki piersiowej.

Pierwszym założonym etapem badań było dokonanie podsumowania aktualnego stanu wiedzy dotyczącego znaczenia wskaźnika sercowo-płucnego w badaniach naukowych. W kolejnych etapach badań założono dokonanie analizy dokładności predykcyjnej wyznaczonego CTR w zestawieniu z wielkością jam serca wyznaczonymi za pomocą echokardiografii oraz tomografii komputerowej w różnych podgrupach chorych. Z uwagi na wystąpienie pandemii COVID-19 podczas okresu trwania badań, dokonano również założonych porównań

Założone etapy badań warunkowały cele szczegółowe poszczególnych prac składających się na rozprawę doktorską, a zatem:

1. Zebranie, uporządkowanie i podsumowanie obecnego stanu wiedzy z uwzględnieniem kwestii spornych, ograniczeń i przydatnych aspektów dotyczących zagadnienia CTR w dostępnej literaturze.
2. Określenie przydatności radiologicznego wskaźnika sercowo-płucnego (CTR) jako predyktora powiększenia prawej komory u chorych z podejrzeniem zatorowości płucnej w przebiegu COVID-19.
3. Weryfikacja przydatności radiologicznego wskaźnika sercowo-płucnego jako potencjalnego markera przerostu lewej komory ocenianych metodą echokardiografii.

OMÓWIENIE

W pierwszej pracy cyklu, którą stanowiła praca przeglądowa pt. Radiological Cardiothoracic Ratio in Evidence-Based Medicine skupiono się na przeglądzie dostępnej w literaturze wiedzy dotyczącej zagadnienia CTR w celu usystematyzowania przeprowadzonych w tym temacie badań.

W dotychczasowej literaturze znaczenie pomiarów CTR postrzegane jest szeroko, w sposób zróżnicowany, czasem wręcz rozbieżnie. Podkreślana jest wielokrotnie wartość CTR jako prostego, szybkiego i niepodnoszącego kosztów parametru mogącego służyć przesiewowej ocenie wielkości serca. Wielokrotnie podnoszony jest fakt, że CTR jest poniekąd informacją dodaną do badania klatki piersiowej wykonywanego z określonych wskazań medycznych co nie wiąże się dla pacjenta z żadnym dodatkowym obciążeniem związanym z większą dawką promieniowania X czy wymagającym specjalnego przygotowania.

Podkreślana była tzw. klasyczna definicja CTR z głównym naciskiem na konieczność jego wyznaczania na radiogramach w projekcji PA. Wiele publikacji skupiało się na odstępstwach od projekcji PA i proponowało inne rozwiązania np. tzw. corrected CTR oparty na pomiarach w radiogramach AP i tomografii komputerowej, który nie wykazywał się większą swoistością ani czułością w detekcji powiększenia sylwetki serca. Opisywano również 2D CTR jako stosunek pomiaru planimetrycznego powierzchni sylwetki serca do powierzchni pól płucnych i cienia środkowego wykazując dużą zgodność pomiędzy 2D CTR a klasycznym CTR jednocześnie wskazując lepszą korelację 2D CTR z frakcją wyrzutową lewej komory.

Podczas trwania badań będących podstawą niniejszej rozprawy doktorskiej ukazała się istotna publikacja oryginalna, stanowiąca uzupełnienie danych zamieszczonych w pracy przeglądowej wchodzącej w skład omawianej dysertacji. W badaniu Simkus et al. pt. Limitations of cardiothoracic ratio derived from chest radiographs to predict real heart size; comparison with magnetic resonance imaging[11], badacze na podstawie porównania wartości CTR z wymiarami jam serca uzyskanymi metodą rezonansu magnetycznego wykazali, że parametry te słabo, ale w sposób istotny statystycznie korelują z wartością CTR. W konkluzji badacze sformułowali postulat unikania decyzji klinicznych opartych na pośrednich wartościach CTR (0,45-0,55) i zasugerowali stosowanie normatywy CTR >0,55 jako kryterium wskazującego na rzeczywiste powiększenie serca. Omawiając kwestię zależności CTR i rezonansu magnetycznego w pracy przeglądowej wchodzącej w skład rozprawy doktorskiej przytoczono badanie, w którym wykazano, że u pacjentów z kardiomiopatią rozstrzeniową i CTR bliskim wartości normatywnych na wartość CTR wpływ miała rotacja serca w wymiarze poprzecznym. Objętości jam serca obliczone metodą rezonansu magnetycznego (złoty standard oceny objętości jam serca) konfrontowano z CTR również u dzieci z częstymi wadami serca. Wykazano, że wyższy CTR był związany ze zwiększoną objętością całkowitą serca u dzieci z niedomykalnością zastawki pnia płucnego i aortalną, CTR nie korelował natomiast z objętościami komór serca u pacjentów z przeciekiem lewo-prawym i kardiomiopatią przerostową.

Reasumując dotychczasowy stan wiedzy należy wskazać, że przy zachowaniu świadomości jego ograniczeń, wartość CTR może być używany w stratyfikacji ryzyka, ocenie leczenia czy rokowaniu w różnych schorzeniach serca i patologiach przebiegających z zajęciem serca.

W drugiej pracy rozprawy doktorskiej pt. Radiological Cardiothoracic Ratio as a Potential Predictor of Right Ventricular Enlargement in Patients with Suspected Pulmonary Embolism Due to COVID-19, grupę badaną stanowiło 61 chorych (wiek 67,18 ± 12,47 lat) z potwierdzonym COVID-19, u których w oparciu o badanie fizykalne i badania laboratoryjne sformułowano podejrzenie zatorowości płucnej. U wszystkich pacjentów wykonano ze wskazań klinicznych w odstępie maksymalnie 48 godzin badania angiografii tomografii komputerowej (CTA) tętnic płucnych oraz radiogram przeglądowy klatki piersiowej w projekcji AP.

Radiogram klatki piersiowej wykonywano z uwagi na stan kliniczny chorych, w pozycji leżącej, w projekcji przednio-tylnej (AP), za pomocą aparatu rentgenowskiego przyłóżkowego. Radiogram wykonywano w miarę możliwości na wstrzymanym oddechu, na maksymalnym wdechu. Dokonywano pomiaru maksymalnej szerokości sylwetki serca (C width) oraz pomiaru maksymalnej szerokości klatki piersiowej (T width). Wartość wskaźnika sercowo-płucnego uzyskiwano korzystając z formuły: CTR = C widht / T widht. Powiększenie sylwetki serca stwierdzano, gdy CTR na radiogramie klatki piersiowej w projekcji AP >0.55.

Badania CTA tętnic płucnych wykonywano według wystandaryzowanego protokołu badania angiograficznego. Uzyskane obrazy badania CTA tętnic płucnych były oceniane przez 2 lekarzy radiologów posiadających doświadczenie w ocenie badań angiograficznych serca i naczyń. Zatorowość płucną (PE+) rozpoznawano w przypadku stwierdzenia ubytków zakontrastowania naczyń tętniczych płucnych. W celu oceny powiększenia prawej komory dokonywano wymiarowania obu komór serca. Radiolodzy oceniający wymiary komór nie dysponowali w chwili pomiaru wiedzą dotyczącą wartości CTR. Powiększenie prawej komory rozpoznawano na podstawie stosunku wymiaru prawej komory i lewej komory (RV/LV) w badaniu CTA tętnic płucnych, stosując 2 różne punkty odcięcia: ≥0.9 i ≥1.0.

Średnia wartość CTR w badanej grupie chorych wynosiła 0.57 ± 0.05. Radiologicznie powiększenie sylwetki serca stwierdzono u 60.6% badanych. Na podstawie wykonanego badania CTA tętnic płucnych zatorowość płucną rozpoznano u 45.9% badanych. Stosunek RV/LV wyniósł 0.96 ± 0.23. Powiększenie prawej komory zależnie od przyjętego kryterium RV/LV ≥0.9 lub RV/LV ≥1.0 udokumentowano u 44.3% lub 29.5%. W analizie porównawczej podgrup wyodrębnionych na podstawie punktu odcięcia CTR = 0.55 wykazano, że chorzy z powiększoną sylwetką serca cechują się istotnie statystycznie wyższymi wartościami stosunku RV/LV w badaniu CTA tętnic płucnych niż chorzy z niepowiększoną sylwetką serca, istotnie częściej spełniają również kryterium powiększenia prawej komory (zarówno definiowane jako RV/LV ≥0.9, jak i jako RV/LV ≥1.0).

Porównując podgrupy wyodrębnione na podstawie punktów odcięcia RV/LV ≥0.9 i RV/LV ≥1.0 udokumentowano, że chorzy z powiększoną prawą komorą mieli istotnie statystycznie wyższe wartości wskaźnika CTR aniżeli chorzy z niepowiększoną prawą komorą. U chorych z powiększoną prawą komorą istotnie statystycznie częściej w zestawieniu z chorymi z niepowiększoną prawą komorą obserwowano powiększenie sylwetki serca (definiowane jako CRT >0.55 na radiogramie klatki piersiowej w projekcji AP).

W porównaniu podgrup wydzielonych na podstawie rozpoznania zatorowości płucnej stwierdzono, że chorzy z potwierdzoną zatorowością płucną charakteryzowali się istotnie statystycznie wyższymi CRT i RV/LV niż chorzy z wykluczoną zatorowością płucną. U chorych z potwierdzoną zatorowością płucną w porównaniu z chorymi z wykluczoną zatorowością płucną istotnie statystycznie częściej stwierdzano powiększenie sylwetki serca. Badane podgrupy nie różniły się natomiast częstością występowania powiększenia prawej komory w badaniu CTA tętnic płucnych. Badanie wykazało, że CTR u chorych z podejrzeniem zatorowości płucnej w przebiegu COVID - 19 może stanowić predyktor powiększenia prawej komory serca przy czym zwłaszcza niższe wartości CTR mogą wskazywać na brak powiększenia prawej komory serca.

W trzeciej pracy cyklu doktorskiego pt. Radiological cardiothoracic ratio as a potential marker of left ventricular hypertrophy assessed by echocardiography, badaniem objęto

96 pacjentów poradni kardiologicznej (w wieku 54,90 ± 10,38 lat).

U wszystkich badanych zmierzono podstawowe pomiary antropometryczne oraz wykonano badania obrazowe: radiogram klasyczny (CR) klatki piersiowej w projekcji PA oraz badanie echokardiograficzne.

Radiogram klatki piersiowej wykonywano metodą standardową w pozycji stojącej, w projekcji tylno-przedniej (PA), na wstrzymanym oddechu, podczas fazy maksymalnego wdechu. Zmierzone zostały maksymalna szerokość sylwetki serca (C width) oraz maksymalna szerokość klatki piersiowej (T width). Wartość CTR uzyskiwano dzieląc zmierzoną wartość C width przez wartość T width. Przyjmując kryterium CTR >0.50 rozpoznawano powiększenie sylwetki serca.

Przezklatkową echokardiografię wykonywano za pomocą standardowego protokołu badania. Zmierzono wymiary światła i grubość ścian lewej komory serca: wymiar końcoworozkurczowy lewej komory (LVEDd), wymiar końcowoskurczowy lewej komory (LVESd), wymiar rozkurczowy przegrody międzykomorowej (IVSDd) oraz wymiar rozkurczowy ściany tylnej (PWDd). Wymiary światła i grubość ścian lewej komory posłużyły do estymacji masy mięśnia lewej komory (LVM), indeksu masy mięśnia lewej komory (LVMI) oraz względnej grubości ściany lewej komory (RWT).

Estymowane wartości LVMI i RWT wykorzystano jako kryteria klasyfikacji 4 typów zasadniczych geometrii lewej komory: prawidłowej geometrii (NG), przebudowy koncentrycznej (CR), przerostu koncentrycznego (CH) i przerostu ekscentrycznego (EH).

Badanie echokardiograficzne oraz radiogram klatki piersiowej wykonywano w możliwie jak najmniejszym odstępie czasu, nie dłuższym niż 7 dni.

Przerost lewej komory (LVH) dotyczył 84.4% badanych, u 49.0% badanych stwierdzono CR, u 15.6% badanych CH, a u 19.8% badanych EH. Badaną grupę charakteryzował CTR wynoszący 0.51 ± 0.04. Powiększenie sylwetki serca rozpoznano u 30.2% chorych.

Porównując podgrupy chorych wyodrębnione na podstawie kryterium CTR wykazano, że chorzy z powiększoną sylwetką serca na radiogramie klatki piersiowej w projekcji PA cechują się znamiennie częściej występowaniem przerostu lewej komory (LVH) w badaniu echokardiograficznym niż chorzy z prawidłową sylwetką serca. Chorych z powiększeniem sylwetki serca i chorych z prawidłową sylwetką serca różnicuje istotnie częstsze występowanie w pierwszej w tych podgrup przerostu koncentrycznego lewej komory.

Wyniki naszych badań wykazały, że CTR może być pomocnym wskaźnikiem w celu predykcji LVH zwłaszcza w podgrupie pacjentów z przerostem koncentrycznym. Podkreślić należy wysoką czułość, swoistość i dokładność przy zachowaniu warunku CTR>0,49. Na podstawie opracowanych danych można wnioskować, że każdorazowo CTR>0,49 powinien nieść za sobą konsekwencję dalszej inwestygacji dotyczącej zwłaszcza grubości ścian LV.

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WNIOSKI

1. Na podstawie analizy dotychczasowej literatury, przy zachowaniu świadomości jego ograniczeń, CTR może być używany w stratyfikacji ryzyka, ocenie leczenia czy rokowaniu w różnych schorzeniach serca i patologiach przebiegających z zajęciem serca.

2.1. U pacjentów z podejrzeniem zatorowości płucnej wtórnej do COVID-19, radiologiczny wskaźnik sercowo-płucny można uznać za czynnik prognostyczny dla powiększenia prawej komory.

2.2. Uwzględniając, że swoistość CTR jest znacznie wyższa niż jego czułość, szczególnie niższe wartości CTR mogą wskazywać na brak powiększenia prawej komory u pacjentów z COVID-19.

3.1. Radiologiczny wskaźnik sercowo-płucny może stanowić przydatny marker przerostu lewej komory ocenianego według standardowych kryteriów echokardiograficznych, pod warunkiem standaryzacji jego punktu odcięcia w danej populacji badanych.

3.2 Spośród ocenianych echokardiograficznie typów geometrii lewej komory, radiologiczny wskaźnik sercowo-płucny można z wysoką dokładnością predykcyjną uznać za marker przerostu koncentrycznego, a także w dalszej kolejności za marker przerostu ekscentrycznego lewej komory. Należy zachować dużą ostrożność przy predykcji remodelingu koncentrycznego lewej komory na podstawie wartości radiologicznego wskaźnika sercowo-płucnego.

STRESZCZENIE

Badanie radiologiczne klatki piersiowej w projekcji PA jest jednym z najczęściej zlecanych i wykonywanych wśród wszystkich badań radiologicznych. Radiogram klatki piersiowej jest szeroko stosowaną formą oceny płuc i śródpiersia w wielu dziedzinach medycyny m.in. w pulmonologii, pediatrii, onkologii, bywa wykorzystywany także jako badanie przesiewowe w ocenie wielkości sylwetki serca. Powszechnie używanym parametrem oceny wielkości sylwetki serca jest tzw. wskaźnik sercowo-płucny (CTR – cardiothoracic ratio), po raz pierwszy opisany już w 1919 r.

Wskaźnik sercowo-płucny określany jest jako stosunek największego poprzecznego wymiaru sylwetki serca do największego poprzecznego wymiaru klatki piersiowej mierzonego do wewnętrznych powierzchni żeber na radiogramie klatki piersiowej w projekcji PA. Parametr ten jest łatwy do wyznaczenia i nie wydłuża istotnie interpretacji obrazów radiologicznych, zwłaszcza przy możliwościach narzędziowych współczesnych przeglądarek obrazów DICOM. Za wartości prawidłowe uznaje się przedział pomiędzy 0,42 a 0,50. Wartość powyżej 0,50 jest uznawana za nieprawidłową i może świadczyć o kardiomegalii.

Celem badań była ocena zasadności dalszego stosowania CTR w przesiewowej ocenie powiększenia sylwetki serca, zwłaszcza w kontekście dokonującego się rozwoju technologicznego w medycynie, powszechnej dostępności echokardiografii i tomografii komputerowej oraz coraz większej dostępności rezonansu magnetycznego.

Niniejszą rozprawę doktorską stanowi cykl trzech artykułów naukowych składający się z jednej pracy przeglądowej oraz dwóch prac oryginalnych. W pracy przeglądowej dokonano analizy i syntezy dostępnych dotychczas doniesień naukowych dotyczących wskaźnika sercowo - płucnego. Na podstawie systematycznego przeglądu literatury wykazano, że CTR jako proste, tanie i szybkie narzędzie nadal pozostaje ważnym parametrem w ocenie pacjenta w wielu sytuacjach klinicznych. Przy zachowaniu świadomości jego ograniczeń, CTR może być używany w stratyfikacji ryzyka, ocenie leczenia czy rokowaniu w różnych schorzeniach, nie tylko bezpośrednio związanych z kardiologią. W kilku badaniach sygnalizuje się wątpliwości wiązania CTR z parametrami funkcji serca, zwłaszcza z frakcją wyrzutową lewej komory.

Na okres prowadzenia badań będących przedmiotem niniejszego cyklu publikacji nałożyła się pandemia COVID-19, stąd też w pierwszej pracy oryginalnej oceniano przydatność wskaźnika sercowo-płucnego jako potencjalnego predyktora powiększenia prawej komory serca u chorych

z podejrzeniem zatorowości płucnej w przebiegu COVID-19. Na podstawie uzyskanych wyników badań angiografii tomografii komputerowej tętnic płucnych wykazano, że u chorych z podejrzeniem zatorowości płucnej w przebiegu COVID-19, radiologiczny wskaźnik sercowo-płucny może stanowić przydatny predyktor powiększenia prawej komory serca.

W drugiej pracy oryginalnej dokonano analizy przydatności wskaźnika sercowo-płucnego jako potencjalnego markera przerostu lewej komory ocenianej metodą echokardiografii. Wykazano, że radiologiczny wskaźnik sercowo-płucny może stanowić umiarkowanie przydatny marker przerostu lewej komory ocenianego według standardowych kryteriów echokardiograficznych, pod warunkiem standaryzacji jego punktu odcięcia w danej populacji badanych. CTR można uznać z wysoką dokładnością predykcyjną przede wszystkim za marker przerostu koncentrycznego, w dalszej kolejności za marker przerostu ekscentrycznego; zachowując jednocześnie dużą ostrożność przy predykcji remodelingu koncentrycznego lewej komory.

Podsumowując, uzyskane wyniki badań wskazują na przydatność pomiarów wskaźnika sercowo-płucnego dokonywanych podczas oceny radiogramów klatki piersiowej w ocenie wielkości sylwetki serca w określonych sytuacjach klinicznych, co wpisuje się w dotychczas zebrane przez innych badaczy dane oparte o zasadę evidence-based medicine. Zasadne jest zatem rutynowe stosowanie oceny CTR podczas analizy radiogramów klatki piersiowej jako narzędzia diagnostycznego we wstępnej przesiewowej ocenie wielkości sylwetki serca, narzędzia w zasadzie niepodnoszącego kosztów, ani niezwiększającego obciążenia czasowego personelu.

SUMMARY:

Chest radiograph in PA projection is one of the most ordered and performed one among all the radiological examinations. Chest radiograph is a broadly used form of lung and mediastinum evaluation in many medical fields, e.g. in pulmonology, paediatrics, oncology, it is also used as a screening test in the assessment of the heart silhouette size. Cardiothoracic ratio (CTR), described first in 1919, is a commonly used parameter for assessing the heart silhouette size.

The cardiothoracic ratio is defined as the ratio of the largest transverse heart silhouette dimension to the largest transverse chest dimension, measured to the internal rib surface on a chest PA radiograph. This parameter is very easy to determine and does not prolong the interpretation of the radiological images in any significant way, especially considering the functional possibilities of the current DICOM image viewers. Values within the range of 0.42 and 0.50 are considered normal. Any value above 0.50 is deemed incorrect and may be a symptom of cardiomegaly.

The aim of the study was to assess the expediency of continuing the CTR for screening of enlarged heart silhouette, particularly in the context of the ongoing technological progress in medicine, common availability of echocardiography and computer tomography, as well as the increasing availability of magnetic resonance.

This doctoral dissertation is a cycle of three scientific articles consisting of one review study and two original studies. The review article presents an analysis and synthesis of the scientific reports on the cardiothoracic ratio, available at the time. Based on a systematic literature overview, it was demonstrated that the CTR, as s simple, low-cost and fast tool, remains an important parameter for patient assessment in numerous clinical situations. If the limitations of this method are kept in mind, the CTR can be used in risk stratification, treatment assessment or prognosticating in various ailments, not only those directly related to cardiology. Several studies indicate doubts regarding the association between the CTR and cardiac function parameters, particularly left ventricular ejection fraction.

The studies which are the subject of this cycle of publications coincided with the COVID-19 pandemic, which is why the first original article assessed the usefulness of the cardiothoracic ratio as a potential predictor for the right ventricle enlargement in patients with suspected pulmonary embolism secondary to COVID-19. Based on the results of CT angiography of the pulmonary arteries, it was demonstrated that in patients with suspected pulmonary embolism secondary to

COVID-19, the radiological cardiothoracic ratio can be a useful predictor for the right cardiac ventricle enlargement.

The second original article analysed the usefulness of the cardiothoracic ratio as a potential marker for left ventricle hypertrophy assessed via echocardiography. It was demonstrated that the radiological cardiothoracic ratio may be a moderately useful marker for left ventricle hypertrophy assessed using standard echocardiography criteria, provided that its cut-off point in the given population of subjects is standardized. The CTR can be considered, with a high predictive accuracy, mainly a marker for concentric hypertrophy, then a marker for eccentric hypertrophy, while exercising caution when predicting concentric remodelling of the left ventricle.

To sum up, the results of the studies indicate that measurement of the cardiothoracic ratio made in chest radiographs is useful for assessing the heart silhouette size in specific clinical situation, which concurs with the data collected by others research based on the principle of evidence-based medicine. Therefore, it is expedient to routinely use the CTR assessment when analysing chest radiographs as a diagnostic tool in preliminary screening of the heart silhouette size, as, essentially, this tool neither increases the costs nor does it increase the burden of time for the staff.

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WYKAZ PUBLIKACJI WŁĄCZONYCH DO ROZPRAWY DOKTORSKIEJ

1. **Radiological cardiothoracic ratio in evidence-based medicine.**

   KRYSTIAN TRUSZKIEWICZ, RAFAŁ PORĘBA, PAWEŁ GAĆ. *J.Clin.Med.* 2021 Vol.10 no.9 art.2016 [9 s.], ryc., IF:4,242, MNiSW 140,00

2. **Radiological cardiothoracic ratio as a potential predictor of right ventricular enlargement in patients with suspected pulmonary embolism due to COVID-19.**

   KRYSTIAN TRUSZKIEWICZ, MAŁGORZATA PORĘBA, RAFAŁ PORĘBA, PAWEŁ GAĆ. *J.Clin.Med.* 2021 Vol.10 no.23 art.5703 [15 s.], ryc., tab., IF 4,242, MNiSW 140,00

3. **Radiological cardiothoracic ratio as a potential marker of left ventricular hypertrophy assessed by echocardiography.**

   KRYSTIAN TRUSZKIEWICZ, PIOTR MACEK, MAŁGORZATA PORĘBA, RAFAŁ PORĘBA , PAWEŁ GAĆ *Radiol Res Pract*. 2022;2022:4931945. IF -0.00, MNiSW: 70 pkt

PRACA NR 1

Journal of Clinical Medicine

MDPI

Review

Radiological Cardiothoracic Ratio in Evidence-Based Medicine

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Abstract: The cardiothoracic ratio (CTR), expressing the relationship between the size of the heart and the transverse dimension of the chest measured on a chest PA radiograph, is a commonly used parameter in the assessment of cardiomegaly with a cut-off value of 0.5. A value of >0.5 should be interpreted as enlargement of the heart. The following review describes the current state of available knowledge in terms of contentious issues, limitations and useful aspects regarding the CTR. The review was carried out on the basis of an analysis of scientific articles available in the PubMed database, searched for using the following keywords: "CTR", "cardiothoracic ratio", "cardiopulmonary ratio", "cardiopulmonary index", and "heart-lung ratio". According to the accumulated knowledge, the CTR can still be used as an important parameter that can be easily determined in establishing enlargement of the heart. However, an increased CTR does not directly relate to heart function. In the era following the development of diagnostic methods such as computed tomography, magnetic resonance imaging, and ultrasonography, CTR modifications based on these methods are used with varying clinical usefulness. It is important to consider the definition of the CTR and remember to base measurements on PA radiographs, as attempts to mark it in other projections face many limitations.

Keywords: cardiothoracic ratio; chest radiography; heart enlargement

Citation: Truszkiewicz, K.; Poręba, R.; Gać, P. Radiological Cardiothoracic Ratio in Evidence-Based Medicine. *J. Clin. Med.* **2021**, *10*, 2016. https://doi.org/10.3390/jcm10092016

Academic Editor: Patrick Martineau

Received: 18 March 2021
Accepted: 5 May 2021
Published: 8 May 2021

1. Introduction

A chest PA examination, apart from its usefulness in oncology, pulmonology, pediatrics, etc., is also used as a screening tool to assess the size of the heart's silhouette. A commonly used parameter for the heart's evaluation is the cardiothoracic ratio (CTR), first described in 1919 [1]. The cardiothoracic ratio is defined as the ratio of the greatest transverse dimension of the heart to the greatest transverse dimension of the chest cavity measured to the inner surface of the ribs on the PA radiograph [1] (Figure 1). This parameter is easy to determine and does not significantly extend the interpretation of X-ray images, especially with the capabilities of modern DICOM image viewer tools, which may be one of the reasons for not adopting the automatic CTR measurement method [2]. Normal values range between 0.42 and 0.50, which should not be presented as a percentage, but as a ratio. A value above 0.50 is considered abnormal and may indicate cardiomegaly [3]. Unfortunately, when assessing the cardiac silhouette on a chest radiograph, it can be difficult to distinguish true enlargement of the heart from enlargement as a result of pericardial disease (e.g., effusion). Despite this, the universality of the CTR in various populations can be proved, for example, a study conducted in Ghana on a group of almost 2000 patients demonstrated that the mean (normal) CTR in the population was <0.5. According to the investigators, the mean CTR for their study population was 0.452. The researchers also found a difference in the mean CTR value for women (0.467) and men (0.459) and established its variability with age (the index increases with age). Patients also showed an increase in chest width until the sixth decade of life, after which this index decreased [4].

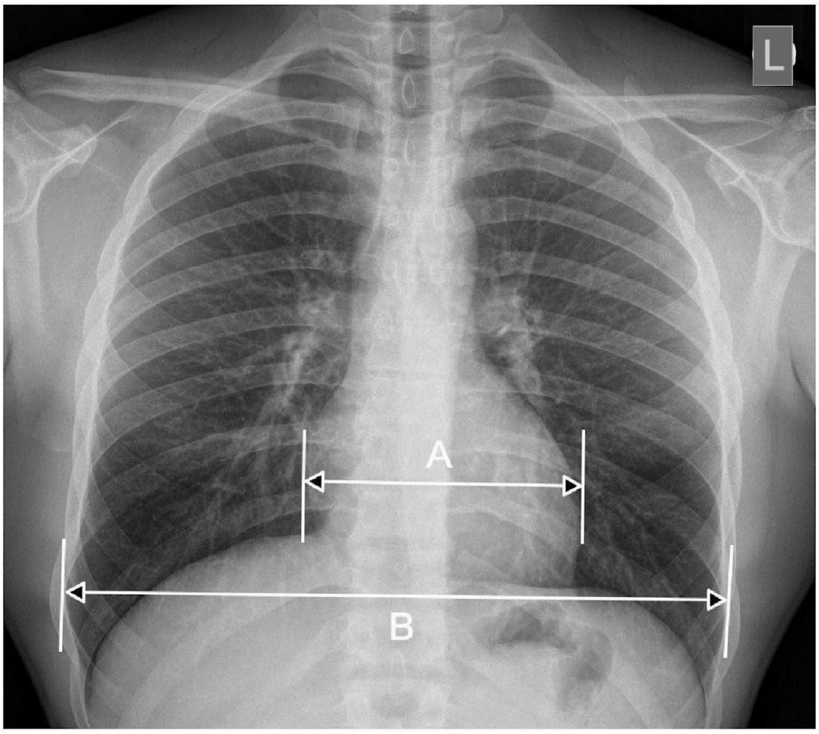

Figure 1. The method of determining the CTR. The CTR is determined on the basis of the ratio of the transverse heart dimension [A] to the transverse dimension of the chest (internal ribs) [B] measured on the radiograph in the chest PA projection: CTR = A/B.

The assessment of the heart's silhouette on a chest radiograph, in addition to the CTR mentioned above, may allow us to obtain additional, clinically useful information at a much lower dose of ionizing radiation (between 80 and 100 times) compared with computed tomography. Assessing the silhouette of the heart enables, among others suspicion of aortic dilatation, information about the presence of rings of implanted valves, calcifications in the projection of the valve fields, assessment of the position of pacemaker electrodes, etc. Additionally, it should be remembered that chest radiographs are not performed only to determine the CTR; it is determined along with other diagnostic purposes of the study.

2. CTR—The Importance of Radiograph Projection

The cardiothoracic ratio should only be determined by a PA radiograph projection. Although in the literature we find appropriate values of the coefficient, for example, for the AP projection [5], we should approach them with care and be aware of their limitations [5]. Chest radiograph, and thus also CTR determination, is an easy and beneficial parameters in patient assessment in hospital emergency departments (HEDs) and in the course of treatment and patient care in intensive care units (ICUs) [6]. The clinical condition of such patients, however, often does not allow for the execution of a chest radiograph in the PA projection, which is most often substituted with bedside examinations of the AP projection. We must remember the basic limitations related to determining the CTR in such clinical situations. First, the width of the heart, located in the mediastinum closer to the anterior chest wall, is greater if the X-ray beam is directed from the front to the rear. Secondly, the distance between the radiation source (lamp) and the detector (cassette) is shorter than when taking PA radiographs (for PA radiographs, approx. 180–200 cm) [7], which results in the obtained radiograph enlarging both the silhouette of the heart and the transverse dimensions of the chest. Thirdly, the clinical condition of such patients often does not allow them to perform a full inhalation or to maintain it for an appropriate time, which results in unreliable measurements of the transverse dimensions of the chest [8]. It should also be remembered that the conditions for producing bedside radiographs are highly variable.

The above-described variables and the inconvenience in determining the CTR via AP radiographs were reflected in numerous research studies that sought methods to determine this easy parameter. Chon et al. [8] proposed the corrected CTR, calculated from the formula they proposed. However, this measurement requires access to a patient's prior PA radiograph, and the sensitivity and specificity of this measurement were determined to be 61% and 54%, respectively. The study was also limited by the small validation group (18 patients with echocardiographic features of heart failure and 17 without such features).

Kabala and Wilde [9] proposed, based on the results of their work (and on a tomographic and radiographic model), to define the enlargement of the heart silhouette based on AP radiographs as CTR > 55% and the width of the heart shape >165 mm for men and 150 mm for women (sensitivity 92%, specificity 96%). A limitation of this study was the selection of the group. The researchers selected people with histories suggesting symptoms of heart failure, including their radiological features, and the results were not correlated with other diagnostic methods, e.g., echocardiography.

3. CTR—The Meaning of the Breathing Phase, the Anterior-Posterior Heart Dimension

Another variable that significantly affects the CTR value is the respiratory phase; the silhouette of the heart is larger during exhalation and smaller if the radiograph of the same patient is taken during inspiration. The dimensions of the chest are also variable in both breathing phases, but the work of Tomita et al. [10], based on the multi-parameter study of the dimensions of the chest and heart silhouette, the computed tomography of the chest in inspiration and exhalation, and the determination of the CTR in both phases, proved that the developed CTR under these conditions is significantly higher ($p < 0.0001$) in exhalation than in inspiration. This indirectly proves a significant disproportion of changes in lung size and the cardiac silhouette during respiratory phases, and emphasizes the importance of the pre-evaluation of data prior to CTR determination. These data are also confirmed in populations of children. The textbook Pediatric Radiology [11] describes significant changes in the size of the heart silhouette depending on the respiratory phase, using the example of computed tomography of the chest performed on a crying child. As in the adult population, the CTR was higher during exhalation and significantly lower during inspiration. Due to the inability to hold breath in the population of newborns, infants, and young children, the CTR is of limited value in the diagnosis and evaluation of congenital heart defects associated with enlargement. The situation is quite different for the adult population with congenital heart disease undergoing repair surgery. In a group of over 3000 adults with congenital heart disease, the CTR was shown to be a simple, reproducible factor correlating with cardiac function and may be an independent predictor of long-term mortality [12].

The CTR is determined (according to its definition) on the basis of a flat chest PA radiograph. Assessment of cardiomegaly on the basis of the CTR may not always be appropriate due to the inability to account for changes in the anterior-posterior heart size and changes in the long axis of the heart. Researchers from Japan [13] showed that the CTRs in these patients is influenced by the transverse rotation of the heart in the counterclockwise dimension. Such rotation cannot be reliably assessed on a flat radiograph, and the study did not find an appropriate method of including it in the CTR assessment literature. In the 25 year prospective Whitehall Study, researchers added heart measurements in three axes to the classic measurement of the CTR: the long axis, the broad axis determined on the PA radiograph, and the horizontal axis determined in the anterior-posterior dimension on the radiograph in the profile projection. Using the obtained values in an appropriate mathematical algorithm, they determined the heart volume and correlated it with the body surface of the relative heart volume [14], (Figure 2). The study concluded that there was no higher value of the relative heart volume and thus determined the classical CTR for predicting mortality from ischemic heart disease [14].

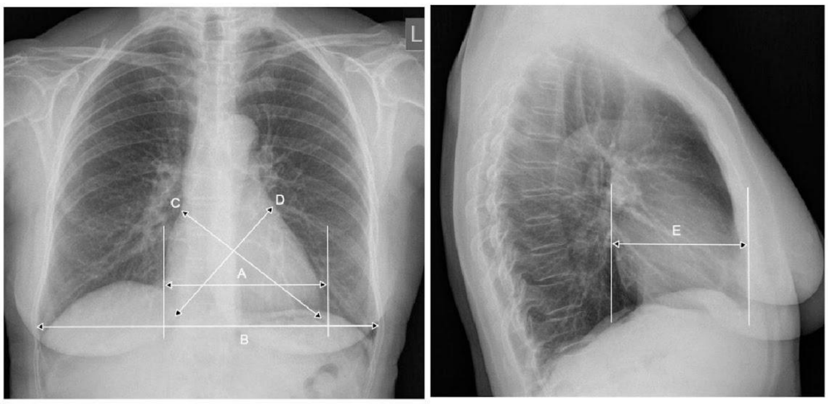

Figure 2. Additional parameters taken into account in determining the heart volumes in the Whitehall Study: A—the transverse dimension of the heart, B—the transverse dimension of the chest, C—the long axis of the heart, D—the broad axis of the heart, and E—the horizontal axis of the heart.

4. CTR as a Prognostic Factor

The CTR was found to be one of the prognostic factors in several groups of diseases. An example is the population of people undergoing hemodialysis. A large, prospective, cohort study on a group of almost 3500 people with a four-year follow-up showed that in people undergoing hemodialysis, a higher CTR is associated with a higher risk for both general and cardiovascular reasons [15].

In an animal model, it was shown that chronic vitamin D deficiency is associated with myocardial remodeling, leading to fibrosis, myocardial hypertrophy, myocarditis, and heart systolic disorders. Based on these observations, a study was conducted on a group of chronic hemodialysis patients to assess the impact of vitamin D deficiency in conjunction with CTR determination on the prognosis in this group. The study found that the CTR was higher in patients with vitamin D deficiency, and may be an independent prognostic factor of vitamin D deficiency in this group of patients [16].

It was also shown in the group of hemodialysis patients that a CTR > 55% is one of the most important independent factors influencing the two-year all-cause mortality rate [17]. Hence, the suggestion to analyze the heart condition in patients at the start of hemodialysis. In a large group of almost 1800 people with a four-year follow-up, the CTR as a simple factor was shown to be a good prognostic factor for poor prognosis in patients with rheumatic heart disease undergoing heart valve replacement surgery. A baseline CTR > 0.6 was shown to be an independent, poor prognostic factor for death during perioperative hospitalization and during the first year following valve replacement [18].

5. CTR and Heart Function

At the time of the development of the CTR, and for many years of its use, values > 0.5 were interpreted not only as enlargement of the heart but also as impaired heart function (left and/or right ventricle). Interesting conclusions were drawn by researchers from London, who related the CTR measured on radiographs of PA and AP to the measurement data obtained in echocardiography in patients treated in the emergency mode. The first conclusions were similar to those described several times above and concern a limited CTR value determined on AP radiographs; the researchers demonstrated that this a CTR was not correlated with left or right ventricular dysfunction. According to the researchers, the CTR determined on the PA radiograph has moderate sensitivity and specificity but low positive predictive value in the diagnosis of right or left ventricular systolic disorders. The researchers highlighted the problem of a lack of correlation between a "big heart" and its dysfunction. This is probably due to the development of diagnostics and the implementation of prior treatment; therefore, a large heart cannot be equated to a heart with the presence of dysfunction [19]. It is important to know whether the CTR may normalize or decrease with the introduction of treatment and whether the CTR may be a prognostic factor in this situation. Breur et al. assessed the effect of pacemaker therapy in patients with isolated congenital total atrioventricular block. The following were taken as heart size markers: the left ventricular end-diastolic diameter (LVEDD), the left ventricular shortening fraction (FS), and the CTR. The study showed that in patients without pacemaker implantation, CTR increases by 0.02%/month, and in patients with pacemakers, it decreases by 0.19%/month; the difference was statistically significant. It was proven that early pacemaker implantation results in a reduction in the size of the heart, also in the assessment of the CTR. The conclusion was that the progressive increase or persistently high CTR (and LVEDD) values in asymptomatic patients should be taken into account when implanting an electrostimulator in order to avoid the development of congestive heart failure [20].

Researchers from Ireland tried to link the classical one-dimensional CTR and their two-dimensional CTR with the left ventricular ejection fraction [21]. The 2D CTR was defined as the ratio of the number of pixels covering a previously determined area of the heart (the cardiac area) to the number of pixels covering the surface of the lung fields and the middle shadow (the whole thorax area) (Figure 3). The ejection fraction was determined by radioisotope studies. The researchers demonstrated a strong correlation between the classic CTR and 2D CTR ($r = 0.82$); however, on comparing both coefficients with the left ventricular ejection fraction, they concluded that an increased 2D CTR better correlated with a reduced ejection fraction ($r = -0.52$) than the classic CTR ($r = -0.45$). They proposed a value of a 0.23 2D CTR (or a ratio of 1/4) or less as the correct value, which should indirectly indicate a fraction of $\geq$55%.

On the basis of computed tomography studies, it was shown that the size of the left ventricle can be more accurately predicted on the basis of a simple and highly reproducible measurement of the left ventricular surface on axial chest computed tomography scans than on the CTR [22]. Images for measurements of the left ventricular surface were obtained in two groups: gated ECGs of CT examinations with contrast enhancement and gated ECGs of examinations without the use of a contrast agent; CTR measurement was performed on topographic scans. Despite the good and repeatable results of measurements of the left ventricular parameters thus obtained, the method of its determination should be considered a limitation when comparing them with the CTR (the limitations of the CTR determined in this way are described later in this study).

However, it was shown that a baseline CTR > 0.5 in patients with chronic heart failure is associated with higher mortality and higher hospitalization rates, and a routine PA radiograph along with CTR measurement was indicated as an important part of the management of such patients. The CTR in this case can be used as a value to stratify cardiovascular risk [23].

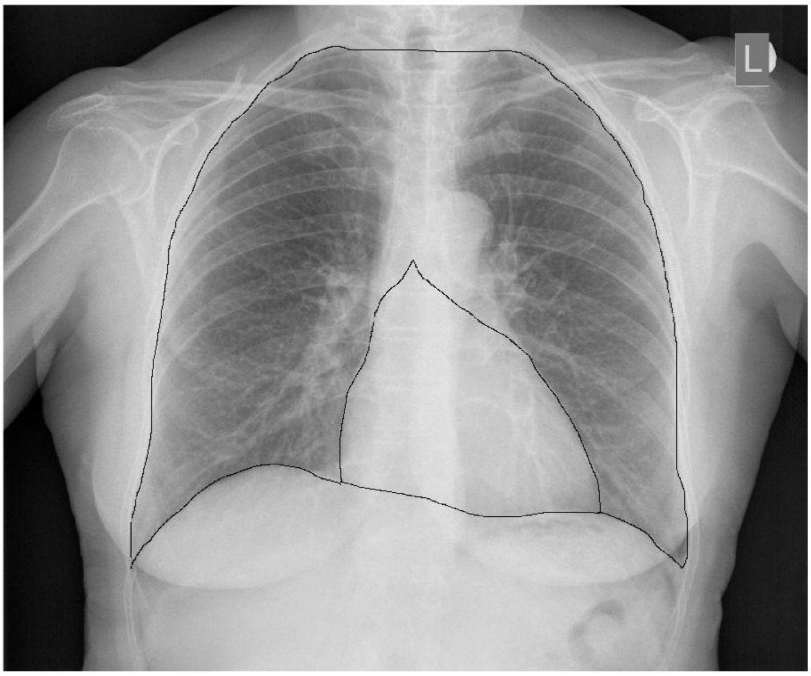

Figure 3. Demarcation lines delineating the surface areas used to determine the 2D CTR.

6. CTR in the Pediatric Population

Due to the above-described limitations of the use of the CTR in children, there are several studies investigating this problem in the literature.

Canadian researchers from Toronto conducted a retrospective study of 127 children (mean age 11.2 ± 5.5 years) with the most common structural and myopathic congenital myocardial defects, in which they checked the correlation of the CTR with the volume of the heart cavities measured by magnetic resonance [24]. It was shown that a higher CTR is associated with an increased total heart volume in children with aortic and pulmonary valve insufficiency; however, significant differences in the volume of individual chambers and the size of the CTR limit its use in monitoring the patient's heart condition. The CTR did not correlate with ventricular volumes in patients with left-right shunt and hypertrophic cardiomyopathy (HCM). In recent cases, the additional coefficient determined on the lateral radiograph did not offer additional value in assessing the size of the heart.

In an interesting case report of an eight-year follow-up on a girl with isolated congenital complete atrioventricular block (ICCAVB) with long-term serum NT-proBNP measurement in conjunction with CTR measurement [25], the girl was born by caesarean section in the 36th week of pregnancy due to abnormal HR values, and then she was diagnosed with ICCAVB, without the need for pacemaker implantation. NT-proBNP is one of the end products (with biologically active BNP) of pre-proBNP metabolism, released by the muscle cells of the heart ventricles when their stress increases (overload or volume). It became natural to associate it with the CTR, which is also used to assess patients with heart failure. In the described case, a large positive correlation was found between the CTR and the level of NT-proBNP in the serum ($p < 0.05$). As a conclusion, it was proposed that in children with ICCAVB, measuring the CTR during their follow-up cab be a useful tool in assessing the load on the heart.

The CTR measurement was found to have a role during the fetal stage. Obstetricians from Thailand performed CTR measurements using ultrasound in fetuses from pregnancies at risk of Bart's hemoglobin disease and demonstrated that such measurements have a great prognostic value [26]. Researchers demonstrated a significant increase in the CTR in affected fetuses during the late first/early second trimester of pregnancy. They showed the 13th week of pregnancy as the median increase in the CTR, and all fetuses with the disease were selected up to 23 weeks of gestation. The study also assessed the flow parameters of the middle cerebral artery (MCA-PSV) and showed that only slightly more than 9% of the fetuses developed abnormal flow in this artery before the CTR increased. The conclusion drawn was that the discovery will help identify Bart's hemoglobin disease in earlier pregnancy and, therefore, more appropriate individualized pregnancy ultrasound regimens can be developed.

Another example of the use of a modified form of CTR in fetal life is the prediction of lethal obstruction of the pulmonary veins in fetuses diagnosed by prenatal ultrasound of a single ventricle with the coexistence of total abnormal pulmonary vein connection (TAPVC). Researchers from Japan using the cardiothoracic area ratio (CTAR), calculated as the ratio of the heart area to the thoracic area on the ultrasound data, showed that a reduced prenatal CTAR is a good predictor of lethal obstruction of the pulmonary veins after birth [27]. Such information allows time for the preparation of parents and, above all, for the development of an appropriate procedure to follow after the birth of a child with this syndrome of defects.

7. Post-Mortem Examinations—An Attempt to Evaluate CTR

The CTR is also applicable in autopsy. A benefit of such studies is the negligible harmful effect of ionizing radiation on the study group. Researchers from Switzerland, based on post-mortem computed tomography studies, proposed the new CTR formula for the diagnosis of cardiomegaly [28]. In determining the new CTR formula, apart from heart and chest measurements in axial scans of computer tomography, researchers took into account several additional variables: BMI, age, and sex. Thus, they developed a special mathematical formula: Score = 25 $\times$ CTR + 3 $\times$ sex + 1 $\times$ age/5 (years) + 0.2 $\times$ BMI. They proposed a CTR score $\geq$32 as the cut-off point, which allows for the diagnosis of cardiomegaly. To facilitate the calculations, an online calculator was offered (http://calc.chuv.ch/CTR (accessed on 8 May 2021)). The values calculated in this way are characterized by 84.04% sensitivity, 78.79% specificity, and 81.87% of correctly classified cases.

The researchers came to an interesting conclusion on the basis of earlier post-mortem CT research. They found large discrepancies in the CTR measurements on the CT pilot images and the measurements on the axial chest scans performed. Their conclusions indicated a very large upward overestimation of the CTR in the pilot CT scans; hence, these should not be trusted [29].

8. Conclusions

As demonstrated in the review above, the CTR as a simple, cheap, and quick tool still remains an important parameter in patient assessment in many clinical situations. In many cases, it has been shown that an increased CTR may be a good, initial parameter of the heart size preceding a more accurate assessment of the size of the heart and its cavities in echocardiography, computed tomography (increasingly available, but burdened with a much higher dose of ionizing radiation) and magnetic resonance imaging [30]. When aware of its limitations, it can be used in risk stratification, treatment assessment, or prognosis in various diseases, not only directly related to cardiology. Although it may seem that in 2021 talking about the clinical usefulness of the CTR may be an anachronism (mainly due to its low negative predictive value), according to the authors, given the discussed literature data, further research on the CTR is needed, especially regarding the comparison of the CTR with data from rapidly developing diagnostic methods such as multislice computed tomography and magnetic resonance imaging.

Author Contributions: Conceptualization, R.P. and P.G.; resources, K.T. and P.G.; writing—original draft preparation, K.T.; writing—review and editing, R.P. and P.G.; visualization, K.T.; supervision, P.G.; funding acquisition, P.G. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding. The APC was funded by Wroclaw Medical University.

Conflicts of Interest: The authors declare no conflict of interest.

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Radiological Cardiothoracic Ratio as a Potential Predictor of Right Ventricular Enlargement in Patients with Suspected Pulmonary Embolism Due to COVID-19

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Abstract: The aim of the study was to determine the usefulness of the radiological cardiothoracic ratio (CTR) as a predictor of right ventricular enlargement in patients with suspected pulmonary embolism during COVID-19. The study group consisted of 61 patients with confirmed COVID-19, suspected of pulmonary embolism based on physical examination and laboratory tests (age: 67.18 ± 12.47 years). Computed tomography angiography (CTA) of pulmonary arteries and chest radiograph in AP projection with cardiothoracic ratio assessment were performed in all patients. Right ventricular enlargement was diagnosed by the ratio of right ventricular to left ventricular (RV/LV) dimensions in pulmonary CTA with two cut-off points: ≥0.9 and ≥1.0. Heart silhouette enlargement was found when CTR on the chest radiograph in the projection AP > 0.55. The mean values of RV/LV and CTR in the studied group were 0.96 ± 0.23 and 0.57 ± 0.05, respectively. Pulmonary embolism was diagnosed in 45.9%. Right ventricular enlargement was documented in 44.3% or 29.5% depending on the adopted criterion RV/LV ≥ 0.9 or RV/LV ≥ 1.0. Heart silhouette enlargement was found in 60.6%. Patients with confirmed pulmonary embolism (PE+) had a significantly higher RV/LV ratio and CTR than patients with excluded pulmonary embolism (PE−) (RV/LV: PE+ 1.08 ± 0.24, PE− 0.82 ± 0.12; CTR: PE+ 0.60 ± 0.05, PE− 0.54 ± 0.04; $p < 0.05$). The correlation analysis showed a statistically significant positive correlation between the RV/LV ratio and CTR (r = 0.59, $p < 0.05$). Based on the ROC curves, CTR values were determined as the optimal cut-off points for the prediction of right ventricular enlargement (RV/LV ≥ 0.9 or RV/LV ≥ 1.0), being 0.54 and 0.55, respectively. The sensitivity, specificity, and accuracy of the CTR criterion >0.54 as a predictor of RV/LV ratio ≥0.9 were 0.412, 0.963, and 0.656, respectively, while those of the CTR criterion >0.55 as a predictor of RV/LV ratio ≥1.0 were 0.488, 0.833, and 0.590, respectively. In summary, in patients with suspected pulmonary embolism during COVID-19, the radiographic cardiothoracic ratio can be considered as a prognostic factor for right ventricular enlargement, especially as a negative predictor of right ventricular enlargement in the case of lower CTR values.

Keywords: cardiothoracic ratio; chest radiograph; computed tomography angiography; COVID-19; pulmonary embolism; right ventricular enlargement

Citation: Truszkiewicz, K.; Poręba, M.; Poręba, R.; Gać, P. Radiological Cardiothoracic Ratio as a Potential Predictor of Right Ventricular Enlargement in Patients with Suspected Pulmonary Embolism Due to COVID-19. *J. Clin. Med.* **2021**, *10*, 5703. https://doi.org/10.3390/jcm10235703

Academic Editor: Patrick Martineau

Received: 24 October 2021
Accepted: 2 December 2021
Published: 4 December 2021

1. Introduction

The virus SARS-CoV-2 causes a complex of symptoms of a viral respiratory infection, in severe cases causing acute respiratory failure and death [1]. During the pandemic, patients started demonstrating numerous complications other than strictly respiratory ones, e.g., concerning the nervous, vascular, and cardiopulmonary system [2,3]. The literature provides numerous reports regarding a series of cardiovascular complications secondary to COVID-19 [4,5]. Well-recognized cardiac manifestations of COVID-19 are heart damage secondary to cardiac ischemia and/or myocardial infarction as well as myocarditis [6–8]. Others include arrhythmias, cardiogenic shock and cardiomyopathy [6]. Another issue related to the COVID-19 infection is the frequent occurrence of pulmonary embolism and deep vein thrombosis, more common than in the course of other viral infections (e.g., the H1N1 flu virus) [9,10]. Meta-analysis demonstrated respectively 16.5% and 14.8% occurrence of acute pulmonary embolism and deep vein thrombosis in patients infected with COVID-19, whereas more than a half of the patients with pulmonary embolism did not suffer from deep vein thrombosis [11].

In its natural course, pulmonary embolism causes more or less intensive overload of the right cardiac ventricle. It is estimated that about 45% patients with acute pulmonary embolism will develop right ventricular insufficiency [12], and as much as 3.8% of them will develop chronic thromboembolic pulmonary hypertension [13]. The right ventricular insufficiency develops because of increased secondary load caused by pulmonary artery occlusion. Once the compensation mechanisms of the right ventricle are exceeded, the right ventricle becomes enlarged and the right ventricular projection is further decreased, leading to a reduced supply of the myocardium with oxygenated blood and ischemia [14].

Apart from the pulmonary embolism, the right ventricular enlargement may cause pulmonic valve stenosis, pulmonary hypertension, arterial and/or ventricular septal defects, tricuspid valve regurgitation, hypertrophic cardiomyopathy, congenital defects, etc. An assessment of the RV size and functions can be made via echocardiography, computed tomography and magnetic resonance [15–17]. Although very useful, in COVID-19 infected patients, the echocardiography methods should not be used routinely, due to the risk of transmitting the infection to the personnel. On the other hand, high concurrence of CT and MR measurements is emphasized [16,17].

A test of choice, characterized by high sensitivity and specificity for diagnosing acute pulmonary embolism is pulmonary artery computed tomography angiography (CTA) [18]. Apart from assessment of the pulmonary embolism itself, the test can be used to evaluate RV enlargement, the morphology of the interventricular septum, etc. An additional, important parameter that can be specified in the pulmonary artery CTA is the RV/LV ratio. This parameter is defined as the ratio of the maximum RV dimension to the corresponding LV dimension, measured from endocardium to endocardium on axial CTA scans, which are the closest to a four-chamber projection, or a reconstructed four-chamber projection. Values of more than 0.9 are considered abnormal [19], and they signify a considerably higher risk of an adverse course of the embolism. It is emphasized that this ratio is highly sensitive (about 92%) for the evaluation of right ventricle insufficiency, and it was considered an independent predictor for a poor prognosis in PE patients [20]. The value of this ratio in the risk stratification for PE patients is also emphasized by the 2019 guidelines issued by ESC and ERS, concerning the diagnostics and treatment in acute pulmonary embolism [21]. Additionally, a large meta-analysis, also cited by the aforesaid guidelines, indicates that a ratio of RV/LV $\geq$ 1.0 involves a 2.5-fold increase in the risk of death for any reason and a 5-fold increase in the risk of PE-related death [22].

The cardiothoracic ratio is an easy to calculate indicator in the assessment of myocardial enlargement. It is defined as the ratio of the largest transverse heart dimension to the largest transverse chest dimension, measured to the internal rib surface on a chest radiograph [23]. Any value above 0.50 is considered incorrect and may be a sign of cardiomyopathy [24]. Values > 0.55 were considered incorrect for radiographs in the AP projection [25,26], which, in relation to the health condition of patients hospitalized with acute respiratory failure secondary to COVID-19, is the basic radiographic projection.

The purpose of the study was to determine the usefulness of the cardiothoracic ratio (CTR) as a predictor of right ventricular enlargement in patients with suspected pulmonary embolism secondary to COVID-19.

2. Materials and Methods

The study group consisted of 61 patients with confirmed COVID-19, in which pulmonary embolism was suspected based on a physical examination and laboratory tests. Group size was determined using a sample size calculator. The selection conditions were as follows: population size 2 million, fraction size 0.2, maximum error 10%, confidence level 95%. The required minimum size of the study group was 61. The criteria of inclusion in the study were as follows: age $\geq$ 18 years, a positive result of a nasopharynx smear test against SARS-CoV-2 (detected presence of the N2 gene for SARS-CoV-2 and/or the E gene for *Betacoronaviridae* using the qRT-PCR method), an increased concentration of D-dimers in the blood, a clinically indicated CTA of the pulmonary arteries and an AP chest radiograph performed within 48 h. The criteria of exclusion in the study were as follows: an ambiguous result of the pulmonary artery CTA scan, a diagnosed pulmonary or mediastinal carcinoma, large amounts of fluid in the pleural cavity/cavities, fluid present in the pericardial sac. The anthropometric parameters of the study group of patients are presented in Table 1.

Table 1. General characteristics of the study group.

	X	SD
age [years]	67.18	12.47
BMI [kg/m^2]	28.11	3.84
	%	**n**
gender		
men	63.9	39
women	36.1	22
age		
<60 years	16.4	10
≥60 years	83.6	51
body mass		
normal	22.9	14
overweight	50.8	31
obesity	26.2	16
comorbidities		
a history of myocardial infarction	14.7	9
a history of stroke	13.1	8
arterial hypertension	24.6	15
peripheral arterial disease	9.8	6
diabetes	11.5	7
a history of cancer	13.1	8
COPD	14.7	9
asthma	4.9	3
stomach and duodenal ulcers	4.9	3
chronic kidney disease	3.3	2
hypothyroidism/hyperthyroidism	8.2	5
osteoporosis	13.1	8

BMI—body mass index; COPD—chronic obstructive pulmonary disease; n—number; SD—standard deviation; X—mean.

The studies were performed in one clinic treating patients hospitalized for COVID-19 and its complications. The study was performed in the first half of 2021.

At subsequent stages, the study group was divided into subgroups, following the criteria of age, BMI, gender, enlarged heart silhouette in chest radiograph as well as enlarged right ventricle, and diagnosed pulmonary embolism in the CTA. The criteria for distinguishing the study subgroups and the sizes of the subgroups are listed in Table 2.

Table 2. Criteria for distinguishing the study subgroups.

Differentiating Variable	Selection Criterion	Subgroup	Size of the Subgroup
age	median age (71 years)	A: ≥71 years B: <71 years	A: 33 B: 28
BMI	upper limit of the normative value (25 kg/m^2)	C: overweight/obesity (≥25 kg/m^2) D: normal body mass (<25 kg/m^2)	C: 47 D: 14
gender		E: men F: women	E: 39 F: 22
enlargement of the heart silhouette	cardiothoracic ratio (CTR) on chest radiograph in antero-posterior projection > 0.55	G: enlarged heart silhouette (CTR > 0.55) H: non-enlarged heart silhouette (CTR ≤ 0.55)	G: 37 H: 24
enlargement of the right ventricle	right ventricle diameter to left ventricle diameter ratio (RV/LV) in CTA ≥ 0.9	I: enlarged right ventricle (RV/LV ≥ 0.9) J: non-enlarged right ventricle (RV/LV < 0.9)	I: 27 J: 34
	right ventricle diameter to left ventricle diameter ratio (RV/LV) in CTA ≥ 1.0	K: enlarged right ventricle (RV/LV ≥ 1.0) L: non-enlarged right ventricle (RV/LV < 1.0)	K: 18 L: 43
pulmonary embolism	presence of embolic material in pulmonary arteries on CTA	M: confirmed pulmonary embolism N: excluded pulmonary embolism	M: 28 N: 33

BMI—body mass index; CTA—computed tomography angiography.

The study was performed as part of the research project titled "Radiologic cardiothoracic ratio as a predictor for the size of the heart estimated via echocardiography, computer tomography and magnetic resonance", approved by the local bioethical committee (KB-414/2021).

The methodology of the study comprised an analysis of the basic anthropometric parameters and the following diagnostic images: AP chest radiograph (CR) and computed tomography angiography (CTA) of the pulmonary arteries.

According to the adopted criteria of inclusion in the study, the interval between the pulmonary artery CTA and the AP chest radiograph did not exceed 48 h. In case more than one CR was acquired within 48 h before or after the pulmonary artery CTA, the analysis was performed using the chest radiograph acquired within the shortest interval from the pulmonary artery CTA.

On account of the clinical condition of the patients, chest radiographs were acquired in the lying position, in the anterior–posterior projection (AP), using a bedside X-ray machine. Radiographs were acquired, as far as possible, while the patient was holding their breath, with maximum inhalation, using the X-ray lamp set at 120 kV.

The cardiothoracic ratio (CTR) was assessed using a diagnostic station conforming to the legal regulations for radiologic tests. The maximum cardiac width (C width) and the maximum thoracic width (T width) were measured. The value of the cardiothoracic ratio was calculated using the following formula: CTR = C width/T width. Enlargement of the heart silhouette was diagnosed if, in the AP chest radiograph, the CTR > 0.55. An example of the CTR measurement in the AP chest radiograph is presented in Figure 1.

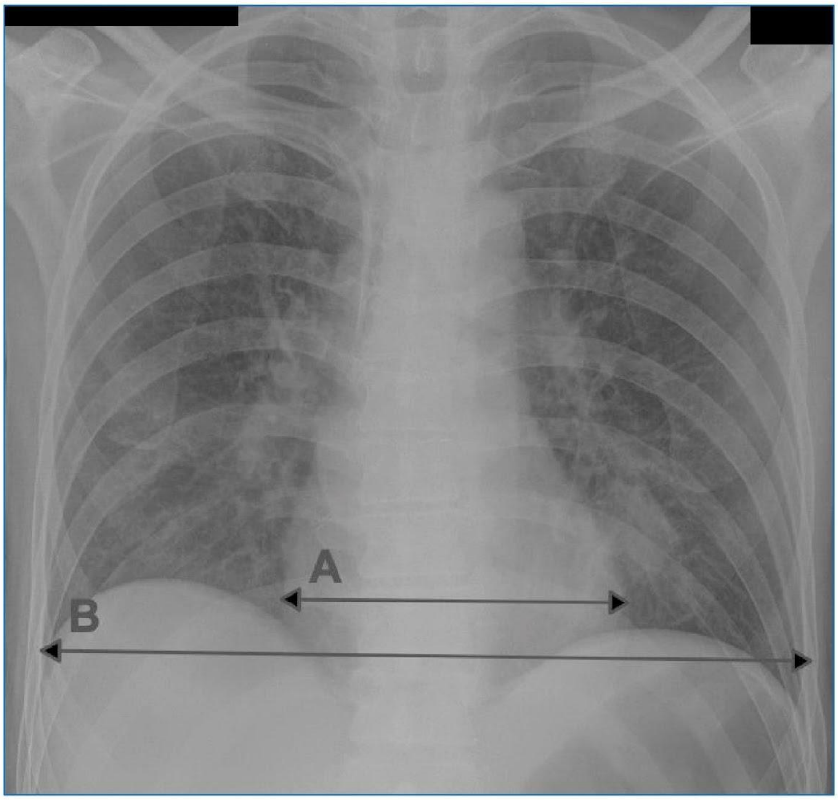

Figure 1. An example of CTR measurement on a chest radiograph in the AP projection. A: transverse dimension of the heart silhouette, B: transverse dimension of the chest.

CTAs of the pulmonary arteries were acquired using a 64-slice computed tomography scanner SOMATOM Definition AS+ (Siemens Healthcare, Erlangen, Germany), in accordance with the standard protocol. In this protocol, the sequence of actions was as follows: tomograph, pre-monitoring and monitoring with the ROI set within the pulmonary trunk/left pulmonary artery at the tracheal bifurcation level, and the proper acquisition with a start triggered by the contrast saturation of 100 HU within the ROI. The acquisition encompassed the area from the pulmonary apices to the costophrenic angles. The exposure kilovolt value was 120 units, with variable mAs values. The scans were performed using intravenous contrast with a constant volume of 60 mL non-ionic contrast, infused with an automatic syringe into the cubital fossa veins, at the infusion rate of 4.0 mL/s. Basic reconstructions were made in axial planes, in 3.0 mm and 0.75 mm slices, along with secondary reconstructions MPR and MIP in frontal and sagittal planes.

The pulmonary artery CTA images required for this analysis were assessed using an application for post-processing of computed tomography images, syngo.CT Cardiac Function (Siemens Healthcare, Erlangen, Germany), by two staff radiologists experienced in the assessment of cardiac and vascular angiography images. Pulmonary embolism (PE+) was diagnosed in cases where filling defects in the pulmonary arteries were found. To assess right ventricle enlargement, the size of both ventricles was measured. The size of the right and left ventricle (RV diameter and LV diameter) was measured based on a multiplanar reconstruction (MPR), in a four-chamber projection, perpendicularly to the long axis of the ventricles, at 1/3 distance between the mitral valve and the apex. The diameter of a ventricle was recognized as the distance between the endocardium of the free wall of the ventricle and the endocardium of the interventricular septum. The papillary muscles were included in the lumen of the chamber. Each time, the average measurement result was considered the final RV diameter and LV diameter values. At the time of the measurement, the radiologists assessing the ventricle dimension had no knowledge of the CTR value. Enlargement of the right ventricle was diagnosed based on the ratio of the right and left ventricle size (RV/LV) in the pulmonary artery CTA, using two different cut-off points: $\geq$0.9 and $\geq$1.0. An example of measuring the RV/LV ratio in the pulmonary artery CTA is presented in Figure 2.

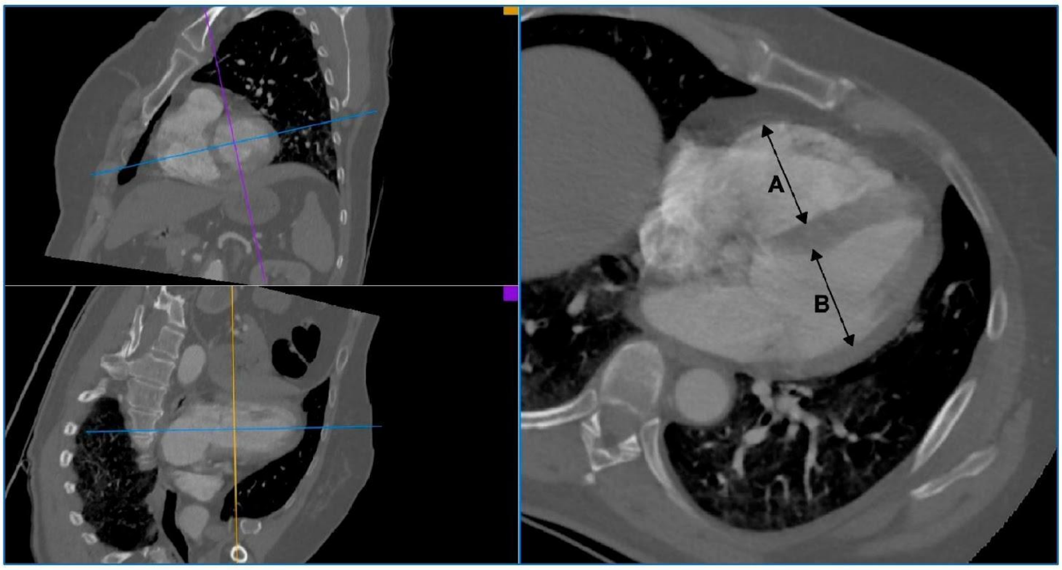

Figure 2. An example of RV/LV ratio measurement in CTA of pulmonary arteries. A: right ventricle diameter, B: left ventricle diameter.

Statistical analysis was performed using the Dell Statistica 13 (Dell Inc., Tulsa, OK, USA) application. For quantitative variables, arithmetic means and standard deviations were calculated. The Shapiro–Willke test was used to verify normal distribution of the variables. Quantitative independent variables with normal distribution were further analyzed using a t test for independent variables. Variables with distribution other than normal were analyzed using the U Mann–Whitney test for independent quantitative variables. Results for the qualitative variables were expressed as a percentage. Qualitative variables were analyzed using the chi-square test. Correlation was analyzed to specify the relationship between the analyzed variables. Pearson correlation coefficients were determined for quantitative variables with normal distribution, and Spearman correlation coefficients for quantitative variables with distribution other than normal. Moreover, the accuracy was tested, with proposed cut-off points for the tests estimated based on the ROC (receiver operating characteristic) curves. The adopted statistical significance level was $p < 0.05$.

3. Results

The average CTR value in the study group of the patients was 0.57 $\pm$ 0.05. Radiological enlargement of the heart silhouette was diagnosed in 60.6% of the subjects. Based on the CTA of the pulmonary arteries, pulmonary embolism was diagnosed in 45.9% of the subjects. The average RV/LV ratio was 0.96 $\pm$ 0.23. Right ventricle enlargement, depending on the adopted criterion of RV/LV $\geq$ 0.9 or RV/LV $\geq$ 1.0, was documented in 44.3% or 29.5% of subjects. The results of the heart silhouette measurement by a chest radiograph and the results of the analyzed variables in the pulmonary artery CTA in the examined group of patients with suspected pulmonary embolism secondary to COVID-19 are presented in Table 3.

Table 3. The size of the heart silhouette in the chest radiograph and selected variables in the CTA examination of the pulmonary arteries in the study group.

	X	SD
C width [mm]	189.10	27.61
T width [mm]	331.59	33.61
CTR	0.57	0.05
RV diameter [mm]	49.55	14.33
LV diameter [mm]	51.66	8.77
RV/LV	0.96	0.23
	%	**n**
CTR > 0.55	60.6	37
RV/LV ≥ 0.9	44.3	27
RV/LV ≥ 1.0	29.5	18
PE+	45.9	28

C width—transverse dimension of the heart silhouette; CTR—cardiothoracic ratio; LV—left ventricle; PE+—pulmonary embolism; RV—right ventricle; T width—transverse dimension of the chest.

A comparative analysis of the subgroups divided on the basis of the CTR cut-off point of 0.55 demonstrated that the patients with enlarged heart silhouette were characterized by statistically significantly higher values of the RV/LV in the pulmonary artery CTA than the patients with non-enlarged heart silhouette; they also significantly more often met the criteria of right ventricle enlargement (both defined as RV/LV ≥ 0.9 and as RV/LV ≥ 1.0). The selected variables of the pulmonary artery CTA in the study subgroups divided on the basis of the criterion of enlarged heart silhouette in the chest radiograph are presented in Table 4.

When comparing the subgroups divided on the basis of the cut-off points RV/LV ≥ 0.9 and RV/LV ≥ 1.0, it was documented that the patients with an enlarged right ventricle had statistically significantly higher CTR values than those with non-enlarged right ventricles. In patients with enlarged right ventricle, the heart silhouette enlargement (defined as CTR > 0.55 in the AP chest radiograph) was observed statistically significantly more often than in patients with non-enlarged right ventricle. The size of the heart silhouette in CR of study subgroups divided on the basis of the criterion of right ventricle enlargement in the pulmonary artery CTA is presented in Table 4.

In a comparison of the subgroups divided on the basis of diagnosed pulmonary embolism, it was found that the patients with confirmed pulmonary embolism had statistically significantly higher CTR and RV/LV than those with excluded pulmonary embolism. In the patients with confirmed pulmonary embolism, enlarged heart silhouette was found statistically significantly more often than in those with excluded pulmonary embolism. These study subgroups demonstrated no differences in the frequency of enlarged right ventricle in the pulmonary artery CTA. The size of the heart silhouette in CR and the selected variables of the pulmonary artery CTA in the study subgroups divided on the basis of the criterion of pulmonary embolism diagnosed in the pulmonary artery CTA are presented in Table 4.

Table 4. The size of the heart silhouette in the chest radiograph and selected variables in the CTA examination of the pulmonary arteries in the study subgroups. (A) Selected variables of pulmonary artery CTA in the study subgroups divided according to the criterion of cardiac enlargement in the chest radiograph. (B) The size of the heart silhouette in the chest radiograph in the study subgroups divided according to the criterion of right ventricular enlargement in the CTA of pulmonary arteries (if RV/LV ≥ 0.9 defines right ventricular enlargement). (C) The size of the heart silhouette in the chest radiograph in the study subgroups divided according to the criterion of right ventricular enlargement in the CTA of pulmonary arteries (if RV/LV ≥ 1.0 defines right ventricular enlargement). (D) The size of the heart silhouette in the chest radiograph and selected variables of the CTA of the pulmonary arteries in the study subgroups divided according to the criterion of pulmonary embolism in the CTA of the pulmonary arteries.

A	**Enlarged Heart Silhouette: CTR > 0.55 (Subgroup G, n = 37)**		**Non-Enlarged Heart Silhouette: CTR ≤ 0.55 (Subgroup H, n = 24)**		*p*
	X	**SD**	**X**	**SD**	
RV diameter [mm]	53.12	15.42	44.04	10.53	0.014
LV diameter [mm]	51.65	9.43	51.67	7.83	0.994
RV/LV	1.03	0.24	0.85	0.18	0.004
	%	n	%	n	
RV/LV ≥ 0.9	59.5	22	20.8	5	0.003
RV/LV ≥ 1.0	40.5	15	12.5	3	0.019
PE+	54.0	20	33.3	8	0.057
B	**Enlarged Right Ventricle: RV/LV ≥ 0.9 (Subgroup I, n = 27)**		**Non-Enlarged Right Ventricle: RV/LV < 0.9 (Subgroup J, n = 34)**		*p*
	X	**SD**	**X**	**SD**	
C width [mm]	198.80	24.65	181.39	27.73	0.013
T width [mm]	333.56	31.60	330.03	35.51	0.688
CTR	0.60	0.05	0.55	0.04	<0.001
	%	n	%	n	
CTR > 0.55	81.5	22	44.1	15	0.003
C	**Enlarged Right Ventricle: RV/LV ≥ 1.0 (Subgroup K, n = 18)**		**Non-Enlarged Right Ventricle: RV/LV < 1.0 (Subgroup L, n = 43)**		*p*
	X	**SD**	**X**	**SD**	
C width [mm]	199.11	28.16	184.91	26.59	0.067
T width [mm]	332.00	31.56	331.42	34.79	0.951
CTR	0.60	0.06	0.56	0.04	0.003
	%	n	%	n	
CTR > 0.55	83.3	15	51.2	22	0.019 *
D	**Confirmed Pulmonary Embolism (Subgroup M, n = 28)**		**Excluded Pulmonary Embolism: (Subgroup N, n = 33)**		*p*
	X	**SD**	**X**	**SD**	
C width [mm]	199.49	26.06	176.85	24.53	0.001
T width [mm]	334.09	33.64	328.64	33.94	0.533
CTR	0.60	0.05	0.54	0.04	<0.001
RV diameter [mm]	56.04	15.32	41.89	8.09	<0.001
LV diameter [mm]	51.88	9.43	51.39	8.09	0.831
RV/LV	1.08	0.24	0.82	0.12	<0.001
	%	n	%	n	
CTR > 0.55	85.7	24	39.4	13	0.002
RV/LV ≥ 0.9	57.1	16	33.3	11	0.062
RV/LV ≥ 1.0	39.3	11	21.2	7	0.122

* Statistical significance; C width—transverse dimension of the heart silhouette; CTR—cardiothoracic ratio; LV—left ventricle; PE+—pulmonary embolism; RV—right ventricle; T width—transverse dimension of the chest.

A correlation analysis demonstrated the existence of a statistically significant positive correlation between RV/LV and CTR (r = 0.59, $p < 0.05$), (Figure 3).

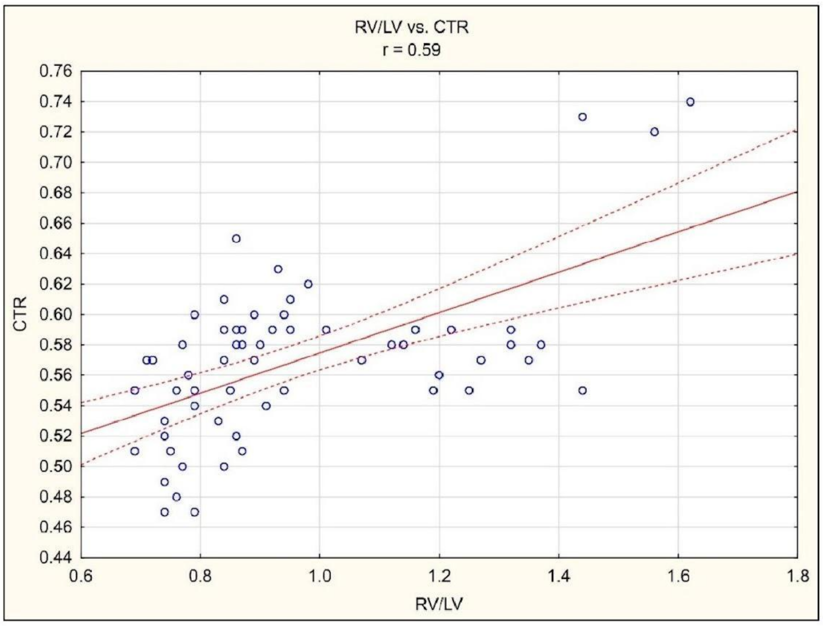

Figure 3. Correlation between RV/LV ratio in CTA of pulmonary arteries and CTR in chest radiograph in the AP projection.

The demonstrated correlation occurred in all the divided subgroups, except for the group with excluded pulmonary embolism. The results of an analysis of the heart silhouette size in the chest radiograph and the size of the right ventricle in the pulmonary artery CTA in the whole study group and study subgroups are presented in Table 5.

Table 5. Correlation of the size of the heart silhouette in the chest radiograph and the size of the right ventricle in the CTA of the pulmonary arteries in the study group and subgroups.

Group/Subgroup	RV/LV vs. CTR Correlation	
	Correlation Coefficient (r)	*p*
whole study group	0.59	<0.001
subgroup A: ≥71 years	0.61	<0.001
subgroup B: <71 years	0.55	0.002
subgroup C: overweight/obesity (BMI ≥ 25 kg/m^2)	0.61	<0.001
subgroup D: normal body mass (BMI < 25 kg/m^2)	0.58	0.029
subgroup E: men	0.44	0.005
subgroup F: women	0.78	<0.001
subgroup G: enlarged heart silhouette (CTR > 0.55)	0.52	0.001
subgroup H: non-enlarged heart silhouette (CTR ≤ 0.55)	0.42	0.039
subgroup I: enlarged right ventricle (RV/LV ≥ 0.9)	0.47	0.013
subgroup J: non-enlarged right ventricle (RV/LV < 0.9)	0.44	0.010
subgroup K: enlarged right ventricle (RV/LV ≥ 1.0)	0.67	0.002
subgroup L: non-enlarged right ventricle (RV/LV < 1.0)	0.56	<0.001
subgroup M: confirmed pulmonary embolism	0.43	0.012
subgroup N: excluded pulmonary embolism	0.29	0.127

CTR—cardiothoracic ratio; LV—left ventricle; RV—right ventricle.

The ROC curves were used to determine CTR values constituting optimal cut-off points for the prediction of right ventricle enlargement (RV/LV ≥ 0.9 or RV/LV ≥ 1.0), amounting to 0.54 and 0.55, respectively (Figure 4A,B).

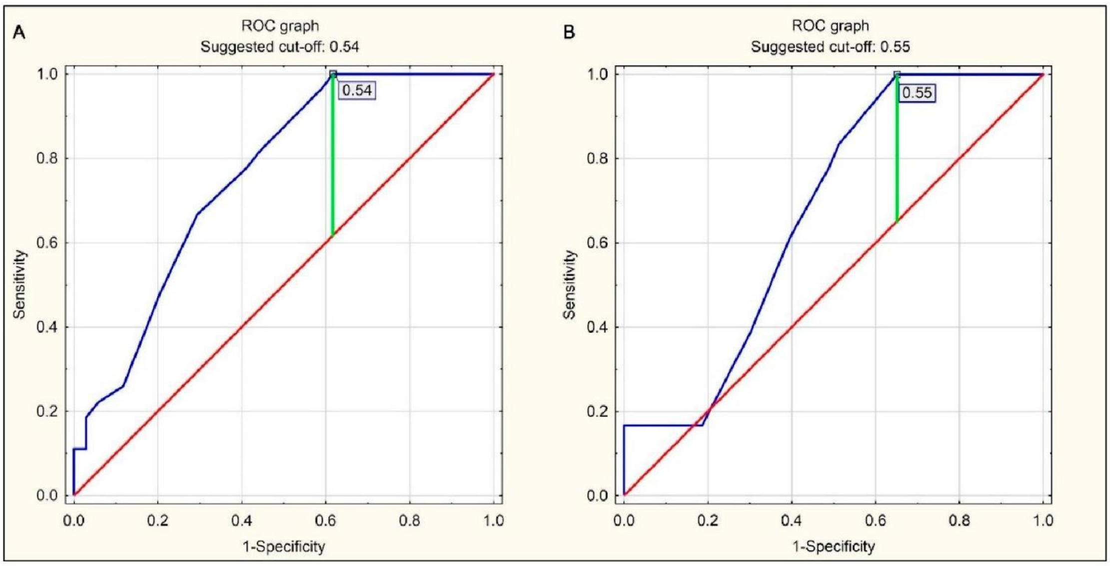

Figure 4. ROC curves for predicting right ventricular enlargement (RV/LV ratio ≥ 0.9 or RV/LV ratio ≥ 1.0 in pulmonary CTA) using the CTR value on the chest radiograph in the AP projection. (**A**) Right ventricular enlargement defined as RV/LV ≥ 0.9 in pulmonary CTA. (**B**) Right ventricular enlargement defined as RV/LV ≥ 1.0 in pulmonary CTA.

The sensitivity, specificity, and accuracy of CTR > 0.54 as a predictor for RV/LV ≥ 0.9 were 0.412, 0.963, and 0.656, respectively, while those of CTR > 0.55 as a predictor for RV/LV ≥ 1.0 were 0.488, 0.833, and 0.590, respectively. The test accuracy analysis indicated that the predictors had a significantly higher specificity than sensitivity. The results of the accuracy analysis for the radiological cardiothoracic ratio as a predictor of right ventricle enlargement in the pulmonary artery CTA for the whole study group are presented in Table 6.

Table 6. Sensitivity, specificity, and accuracy of the radiographic cardiothoracic ratio as a predictor of right ventricular enlargement in pulmonary CTA. (A) In the whole group. (B) In subgroups divided according to the age criterion. (C) In subgroups divided according to the BMI criterion. (D) in subgroups divided according to the gender criterion. (E) in subgroups divided according to the pulmonary embolism criterion.

A	Prediction of Right Ventricular Enlargement (RV/LV ≥ 0.9)	Prediction of Right Ventricular Enlargement (RV/LV ≥ 1.0)
CTR value that is the optimal cut-off point for prediction based on the ROC curve	>0.54	>0.55
sensitivity	0.412	0.488
specificity	0.963	0.833
accuracy	0.656	0.590
positive predictive value	0.933	0.875
negative predictive value	0.565	0.405
likelihood ratio of a positive result	11.118	2.930
likelihood ratio of a negative result	0.611	0.614

Table 6. *Cont.*

	Subgroup A: ≥71 Years		**Subgroup B: <71 Years**	
B	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 0.9)**	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 1.0)**	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 0.9)**	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 1.0)**
CTR value that is the optimal cut-off point for prediction based on the ROC curve	>0.55	>0.55	>0.58	>0.58
sensitivity	0.556	0.455	0.875	0.810
specificity	0.933	0.909	0.417	0.429
accuracy	0.727	0.606	0.679	0.714
	Subgroup C: Overweight/Obesity (BMI ≥ 25 kg/m^2)		**Subgroup D: Normal Body Mass (BMI < 25 kg/m^2)**	
C	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 0.9)**	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 1.0)**	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 0.9)**	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 1.0)**
CTR value that is the optimal cut-off point for prediction based on the ROC curve	>0.59	>0.55	>0.73	>0.73
sensitivity	0.882	0.488	1.000	1.000
specificity	0.385	0.750	0.077	0.083
accuracy	0.745	0.511	0.143	0.214
	Subgroup E: Men		**Subgroup F: Women**	
D	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 0.9)**	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 1.0)**	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 0.9)**	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 1.0)**
CTR value that is the optimal cut-off point for prediction based on the ROC curve	>0.59	>0.55	>0.58	>0.58
sensitivity	0.789	0.348	0.933	0.882
specificity	0.300	0.769	0.429	0.400
accuracy	0.538	0.487	0.773	0.773
	Subgroup M: Confirmed Pulmonary Embolism		**Subgroup N: Excluded Pulmonary Embolism**	
E	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 0.9)**	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 1.0)**	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 0.9)**	**Prediction of Right Ventricular Enlargement (RV/LV ≥ 1.0)**
CTR value that is the optimal cut-off point for prediction based on the ROC curve	>0.62	>0.72	>0.54	>0.55
sensitivity	0.917	1.000	0.591	0.731
specificity	0.238	0.125	0.833	0.500
accuracy	0.485	0.576	0.643	0.714

CTR—cardiothoracic ratio; LV—left ventricle; ROC—receiver operating characteristic; RV—right ventricle.

Table 6 present also the results of an analysis performed in the divided subgroups. The radiological cardiothoracic ratio with the highest accuracy is a predictor of right ventricle enlargement in the pulmonary artery CTA in the subgroups of females, overweight/obese patients, and patients aged ≥ 71 years.

4. Discussion

COVID-19 has become an enormous epidemiological problem for the entire world; we witnessed as numerous health care systems in many countries around the globe collapsed one by one. Apart from acute respiratory failure secondary to pneumonia, this illness involves numerous complications, including cardiovascular ones. In 28 out of the 61 patients in the investigated group, the pulmonary artery CTA scan demonstrated the presence of pulmonary embolism (45.9%), which confirms the weight of the problem in patients hospitalized with diagnosed COVID-19. Similar percentages of pulmonary embolism were reported by researchers from Italy (44.7%) [27] and London (46.2%) [28] for their respective groups. Right ventricular failure is one of the main problems in this patient group.

Dimensioning of the right ventricle is reflected in the guidelines regarding the diagnostics and treatment of pulmonary embolism, and the RV/LV ratio may be a prognostic factor [21]. To assess advanced pneumonia, patients admitted to hospitals often undergo a chest radiograph, usually AP, on account of their health condition. When interpreting these radiographs, it is possible to determine the cardiothoracic ratio, which does not prolong the interpretation task in any significant way. Earlier studies already demonstrated that the CTR could be a prognostic factor for myocardial enlargement in various illnesses [29–32]. Values >0.55 were considered incorrect for radiographs in the AP projection [25,26], and the same value was demonstrated in a study investigating the dependence between CTR in the AP projection and heart measurements in computed tomography [33].

According to our data analysis, such determined CTR can be considered as a prognostic factor for right ventricular enlargement in patients with pulmonary embolism secondary to COVID-19. RV/LV was significantly higher in patients with enlarged heart silhouette than in patients with non-enlarged heart silhouette. CTR was significantly higher in patients with an enlarged right ventricle (higher RV/LV) than in patients with non-enlarged right ventricles (lower RV/LV). There was a positive correlation between RV/LV and CTR. In addition, the accuracy of CTR > 0.54 as a predictor for RV/LV ≥ 0.9 was 65.6%. However, considering that the specificity of prediction is much higher than its sensitivity (over 80% compared to less than 50%), especially lower CTR values may indicate a lack of right ventricular enlargement in patients with COVID-19. The high sensitivity of prediction always indicates the usefulness of the test in confirming a given state, while the high specificity of prediction indicates the usefulness of the test in excluding a given state.

The research published so far also confirms our observations, although the number of these studies is small. Researchers from Iran proved that CTR determined during a chest CT is a strong predictor for mortality in patients with COVID-19, and its values grow together with the affected volume of the pulmonary parenchyma. Just like us, the researchers demonstrated that over half of the patients had increased CTR; in our group it was 60.6% [34]. Considering the lack of any statistically significant difference between CTR determined on a chest radiograph and in computed tomography [35], one can conclude that a clinically indicated radiograph could be one of the screening factors in the evaluation of right ventricle enlargement; also, a study on the association between the CTR and the ventricle size in patients with systolic and diastolic heart failure demonstrated a higher relationship between the CTR and RV than LV size [36].

Researchers from Warsaw reached different conclusions, when they failed to prove a significant CTR value in predicting the right ventricle size in a different group of patients, namely those after a Fallot tetralogy correction [37]. The same applies to the general population of minors with heart defects [38]; it was demonstrated that in healthy children the correlation between the CTR and the size of the heart chambers determined via echocardiography was small [39]. This merits the question of how the surgery and the defect itself affected the shape and consequently the size of the heart silhouette and chest in the radiograph, and did it affect the CTR measurements? Another research work that negated a significant added value of the CTR in the assessment of the right ventricle size was a study on the relation between these parameters in patients with restrictive pulmonary diseases (pure restrictive ventilatory impairment) [40]. In this study, the researchers observed only a small correlation between the CTR and enlarged right ventricle (this study was undoubtedly limited by the size of the study group, which was only 19 patients). The studies performed on the adult population referred to in this paragraph emphasized the lack of any added value provided by the estimation of RV size on a lateral radiograph.

The Iranian researchers, while indicating significantly lower value to estimating heart size using CTR than using echocardiography, at the same time emphasized the prevalence of the radiographic method and cited it as a good, low-cost screening assessment for heart silhouette enlargement [41].

Our study was encumbered by several limitations, which still fail to significantly reduce the value of the results. In terms of the studied group, the limitations included the small size of the study group, the lack of data on pharmacotherapy for chronic diseases, as well as the inability to perform analyses in subgroups of patients with specific comorbidities (due to the insufficient size of the subgroups, which would be created based on the criteria for the occurrence of subsequent comorbidities). The results of the present study are a starting point for further studies on a larger group of patients, which will allow consideration for the importance of comorbidities, as well as their pharmacotherapy. In terms of the research methodology itself, the following limitations should be mentioned. The study did not consider the volume of the pulmonary parenchyma affected by the inflammation, while from a pathophysiological perspective, an increase in the affected volume of the pulmonary parenchyma would increase the afterload of the right ventricle, which may cause an enlargement of the right ventricle, and, in consequence, the CTR. Therefore, these data should be related to the volume of the lungs affected by the inflammation, particularly in the group of patients without diagnosed pulmonary embolism, but with a diagnosed enlargement of the right ventricle or CTR. Additionally, determination of the CTR on an AP radiograph has numerous limitations. Due to the health condition of the patients in the study group, it was not possible to perform a PA radiograph; therefore, it appears that comparing the CTR measurement to the CTR determined in pulmonary CTA could provide added value. Moreover, we had no access to chest radiographs or chest CT scans of the patients that were taken before current hospitalization. It seems that excluding patients with prior CTR and RA/LV increases from the study group could improve the sensitivity and specificity of the assessment for the investigated parameters in the context of pulmonary embolism secondary to COVID-19. Finally, the pulmonary artery CTA was only performed on patients with suspected pulmonary embolism instead of the whole group, making it impossible to determine the number of patients with clinically silent pulmonary embolism.

5. Conclusions

In patients with suspected pulmonary embolism secondary to COVID-19, the radiological cardiothoracic ratio can be considered as a prognostic factor for right ventricular enlargement. Considering that the specificity of prediction is much higher than its sensitivity, especially lower CTR values may indicate a lack of right ventricular enlargement in patients with COVID-19.

Author Contributions: Conceptualization, P.G. and R.P.; methodology, K.T. and P.G.; software, P.G. and R.P.; investigation, K.T. and P.G.; writing—original draft preparation, K.T. and P.G.; writing—review and editing, M.P. and R.P.; visualization, K.T.; supervision, P.G. and R.P.; project administration, P.G.; funding acquisition, P.G. All authors have read and agreed to the published version of the manuscript.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. APC was financed by the Wroclaw Medical University.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Wroclaw Medical University (protocol code KB-414/2021).

Informed Consent Statement: Written informed consent was obtained from the patient(s) to publish this paper.

Data Availability Statement: Study data can be made available upon documented request.

Conflicts of Interest: The authors declare no conflict of interest.

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Radiological cardiothoracic ratio as a potential marker of left ventricular hypertrophy assessed by echocardiography

PUBLISHED

ID 4931945

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Article Type

Research Article

Journal

Radiology Research and Practice

Academic Editor Faggioni Lorenzo Submitted on 2022-06-01 (8 days ago)

Abstract

The aim of the study was to verify the usefulness of the radiological cardiothoracic ratio as a potential marker of left ventricular hypertrophy assessed by echocardiography. The study included 96 patients (mean age: 49.52 ± 9.64 years). Chest radiograph in the PA projection and echocardiography were performed. In CR the measurement of the cardiothoracic ratio (CTR) was performed. Assuming CTR >0.50, heart silhouette enlargement was diagnosed. In echocardiography, 4 types of left ventricular geometry were assessed: normal geometry (NG), concentric remodeling (CR), concentric hypertrophy (CH) and eccentric hypertrophy (EH). It was shown that patients with an enlarged heart silhouette were characterized by a significantly more frequent occurrence of left ventricular hypertrophy (LVH) on echocardiography than patients with a non-enlarged heart silhouette. In the subgroup of patients with LVH compared to the subgroup of patients with normal left ventricular geometry, CTR values are statistically significantly higher, and heart silhouette enlargement is significantly more frequent. The criterion "CTR >0.49" estimates LVH with a sensitivity of 93.3% and specificity of 82.7%, which translates into a high accuracy of 84.4%. By analysing the prediction of left ventricular geometry types, a high accuracy of CH prediction was obtained using the "CTR >0.49" criterion of 80.2% (with a high sensitivity of 84.0% and a satisfactory specificity of 60.0%) and a high accuracy of EH prediction using the "CTR >0.52" criterion of 71.9% (with high sensitivity 80.5% and low specificity 36.8%), as well as low CR prediction accuracy of only 57.3% (with low sensitivity 36.7%, even if high specificity 78.7%). In summary, radiological cardiothoracic ratio may be a moderate marker of left ventricular hypertrophy assessed according to standard echocardiographic criteria, provided that its cut-off point is standardized in each population of subjects.

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1 Introduction

The cardiothoracic ratio (CTR) is defined as the ratio of the greatest transverse dimension of the heart (C wight) to the greatest dimension of the chest measured to the inner edge of the ribs (T wight) on the chest PA radiograph [1]. Normal CTR values were ≤ 0.5, with values >0.5, enlargement of the heart silhouette is suggested. Due to the high variability in the exposure, the patient's position, the distance of the X-ray tube, etc. for routine CTR measurements, no other than PA chest projection should be used, and if necessary, their limitations should be kept in mind [2,3,4,5].

CTR is a widely used, time-saving, and non-cost-effective indicator when interpreting a chest X-ray to assess the size of the heart shape. In the literature, we find publications both about its important value and discrediting its importance in common use.

A large, prospective, cohort study on a group of almost 3.5 thousand 4-year follow-up showed that in people undergoing hemodialysis, higher CTR is associated with a higher risk for both general and cardiovascular reasons [6]. In the group of hemodialysis patients, it has also been shown that CTR > 55% is an important independent factor influencing the 2-year all-cause mortality [7]. Another study conducted on a group of almost 1.8 thousand 4-year follow-up has shown that CTR as a simple indicator is a strong predictor of poor prognosis in patients with rheumatic heart disease undergoing heart valve replacement [8]. CTR in patients with chronic heart failure can be used to stratify cardiovascular risk, and its value> 0.5 is associated with higher mortality and an increase in hospitalizations [9].

Despite the potential clinical applications of CTR described above, a common opinion is that CTR is of low clinical usefulness, which is also reflected in some studies that emphasize, for example, a weak correlation between CTR and the parameters of heart function [10,11,12]. Another study in a group of patients undergoing coronary angiography questioned the validity of the normal cut-off point of 0.5, showing increased mortality in patients undergoing coronary angiography at $0.42 < CTR < 0.49$ [13]. Other shows that despite the easy determination of the parameter and high repeatability be-tween researchers / clinicians, it has low accuracy as a method of distinguishing the normal size of the heart from an enlarged one based on a single cut-off point [14]. In the literature, however, we find little data on the real clinical value of CTR, and there are no studies that would unambiguously tip the balance on one side.

When talking about the "large" left ventricular (LV), we should distinguish at least two terms describing it, namely hypertrophy and dilatation. LV hypertrophy is an in-crease in the mass of the left ventricular secondary to an increase in the thickness of the left ventricular walls. The overgrown left ventricular, in addition to increasing the mass of the miokardium, may be of the correct size or enlarged [15,16]. Left ventricular dilatation is understood as an increase in the internal dimensions of the left ventricular cavity above normal [17].

The main causes of left ventricular hypertrophy (LVH) are arterial hypertension, significant narrowing of the renal arteries, the so-called athlete's heart, aortic stenosis, aortic coarctation, hypertrophic cardiomyopathy, aortic / mitral valve regurgitation, etc. All the above-mentioned diseases, in connection with the increase in left ventricular volume load in certain stages, may lead to left ventricular dilatation [16, 18]. Echocardiography is the most accessible and routinely used method in clinical management to estimate the size of the left ventricular.

The aim of the study was to verify the usefulness of the radiological cardiothoracic ratio as a potential marker of left ventricular hypertrophy assessed by echocardiography.

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2. Materials and Methods

The study included 96 patients examined in the cardiology clinic, recruited for the study based on the inclusion and exclusion criteria. The inclusion criteria for the study were: age ≥18 years, clinical indications for echocardiography and chest radiograph in the PA projection, informed written consent to participate in the study. The exclusion criteria from the study were a large volume of fluid in the pleural cavity / cavities, the presence of fluid in the pericardial sac, the coexistence of chronic respiratory diseases (COPD, bronchial asthma, interstitial lung diseases), past pneumonia in the past 6 months, cancer history, coexistence of diseases systemic diseases, history of congenital heart defects, previous thoracic, cardiosurgical and neurosurgical procedures in the thoracic spine and changes in the therapy of chronic diseases in the past 6 months. The required sample size of 96 people was determined using a sample size calculator, adopting the following calculation criteria: population size 2 million, fraction size 0.5, maximum error 10%, confidence level 95%. The mean age in the study group was 49.52 ± 9.64 years, height 1.67 ± 0.09 m, body mass 73.12 ± 9.88 kg, and BMI 26.30 ± 2.78 kg/m2. The general characteristics of the entire study group are presented in Table 1.

The study was conducted as part of a research project entitled "Radiological cardiothoracic ratio as a predictor of heart size as assessed by echocardiography, computed tomography and magnetic resonance imaging." The assumptions and protocol of the study were positively assessed by the local institutional bioethics committee (KB - 414/2021).

Basic anthropometric measurements were measured in all patients and imaging examinations were performed: chest radiograph in the PA projection and echocardiography.

The chest radiograph was performed using the standard method in the standing position in the posterior-anterior (PA) view. The radiograph was taken with a breath hold, during the maximal inspiration phase, using a kilovolt of the 120 kV X-ray tube. All radiographs met the radiological criteria for the correct acquisition of the X-ray image.

For the purposes of the current study of retrospective CTR measurements in all chest radiographs performed, one specialist in radiology and imaging diagnostics, holding institutional individual certification in the field of cardiovascular radiology, performed it. The measurement of the cardiothoracic ratio (CTR) was performed using a diagnostic radiological station that met the applicable legal requirements for the assessment of X-rays. The maximum width of the heart's silhouette (C width) and the maximum width of the chest (T width) were measured. The CTR value was obtained by dividing the measured C width value by the T width value. Assuming CTR >0.50, enlargement of the heart silhouette was diagnosed. The method of measuring CTR on a chest radiograph in the PA projection is presented in Figure 1.

Transthoracic echocardiography was performed using a standard examination protocol using the ALOKA ProSound 6 (Aloka Inc, Tokyo, Japan). Using the M-mode presentation under the control of a two-dimensional examination (in the parasternal projection in the long axis of the left ventricular), the dimensions of the lumen and the thickness of the walls of the left ventricular were measured: left ventricular end-diastolic diameter (LVEDd), left ventricular end-systolic diameter (LVESd), interventricular septum diastolic diameter (IVSDd) and posterior wall diastolic diameter (PWDd). Left ventricular dimensions and left ventricular wall thickness were used to estimate left ventricular mass (LVM), left ventricular mass index (LVMI), and relative wall thickness (RWT). The following mathematical formulas were used in the estimation: $LVM = 0.8 \times [1.04 \times (LVEDd + PWDd + IVSDd)^3 - LVEDd^3] + 0.6$; LVMI = LVM / BSA (where BSA was the body surface area calculated from Du Bois' formula: $BSA = 0.007184 \times \text{body weight}^{0.425} \times \text{height}^{0.725}$); RWT = (IVSDd + PWDd) / LVEDd.

The estimated LVMI and RWT values were used as criteria for classifying 4 types of left ventricular geometry: normal geometry (NG), concentric remodeling (CR), concentric hypertrophy (CH) and eccentric hypertrophy (EH). NG was diagnosed when RWT $\leq$ 0.45 and LVMI $\leq$ 125 g/m^2 in men or $\leq$ 110 g/m^2 in women; CR when RWT > 0.45 and LVMI $\leq$ 125 g/m^2 in men or $\leq$ 110 g/m^2 in women; CH, when RWT > 0.45 and LVMI > 125 g/m^2 in men or > 110 g/m^2 in women; and EH, when RWT $\leq$ 0.45 and LVMI > 125 g/m^2 in men or > 110 g/m^2 in women. Moreover, patients diagnosed with CR, CH and EH were classified into the general group of patients with left ventricular hypertrophy (LVH). For the purposes of the present study, all echocardiographic examinations were performed by one specialist in cardiology with 20 years of experience.

Echocardiographic examination and chest radiograph were performed in the shortest possible time interval, not longer than 7 days. The mean time interval between the performed imaging examinations was 4.32 ± 1.03 days.

Statistical analysis was performed using the Dell Statistica 13 statistical package (Dell Inc., USA). For quantitative variables, arithmetic means and standard deviations were calculated. The W-Shapiro-Wilk test was used to check the normality of the distribution of variables. The null hypotheses for normally distributed quantitative independent variables were tested with the t-test. The null hypotheses for non-normally distributed variables were tested with the Mann-Whitney U-test. For qualitative variables, percentages were calculated. The null hypotheses for qualitative variables were tested with the chi-square test. To determine the potential linear relationships between the analyzed quantitative variables, a correlation analysis was performed. Pearson's correlation coefficients were established for quantitative variables with a normally distributed, and Spearman's correlation coefficients for quantitative variables with a distribution other than normal. Moreover, an analysis of the prediction accuracy assessment was performed, in which the proposed cut-off points for the predictors were estimated based on ROC (Receiver Operating Characteristic) curves. The level of statistical significance was p <0.05.

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3. Results

LVMI in the studied group of patients was 107.80 ± 31.05 g/m^2, while the RWT - 0.48 ± 0.07. Left ventricular hypertrophy (LVH) was found in 84.4% of patients, CR was found in 49.0% of patients, CH in 15.6%, and EH in 19.8% of patients. The study group was characterized by a CTR of 0.51 ± 0.04. Enlarged heart silhouette was diagnosed in 30.2% of patients. Selected variables from imaging studies are summarized in Table 2.

Comparing the subgroups of patients distinguished based on the CTR criterion, it was shown that patients with an enlarged heart silhouette on the chest radiograph in the PA projection were characterized by a significantly more frequent occurrence of left ventricular hypertrophy (LVH) on echocardiography than patients with a non-enlarged heart silhouette. There is a significant difference between patients with enlarged heart silhouette and patients with a non-enlarged heart silhouette of the more frequent incidence of left ventricular concentric hypertrophy in the first of these subgroups. The left ventricular geometry in the subgroups distinguished based on the heart silhouette enlargement criterion is presented in Table 3.

In a comparative analysis of the subgroups distinguished based on the presence of LVH, it was found that in the subgroup of patients with LVH compared to the subgroup of patients with normal left ventricular geometry, CTR values are statistically significantly higher, and heart silhouette enlargement is significantly more frequent.

When comparing the subgroups of patients with different types of left ventricular geometry in echocardiography, statistically significant higher CTR values were observed in the CR, CH and EH subgroups than in the NG subgroup, and also in the CH and EH subgroups than in the CR subgroup. Moreover, heart silhouette enlargement was significantly more frequent in the subgroup of patients with CR, CH and EH than in the subgroup of patients with NG, and also in the subgroup of patients with CH than in the subgroup of patients with CR. The values of the cardiothoracic ratio in the subgroups distinguished based on the geometry of the left ventricular are presented in Table 4.

The correlation analysis showed the existence of statistically significant positive linear relationships between LVEDd and CTR ($r = 0.38$, $p < 0.05$), LVM and CTR ($r = 0.42$, $p < 0.05$) and between LVMI and CTR ($r = 0.50$, $p < 0.05$), table 5.

The sensitivity and specificity analysis was used to assess the accuracy of CTR values as a predictor of left ventricular hypertrophy and types of left ventricular geometry. The results of the sensitivity and specificity analysis of the standard criterion "CTR > 0.50" (defining the heart silhouette enlargement on the chest radiograph in the PA projection) as well as the CTR criteria determined based on the performed ROC curves presented in Figures 2 and 3 are summarized in Table 6.

The CTR criteria established based on the ROC curves made were each time characterized by higher predictive accuracy than the standard CTR criterion defining the heart silhouette enlargement. In the studied group of patients, the criterion "CTR > 0.49" estimates LVH with a sensitivity of 93.3% and specificity of 82.7%, which translates into a high accuracy of 84.4%. By analyzing the prediction of left ventricular geometry types, a high accuracy of CH prediction was obtained using the "CTR > 0.49" criterion of 80.2% (with a high sensitivity of 84.0% and a satisfactory specificity of 60.0%) and a high accuracy of EH prediction using the "CTR > 0.52" criterion of 71.9% (with high sensitivity 80.5% and low specificity 36.8%), as well as low CR prediction accuracy of only 57.3% (with low sensitivity 36.7%, even if high specificity 78.7%).

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4. Discussion

The results of our research have shown that CTR may be a helpful indicator in the prediction of LVH, especially in the subgroup of patients with concentric hypertrophy. High sensitivity, specificity and accuracy should be emphasized while maintaining the CTR > 0.49 condition. Based on the compiled data, it can be concluded that each time CTR > 0.49 should be associated with the consequence of further investment regarding, in particular, the thickness of the LV walls. However, there are few studies in the literature comparing echocardiographic and CTR values in the assessment of LV size and its wall thickness. In 2006, a publication was published that investigated the correlation of a chest radiograph and a transthoracic ultrasound of the heart in the assessment of cardiomegaly in patients with arterial hypertension. Researchers have demonstrated, like us, that there is a significant correlation ($p < 0.05$) between LV hypertrophy and CTR, while indicating a weak correlation between CTR and LV enlargement [19]. Similarly, it was demonstrated in the study of cardiomegaly during Chagas disease (no correlation between the increased LVEDD size and cardiomegaly determined in CTR) [20].

Other conclusions were presented in the paper, which tried to answer the question whether the cardiomegaly described by CTR is the same as the cardiomegaly described in echocardiography based on the observation of patients with NSTEMI. This study demonstrated a similar negative and positive prediction of cardiomegaly in CTR, indicating that all patients with suspected cardiac enlargement should have an echo. As a limitation of the study, one should consider the specifics of the study group and (which was also noticed by the researchers) assess whether this situation also applies to the wider population [21]. In the context of this information, the strength of our study should be considered to select a more diverse population.

Comparing our research group with the group studied by Costa et al. [22], in completely different populations (patients of cardiology clinics vs patients with chronic kidney disease with hemodialysis introduced for at least six months), a similar percentage of patients with LVH was obtained (84.4% vs. %), however, the analysis of data on the distribution of certain types of geometry indicates the existing differences in the studied groups. Both were dominated by concentric overgrowth (in our population, the sum of CR and CH, i.e. 64.6%, in the cited study 67.4%), but the distribution of eccentric hypertrophy was slightly different (19.8% vs 32.6%). Both studies proved the usefulness of diagnostic CTR in determining LVH. Similar conclusions were presented in the study which investigated the prevalence of hypertension, calcification in the heart valves and LVH in patients undergoing peritoneal dialysis. Researchers have shown that a separate subgroup of patients with LVH has a significantly higher CTR and that LVMI significantly correlates with CTR [23].

A study that assessed the clinical manifestations and course of HCM in the pediatric population showed an increased CTR (all study participants had an average CTR> 0.65), and echocardiography confirmed different LVH morphologies in all patients [24], which may also indirectly prove the usefulness of CTR in determining LVH in the pediatric population. In our opinion, however, it is necessary to demonstrate great caution in determining and interpreting CTR in the pediatric population, especially in the context of the findings of the work, where no correlation has been demonstrated between CTR and LV measurements in echocardiography and the severity of LVH in children with end-stage renal disease and anemia [25].

Researchers from Korea tried to create a system based on several criteria (including electrocardiography, CTR, etc.) that would allow effective prediction of LVH among asymptomatic hypertensive patients. The researchers emphasized the high negative predictive value of CTR in detecting LVH, and the CTR introduced into their method as an additional risk factor significantly improved the accuracy of the LVH suspicion [26]. Similar conclusions were reached by researchers from Brazil who proved that the assessment of the heart shape on radiographs (AP and lateral) together with the assessment of the electrocardiogram show great value in the prognosis of LVH in patients with arterial hypertension. Moreover, they developed the thesis that such a set of tests should be routinely performed in this group of patients to monitor the occurrence of possible LVH [27]. It should be remembered about the subsequent stages of LV remodeling during arterial hypertension and other diseases that, in the final stage, may lead to its significant enlargement (LVD). A review and pooled analysis of CTR in LVD prediction has shown that increased CTR has no value in LVD prediction [28].

This is another of our research on the predictive suitability of CTR. We previously demonstrated that in patients with suspected pulmonary embolism during COVID-19, CRT can be considered as a prognostic factor for right ventricular enlargement, especially as a negative predictor of right ventricular enlargement in the case of lower CTR values [29].

Summing up, it should be emphasized that despite the common belief that the CTR measurement value is low as a marker of LV hypertrophy, our research seems to fit in with the evidence provided by researchers in recent years regarding the predictive utility of the above radiological parameter. The strength of our study is also demonstrated that among the echocardiographically assessed types of left ventricular geometry, the radiological cardiothoracic ratio can be considered with high predictive accuracy as a marker of concentric hypertrophy, and also as a marker of eccentric left ventricular hypertrophy. However, great caution should be exercised when trying to predict concentric remodeling of the left ventricular based on the radiological cardiothoracic ratio.

5. Conclusions

1. Radiological cardiothoracic ratio may be a moderate marker of left ventricular hypertrophy assessed according to standard echocardiographic criteria, provided that its cut-off point is standardized in each population of subjects.

2. Among the echocardiographically assessed types of left ventricular geometry, the radiological cardiothoracic ratio can be considered with high predictive accuracy as a marker of concentric hypertrophy, and also as a marker of eccentric hypertrophy. Caution should be exercised in predicting concentric remodeling based on the radiographic cardiothoracic ratio.

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Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

Conceptualization, Rafał Poręba and Paweł Gać; Funding acquisition, Paweł Gać; Investigation, Krystian Truszkiewicz, Piotr Macek and Rafał Poręba; Methodology, Krystian Truszkiewicz and Paweł Gać; Project administration, Paweł Gać; Resources, Krystian Truszkiewicz; Software, Rafał Poręba and Paweł Gać; Supervision, Rafał Poręba and Paweł Gać; Visualization, Krystian Truszkiewicz; Writing – original draft, Krystian Truszkiewicz and Paweł Gać; Writing – review & editing, Małgorzata Poręba and Rafał Poręba.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. APC was financed by the Wroclaw Medical University.

Data Availability Statement

Study data can be made available upon documented request.

Tables

Table 1. Clinical characteristics of the study group.

	Mean	Standard deviation	Minimum value	Maximum value
Age (years)	49.52	9.64	30.00	65.00
Height (m)	1.67	0.09	1.49	1.89
Body mass (kg)	73.12	9.88	52.89	95.65
BMI (kg/m^2)	26.30	2.78	20.56	32.31
BSA (m^2)	1.82	0.16	1.49	2.15
Systolic BP (mmHg)	137.13	18.47	96.44	177.03
Diastolic BP (mmHg)	87.06	9.06	68.15	111.35
Total cholesterol (mg/dl)	199.90	33.65	111.01	308.39
HDL cholesterol (mg/dl)	53.15	6.62	29.02	86.40
LDL cholesterol (mg/dl)	104.70	15.16	23.19	209.75
Triglycerides (mg/dl)	125.26	36.76	52.83	315.58
Glucose (mg/dl)	121.71	42.83	75.00	312.00
	Number		Percent	
Men	38		39.6	
Women	58		60.4	
Normal body mass	27		28.1	
Overweight	61		63.5	
Obesity	8		8.3	
Arterial hypertension	86		89.6	
Dyslipidemia	59		61.5	
Type 2 diabetes	32		33.3	
Coronary artery disease	10		10.4	
Stroke	5		5.2	

BMI – body mass index, BP – blood pressure, BSA – body surface area, HDL - high-density lipoprotein, LDL – low- density lipoprotein

Table 2. The results of imaging studies in the study group.

	Mean	Standard deviation	Minimum value	Maximum value
	Echocardiography			
LVEDd (mm)	46.94	6.07	36.03	80.01
LVESd (mm)	35.88	6.54	22.44	53.77
IVSDd (mm)	11.91	1.02	9.47	14.21
PWDd (mm)	10.13	1.09	7.34	12.02
LVM (g)	193.44	47.31	97.17	484.71
LVMI (g/m^2)	107.80	31.05	52.99	311.15
RWT	0.48	0.07	0.28	0.64
	Chest radiograph in PA projection			
C widht [mm]	167.24	19.98	131.00	223.00
T widht [mm]	335.59	32.55	259.00	392.00
CTR	0.51	0.04	0.43	0.63
	Number		Percent	
	Echocardiography			
NG	15		15.6	
LVH	81		84.4	
CR	47		49.0	
CH	15		15.6	
EH	19		19.8	
	Chest radiograph in PA projection			
Heart silhouette enlargement (CTR >0.50)	29		30.2	

C widht – transverse dimension of the heart's silhouette, CH – concentric hypertrophy of the left ventricular, CR – concentric remodelling of the left ventricular, CTR – cardiothoracic ratio, EH – eccentric hypertrophy of the left ventricular, IVSDd – interventricular septum diastolic diameter, LVEDd – left ventricular end-diastolic diameter, LVESd – left ventricular end-systolic diameter, LVH – left ventricular hypertrophy, LVM – left ventricular mass, LVMI – left ventricular mass index, NG – normal geometry of the left ventricular, PWDd – posterior wall diastolic diameter, RWT – relative wall thickness, T widht - transverse dimension of the chest

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Table 3. Geometry of the left ventricular in the studied subgroups differing in cardiothoracic ratio.

	Enlarged heart silhouette (CTR > 0.50)	Non-enlarged heart silhouette (CTR ≤ 0.50)	p
NG [a]	0.0 (0)	22.4 (15)	< 0.05
LVH [a]	100.0 (29)	77.6 (52)	< 0.05
CR [a]	37.9 (11)	53.7 (36)	ns
CH [a]	34.5 (10)	7.5 (5)	< 0.05
EH [a]	27.6 (8)	16.4 (11)	ns

[a] qualitative variable expressed as a percentage (number), CH – concentric hypertrophy of the left ventricular, CR – concentric remodelling of the left ventricular, CTR – cardiothoracic ratio, EH – eccentric hypertrophy of the left ventricular, LVH – left ventricular hypertrophy, NG – normal geometry of the left ventricular

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Table 4. Cardiothoracic ratio in the studied subgroups differing in geometry of the left ventricular.

		CTR [b]	Heart silhouette enlargement (CTR > 0.50) [a]
subgroups differing in left ventricular hypertrophy	NG	0.46 ±0.02	0.0 (0)
	LVH	0.52 ±0.04	35.8 (29)
	p	< 0.05	< 0.05
subgroups differing in the type of left ventricular geometry	NG	0.46 ±0.02	0.0 (0)
	CR	0.49 ±0.02	23.4 (11)
	CH	0.53 ±0.04	66.7 (10)
	EH	0.52 ±0.05	42.1 (8)
	p	NG vs. CR, CH, EH: p < 0.05 CR vs. CH, EH: p < 0.05	NG vs. CR, CH, EH: p < 0.05 CR vs. CH: p < 0.05

[a] qualitative variable expressed as a percentage (number), [b] quantitative variable expressed as mean ± standard deviation, CH – concentric hypertrophy of the left ventricular, CR – concentric remodelling of the left ventricular, CTR – cardiothoracic ratio, EH – eccentric hypertrophy of the left ventricular, LVH – left ventricular hypertrophy, NG – normal geometry of the left ventricular

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Table 5. Correlation of the cardiothoracic ratio in the chest radiograph and the size of the left ventricular in the echocardiography.

	CTR	
	r	p
LVEDd (mm)	0.38	< 0.05
LVESd (mm)	- 0.12	ns
IVSDd (mm)	0.13	ns
PWDd (mm)	0.07	ns
LVM (g)	0.42	< 0.05
LVMI (g/m^2)	0.50	< 0.50
RWT	- 0.19	ns

CTR – cardiothoracic ratio, IVSDd – interventricular septum diastolic diameter, LVEDd – left ventricular end-diastolic diameter, LVESd – left ventricular end-systolic diameter, LVM – left ventricular mass, LVMI – left ventricular mass index, PWDd – posterior wall diastolic diameter, RWT – relative wall thickness

Table 6. Sensitivity, specificity and accuracy of the radiographic cardiothoracic ratio as a predictor of left ventricular geometry.

		Sensitivity	Specificity	Accuracy
Prediction of LVH	CTR > 0.50	1.000	0.358	0.458
	CTR > 0.49 *	0.933	0.827	0.844
Prediction of CR	CTR > 0.50	0.633	0.213	0.427
	CTR > 0.49 *	0.367	0.787	0.573
Prediction of CH	CTR > 0.50	0.778	0.667	0.760
	CTR > 0.52 *	0.840	0.600	0.802
Prediction of EH	CTR > 0.50	0.740	0.421	0.677
	CTR > 0.52 *	0.805	0.368	0.719

* optimal cut-off point according to the ROC curve, CH – concentric hypertrophy of the left ventricular, CR – concentric remodelling of the left ventricular, CTR – cardiothoracic ratio, EH – eccentric hypertrophy of the left ventricular, LVH – left ventricular hypertrophy

Figure

Figure 1. The method of measuring CTR on a chest radiograph in the PA projection. CTR=A/B.

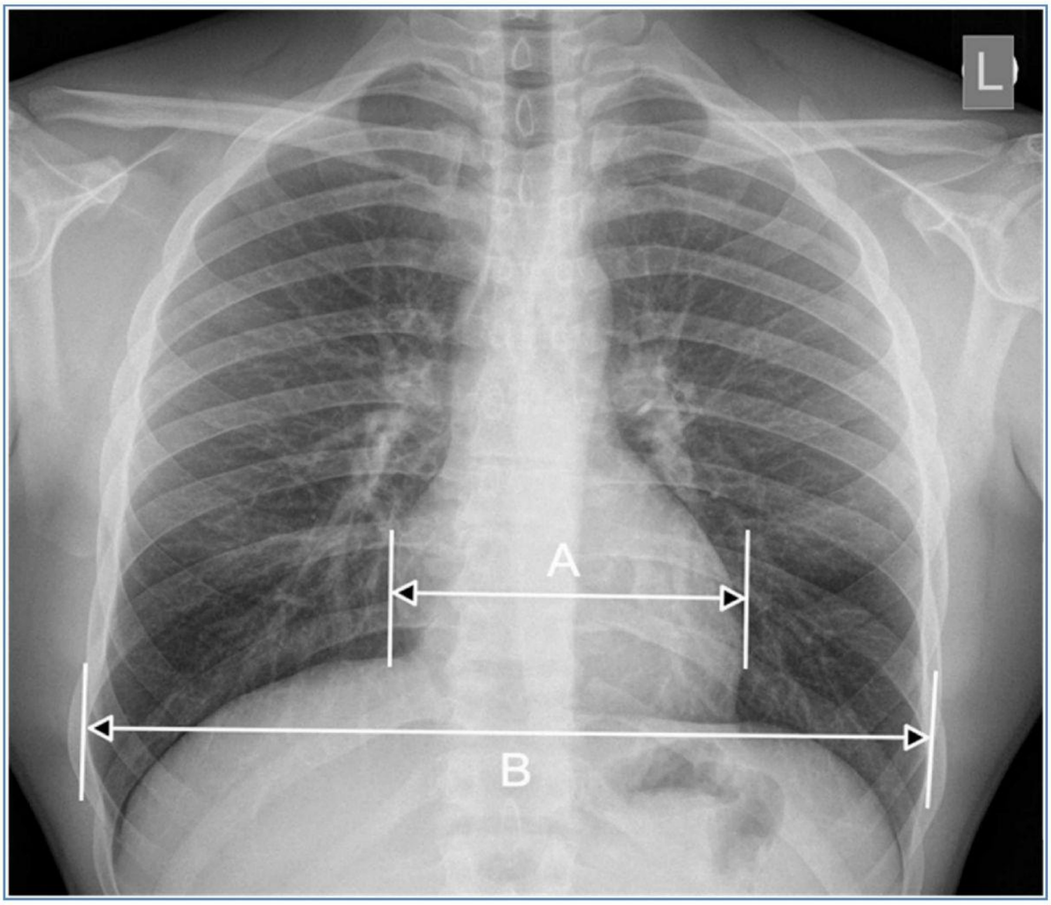

Figure 2. ROC curve for predicting left ventricular hypertrophy using the CTR value on the chest radiograph.

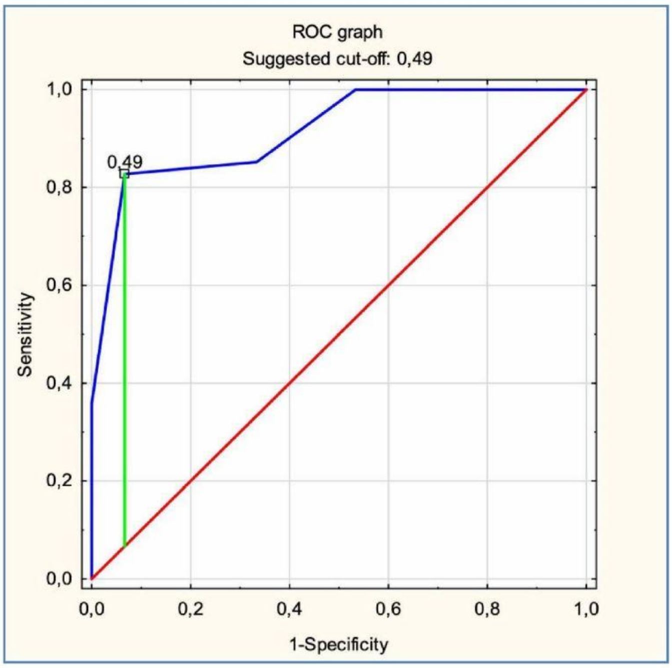

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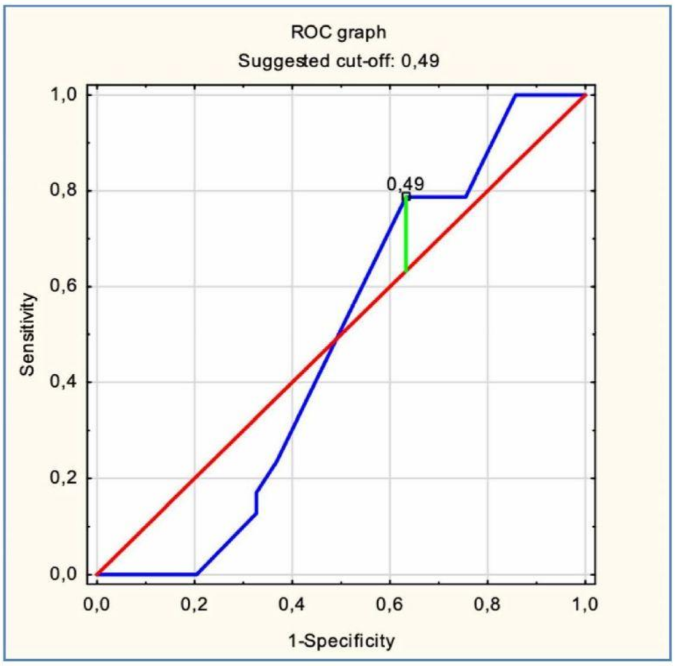
Figure 3. ROC curves for predicting left ventricular geometry using the CTR value on the chest radiograph. **(A)** CR – concentric remodeling of the left ventricular. **(B)** CH – concentric hypertrophy of the left ventricular. **(C)** EH – eccentric hypertrophy of the left ventricular.



A.

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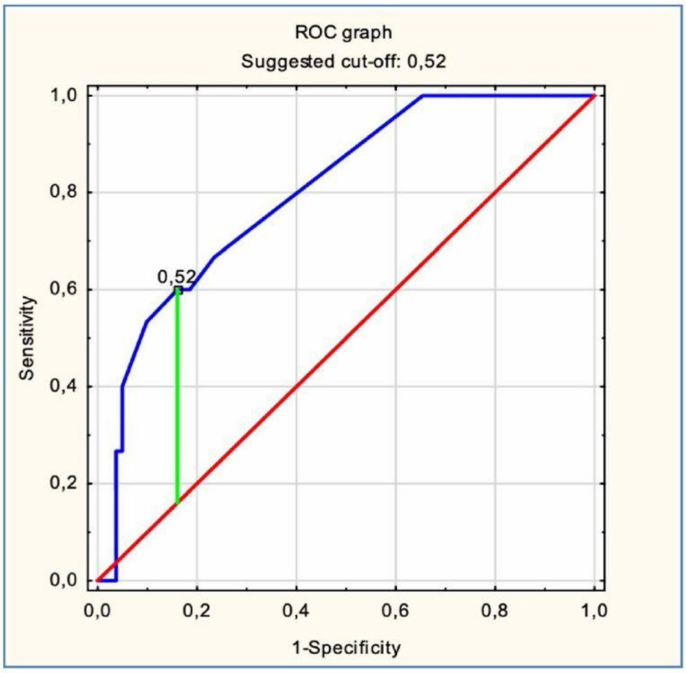
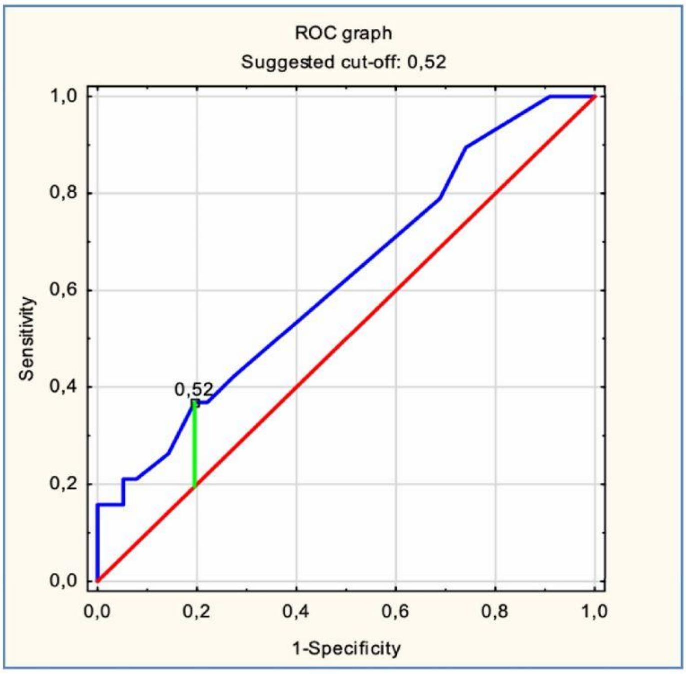

ROC graph
Suggested cut-off: 0,52
0,52
Sensitivity
1-Specificity
0,0
0,2
0,4
0,6
0,8
1,0

548 B.


ROC graph
Suggested cut-off: 0,52
0,52
Sensitivity
1-Specificity
0,0
0,2
0,4
0,6
0,8
1,0

549 C.

OŚWIADCZENIA WSPÓŁAUTORÓW

Wrocław, 06.06.2022

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OŚWIADCZENIE O WSPÓŁAUTORSTWIE

Oświadczam, że w pracy:

1. Truszkiewicz Krystian, Poręba Rafał, Gać Paweł: **Radiological Cardiothoracic Ratio in Evidence-Based Medicine**. *Journal of Clinical Medicine*. 2021; 10(9):2016.
Mój udział polegał na projektowaniu, zebraniu dostępnego piśmiennictwa, przygotowaniu rycin, współredagowaniu merytorycznym i ostatecznym przygotowaniu publikacji

2. Truszkiewicz Krystian, Poręba Małgorzata, Poręba Rafał, Gać Paweł: **Radiological Cardiothoracic Ratio as a Potential Predictor of Right Ventricular Enlargement in Patients with Suspected Pulmonary Embolism Due to COVID-19.**
J. Clin. Med. **2021**, *10*, 5703.
Mój udział polegał na projektowaniu, organizowaniu i nadzorowaniu badań, analizie danych, interpretacji wyników, zebraniu piśmiennictwa naukowego i odniesieniu do niego uzyskanych danych, przygotowaniu rycin, współredagowaniu merytorycznym i ostatecznym przygotowaniu publikacji

3. Truszkiewicz Krystian, Macek Piotr, Poręba Małgorzata, Poręba Rafał, Gać Paweł. **Radiological cardiothoracic ratio as a potential marker of left ventricular hypertrophy assessed by echocardiography.** ***Radiol Res Pract.*** **2022;2022:4931945.**
Mój udział polegał na projektowaniu, organizowaniu i nadzorowaniu badań, analizie danych, interpretacji wyników, zebraniu piśmiennictwa naukowego i odniesieniu do niego uzyskanych danych, przygotowaniu rycin, współredagowaniu merytorycznym i ostatecznym przygotowaniu publikacji

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OŚWIADCZENIE O WSPÓŁAUTORSTWIE

Oświadczam, że w pracy:

1. Truszkiewicz Krystian, Poręba Rafał, Gać Paweł: **Radiological Cardiothoracic Ratio in Evidence-Based Medicine**. *J. Clin. Med.* 2021; 10(9): 2016.
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OŚWIADCZENIE O WSPÓŁAUTORSTWIE

Oświadczam, że w pracy:

1.Truszkiewicz Krystian, Poręba Małgorzata, Poręba Rafał, Gać Paweł: **Radiological Cardiothoracic Ratio as a Potential Predictor of Right Ventricular Enlargement in Patients with Suspected Pulmonary Embolism Due to COVID-19.** *J. Clin. Med.* **2021**, *10*, 5703.
Mój udział polegał na współredagowaniu merytorycznym publikacji

2. Truszkiewicz Krystian, Macek Piotr, Poręba Małgorzata, Poręba Rafał, Gać Paweł. **Radiological cardiothoracic ratio as a potential marker of left ventricular hypertrophy assessed by echocardiography.** ***Radiol Res Pract.*** **2022;2022:4931945.**
Mój udział polegał na współredagowaniu merytorycznym publikacji

Wrocław, 06.06.2022

Prof. dr hab. n. med. Rafał Poręba

Katedra i Klinika Chorób Wewnętrznych, Zawodowych,
Nadciśnienia Tętniczego i Onkologii Klinicznej
Uniwersytetu Medycznego we Wrocławiu
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50 – 556 Wrocław

OŚWIADCZENIE O WSPÓŁAUTORSTWIE

Oświadczam, że w pracy:

1. Truszkiewicz Krystian, Poręba Rafał, Gać Paweł: **Radiological Cardiothoracic Ratio in Evidence-Based Medicine**. *Journal of Clinical Medicine*. 2021; 10(9):2016.
Mój udział polegał na projektowaniu, nadzorowaniu i merytorycznym współredagowaniu publikacji

2. Truszkiewicz Krystian, Poręba Małgorzata, Poręba Rafał, Gać Paweł: **Radiological Cardiothoracic Ratio as a Potential Predictor of Right Ventricular Enlargement in Patients with Suspected Pulmonary Embolism Due to COVID-19.** *J. Clin. Med.* **2021**, *10*, 5703.
Mój udział polegał na projektowaniu, organizowaniu i nadzorowaniu badań, analizie statystycznej danych, interpretacji wyników oraz współredagowaniu merytorycznym publikacji

3. Truszkiewicz Krystian, Macek Piotr, Poręba Małgorzata, Poręba Rafał, Gać Paweł. **Radiological cardiothoracic ratio as a potential marker of left ventricular hypertrophy assessed by echocardiography.** ***Radiol Res Pract.*** **2022;2022:4931945.**
Mój udział polegał na projektowaniu, organizowaniu i nadzorowaniu badań, analizie statystycznej danych, interpretacji wyników oraz współredagowaniu merytorycznym publikacji

Wrocław, 06.06.2022

lek. Piotr Macek

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Uniwersytetu Medycznego we Wrocławiu
ul. Borowska 213
50 – 556 Wrocław

OŚWIADCZENIE O WSPÓŁAUTORSTWIE

Oświadczam, że w pracy:

1. Truszkiewicz Krystian, Macek Piotr, Poręba Małgorzata, Poręba Rafał, Gać Paweł. **Radiological cardiothoracic ratio as a potential marker of left ventricular hypertrophy assessed by echocardiography.** ***Radiol Res Pract.*** **2022;2022:4931945.**
   Mój udział polegał na zbieraniu danych do publikacji

ZGODA KOMISJI BIOETYCZNEJ

1

KOMISJA BIOETYCZNA
przy
Uniwersytecie Medycznym
we Wrocławiu
ul. Pasteura 1; 50-367 WROCŁAW

OPINIA KOMISJI BIOETYCZNEJ Nr KB – 414/2021

Komisja Bioetyczna przy Uniwersytecie Medycznym we Wrocławiu, powołana zarządzeniem Rektora Uniwersytetu Medycznego we Wrocławiu nr 278/XVI R/2020 z dnia 21 grudnia 2020 r. oraz działająca w trybie przewidzianym rozporządzeniem Ministra Zdrowia i Opieki Społecznej z dnia 11 maja 1999 r. (Dz.U. nr 47, poz. 480) na podstawie ustawy o zawodzie lekarza z dnia 5 grudnia 1996 r. (Dz.U. nr 514 z 2020 r.) w składzie:

dr Joanna Birecka (psychiatria)
dr Beata Freier (onkologia)
dr hab. Tomasz Fuchs (ginekologia, położnictwo)
prof. dr hab. Dariusz Janczak (chirurgia naczyniowa, transplantologia)
dr hab. Krzysztof Kaliszewski (chirurgia endokrynologiczna)
dr prawa Andrzej Malicki (prawo)
dr hab. Marcin Mączyński (farmacja)
Urszula Olechowska (pielęgniarstwo)
prof. dr hab. Leszek Szenborn (pediatria, choroby zakaźne)
prof. dr hab. Andrzej Szuba (choroby wewnętrzne, angiologia
ks. prof. Andrzej Tomko (duchowny)
prof. dr hab. Mieszko Więckiewicz (stomatologia)
dr hab. Andrzej Wojnar, prof. nadzw. (histopatologia, dermatologia) przedstawiciel Dolnośląskiej Izby Lekarskiej)
dr hab. Jacek Zieliński (filozofia)

pod przewodnictwem
prof. dr hab. Jerzego Rudnickiego (chirurgia, proktologia)

Przestrzegając w działalności zasad Good Clinical Practice oraz zasad Deklaracji Helsińskiej, po zapoznaniu się z wnioskiem zgłoszonym przez **lek. Krystiana Truszkiewicza** doktoranta Uniwersytetu Medycznego we Wrocławiu do projektu badawczego pt.:

2

„Radiologiczny wskaźnik sercowo-płucny jako predyktor wielkości serca ocenianej metodami echokardiografii, tomografii komputerowej i rezonansu magnetycznego”

w tajnym głosowaniu postanowiła wyrazić zgodę na przeprowadzenie badania w Katedrze i Zakładzie Higieny Uniwersytetu Medycznego we Wrocławiu oraz Samodzielnej Pracowni Nieinwazyjnych Badań Obrazowych Układu Krążenia 4. WSK we Wrocławiu **pod warunkiem zachowania anonimowości uzyskanych danych**.
Badanie będzie prowadzone pod nadzorem dr hab. Pawła Gacia, prof. UMW

Uwaga: Badanie to zostało objęte ubezpieczeniem odpowiedzialności cywilnej Uniwersytetu Medycznego we Wrocławiu z tytułu prowadzonej działalności.

Pouczenie: W ciągu 14 dni od otrzymania decyzji wnioskodawcy przysługuje prawo odwołania do Komisji Odwoławczej za pośrednictwem Komisji Bioetycznej UM we Wrocławiu.

Opinia powyższa dotyczy projektu badawczego będącego podstawą rozprawy doktorskiej.

Przewodniczący Komisji Bioetycznej
przy Uniwersytecie Medycznym

prof. dr hab. Jerzy Rudnicki

Wrocław, dnia 30 kwietnia 2021 r.