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# CT-Base Pulmonary Artery Measurementin the Detection of Pulmonary Hypertension

## *A Meta-Analysis and Systematic Review*

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**Abstract:** To summarize the performance of CT-based main pulmonary artery diameter or pulmonary artery to aorta ratio (PA:A ratio) measurement in detection of pulmonary hypertension by a systematic review and meta-analysis.

A comprehensive literature search was performed to identify studies determining diagnostic accuracy of main pulmonary artery diameter or PA:A ratio measurement for pulmonary hypertension. The Quality Assessment of Diagnostic Accuracy Studies tool was used to assess the quality of the included studies. A bivariate random-effects model was used to pool sensitivity, specificity, positive/negative likelihood ratio (PLR/NLR), and diagnostic odds ratio (DOR). Summary receiver operating characteristic (SROC) curves and area under the curve (AUC) were used to summarize overall diagnostic performance.

This meta-analysis included 20 publications involving 2134 subjects. Summary estimates for main pulmonary artery diameter measurement in the diagnosis of pulmonary hypertension were as follows: sensitivity, 0.79 (95% CI 0.72–0.84); specificity, 0.83 (95% CI 0.75–0.89); PLR, 4.68 (95% CI 3.13–6.99); NLR, 0.26 (95% CI 0.20–0.33); DOR, 18.13 (95% CI 10.87–30.24); and AUC 0.87. The corresponding summary performance estimates for using the PA:A ratio were as follows: sensitivity, 0.74 (95% CI 0.66–0.80); specificity, 0.81 (95% CI 0.74–0.86); PLR, 3.83 (95% CI, 2.70–5.43); NLR, 0.33 (95% CI 0.24–0.44); DOR, 11.77 (95% CI 6.60–21.00); and AUC 0.84.

Both main pulmonary artery diameter and PA:A ratio are helpful for diagnosing pulmonary hypertension. Nevertheless, the results of pulmonary artery measurement should be interpreted in parallel with the results of traditional tests such as echocardiography.

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**Abbreviations**: AUC = area under the curve, CT = computed tomography, DORdiagnostic odds ratio, mPAD = main pulmonary artery diameter, mPAP = mean pulmonary artery pressure, NLR = negative likelihood ratio, PA:Aratio = pulmonary artery to aorta ratio, PH = pulmonary hypertension, PLR = positive likelihood ratio, QUADAS = quality assessment of diagnostic accuracy studies, RHC = right heart catheterization, SROC = summary receiver operating characteristic.

## INTRODUCTION

Pulmonary hypertension (PH) is a progressive disease of multifactorial etiology, it is hemodynamically defined by a mean pulmonary artery pressure (mPAP) $\geq$25 mm Hg.[1,2] PH places a heavy burden on patients because it reduces life quality, work ability, and increases disability. The prognosis of PH is not optimistic, if PH cannot be detected and treated at an early stage, it can lead to progressive right ventricular failure with a high-mortality rate.[3,4] It was reported that in a registry of patients with World Health Organization group 1 PH before the advent of effective medical therapy, the survival rates was only 44% at 5 years, with an estimated median survival of only 2.8 years,[5] and a 5-year survival of 61.1% was found in a recent cohort of idiopathic, heritable, and anorexigen-associated PH patients.[6] Thus, to make an early and accurate diagnostic evaluation of PH will be of great value in facilitating optimal treatment of PH when possible.

The accurate diagnosis of PH remains a clinical challenge, its diagnostic process is complex and requires a high index of clinical suspicion from even the most experienced clinicians. There are several methods to evaluate patients with suspected PH. Echocardiography is commonly used to screen suspected PH patients,[7] one recent published meta-analysis suggested that its pooled sensitivity and specificity were 83% and 72%, respectively, with a modest diagnostic accuracy.[8] In addition, the diagnostic accuracy of echocardiography depends on several factors, including body habitus, detectable tricuspid regurgitation, heart rate, and the experiences of operators, which limit its clinical application.[7,8] Cardiovascular magnetic resonance is another non-invasive diagnostic tool to detect PH, while it seems to only have a moderate sensitivity and specificity.[9] Right heart catheterization (RHC) is the gold standard for the establishment of PH diagnosis. However, it is invasive, and requires exposure to contrast and ionizing radiation when

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appropriate, and does not supply morphologic information.[10] In addition, it is a procedure with some morbidity and mortality even when performed in large-volume medical centers with experienced doctors.[10] Therefore, it highlights the need to develop noninvasive techniques to detect PH.

Since the current available tests have yet proved to be completely satisfactory, the search for improved methods continues. Computed tomography (CT) has been routinely performed in patients with different causes of pulmonary diseases, patients with suspected PH or with non-specific symptoms of PH will undergo CT examination as part of their diagnostic work-up. An increase in the diameter of pulmonary arteries, particularly the main pulmonary artery diameter (mPAD), has been shown to be a useful parameter for detection and assessment of PH,[11] and a number of studies regarding the diagnostic potential of mPAD as well as pulmonary artery to aorta ratio (PA:A ratio) have been extensively studied.[12] But how reliable are pulmonary artery measurements in predicting PH? Studies have come to conflicting answers about whether measurement of mPAD or PA:A ratio can provide adequate diagnostic power and come to similarly conflicting conclusions.[13–15] To help gain more reliable insights, we meta-analyzed the studies based on using mPAD or PA:A ratio measurement to detect PH.

## MATERIALS AND METHODS

This meta-analysis was carried out according to the guidelines of the Preferred Reporting Items for Systematic Reviews, and the methods recommended by the Cochrane Diagnostic Test Accuracy Working Group.[16] Institutional review board approval was not required for this retrospective meta-analysis.

PUBMED and EMBASE were used as search engines to identify relevant publications up to April 2014. The following search terms were used as Medical Headings and/or text words: ''pulmonary artery diameter,'' ''pulmonary artery to aorta ratio,'' ''computed tomography,'' and ''pulmonary hypertension.'' The syntax for the PUBMED searches was as follows: ''pulmonary artery diameter'' OR ''pulmonary artery to aorta ratio'' AND ''computed tomography'' AND ''pulmonary hypertension.'' We also checked the reference lists of the included publications and review articles to identify potential studies.

Inclusion criteria were defined as follows: (1) it should be original article published in English; (2) it examined the ability of mPAD or PA:A ratio measurement for detecting PH in human subjects; (3) there is clear definition of PH and the patients were in stable stage; and (4) it reported sufficient data to calculate sensitivity and specificity. Conference and studies published only as abstracts were excluded for limited information. To avoid selection bias, studies with fewer than 20 patients were also excluded. The quality of the included studies was assessed using the 14-items quality assessment of diagnostic accuracy studies (QUADAS) list.[17] Incase of disagreement, the 2 reviewers arrived at a consensus.

Two reviewers independently extracted data, in studies containing both a training group and a validation group, each group was treated as a single study in the meta-analysis. Using bivariate regression, the pooled estimates of sensitivity and specificity were used as the main outcome measures, this bivariate approach also investigates potential between-study heterogeneity and takes into account possible correlation between sensitivity and specificity, based on the pooled estimates of sensitivity and specificity, we calculated positive likelihood ratios (PLR), negative likelihood ratios (NLR), and diagnostic odds ratios (DOR), which we used as an overall index of diagnostic accuracy. Summary receiver operating characteristic (SROC) curves and area under the curve (AUC) were also calculated to summarize the overall diagnostic performance.

Heterogeneity was assessed using the $I^2$ inconsistency test. $I^2 > 50\%$ indicated substantial heterogeneity, which was then analyzed through meta-regression to investigate the possible source of heterogeneity.[17] Post-test probability was calculated using the overall prevalence of 20% with Fagan nomograms. Potential publication bias was evaluated by Deeks's funnel plot.[18] All analyses were performed using the ''Midas'' module in STATA 12.0 (Stata Corp., College Station, TX) and MetaDiSc 1.4 for Windows (XI, Cochrane Colloquium, Barcelona, Spain). All statistical tests were 2-sided, a $P$ value less than 0.05 was considered for statistical significance.

## RESULTS

After systematically literature search, a total of 378 publications, of which 51 potentially relevant studies were selected for further evaluation, and finally, 20 publications were included.[19–38] Studies were excluded mainly because they did not report sufficient data to construct $2 \times 2$ tables, or they did not perform CT examinations. Figure 1 outlines the process of selecting studies.

### Quality of Reporting and Study Design

The final set of 20 publications (21 studies) involved 2134 subjects, comprising 1268 PH patients, and 866 subjects without PH. Of the included studies, 19 studies examined the ability of mPAD to distinguish PH from non-PH subjects, and 10 assessed the ability of the PA:A ratio to do so. Included studies were published between 1984 and 2014. In all included studies, most studies used RHC as the gold standard to diagnose PH, which is widely considered as an acceptable basis for PH diagnosis, 3 studies only used echocardiography as diagnostic reference.[25,37,38] Of the 20 publications, 15 had QUADAS scores $\geq 9$, suggesting the reliable of our results. Tables 1 and 2

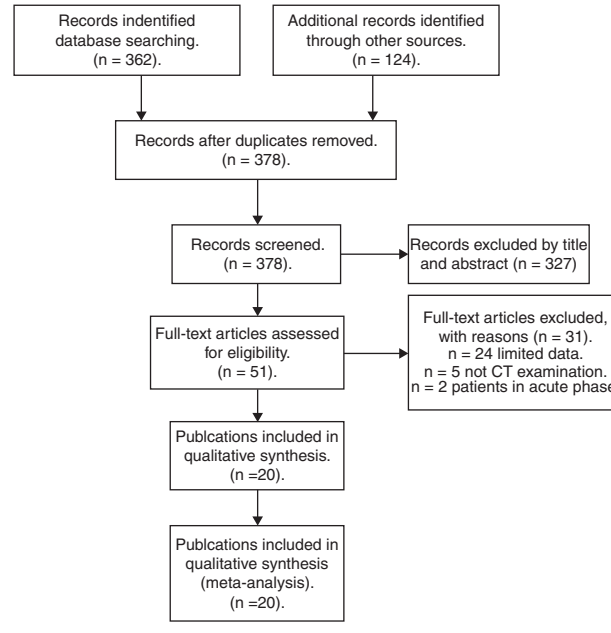


**FIGURE 1.** Flow diagram of study selection.

**TABLE 1.** Clinical Summary of Included Studies

| First Author (Ref) | Year | Origin | Sample Size | Technique | Contrast | Mean Time Interval | Standard | Cut-Off Value mPAP (mm Hg) | Etiology | Study Design | Blind | Consecutive | QUADAS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kuriyama K (19) | 1984 | USA | 27 | General chest CT | Y | 1 month | RHC | 18 | CPD | R | NA | NA | 5 |
| Edwards PD (20) | 1998 | UK | 112 | General chest CT | N | NA | RHC | 20 | Mixed | R | Y | NA | 6 |
| Tan RT (21) | 1998 | USA | 45 | General chest CT | Partly | 1 month | RHC | 20 | PLD or PVD | R | Y | NA | 7 |
| Ng CS (22) | 1999 | UK | 50 | General chest CT/HRCT | Partly | 21.6 days | RHC | 20 | CPD or PLD | R | Y | NA | 7 |
| Pérez-Enguix D (23) | 2007 | Spain | 59 | HRCT | NA | NA | RHC ECG | NA | Mixed | P | NA | Y | 8 |
| Alhamad EH (24)a | 2011 | Saudi Arabia | 100 | General chest CT | N | 3 days | RHC | 25 | ILD | P | Y | Y | 12 |
| Alhamad EH (24)b | 2011 | Saudi Arabia | 34 | General chest CT | N | 3 days | RHC | 25 | Mixed | P | Y | Y | 12 |
| Burger IA (25) | 2011 | Switzerland | 100 | General chest CT | NA | NA | ECG | RV/RA gradient >30 mm Hg | Mixed | R | Y | Y | 10 |
| Chan AL (26) | 2011 | USA | 101 | General chest CT | Partly | 3 days | RHC | 25 | Mixed | R | Y | Y | 9 |
| Condliffe R (27) | 2011 | UK | 67 | CTPA | Y | 3 months | RHC | 25 | SS | R | Y | Y | 10 |
| Davarpanah AH (28) | 2011 | USA | 101 | CTPA | Y | NA | RHC ECG | 25 | Mixed | R | Y | Y | 11 |
| Dornia C (29) | 2012 | Germany | 172 | General chest CT | Y | 3 months | RHC | 25 | CPD PPH | R | Y | NA | 11 |
| Rajaram S (30) | 2012 | UK | 77 | CTPA | Y | 2 days | RHC | 25 | CTD | R | Y | Y | 10 |
| Kam JC (31) | 2013 | USA | 40 | General chest CT | Partly | NA | RHC | 20* | CPD | R | NA | NA | 11 |
| Lange TJ (32) | 2013 | Germany | 78 | General chest CT | Y | 100 days | RHC | 25 | Mixed | R | Y | Y | 11 |
| Mahammedi A (33) | 2013 | USA | 400 | HRCT | Y | 3 months | RHC | 25 | CPD | R | Y | NA | 10 |
| Corson N (34) | 2014 | USA | 289 | General chest CT | Partly | 7 months | RHC | 25 | Mixed | R | Y | NA | 12 |
| Iyer AS (35) | 2014 | USA | 60 | General chest CT | NA | 4 months | RHC | 25 | Severe COPD | R | Y | Y | 11 |
| McCall RK (36) | 2014 | USA | 48 | General chest CT | NA | 6 months | RHC | 25 | Scleroderma | R | Y | NA | 10 |
| Sertogullarindan B (37) | 2014 | Turkey | 124 | General chest CT | Y | NA | ECG | sPAP>35 | BSP | P | NA | NA | 10 |
| Siegel Y (38) | 2014 | USA | 50 | CTPA | Y | 6 months | ECG | NA | Mixed | P | NA | NA | 10 |

BSP = biomass smoking exposure, COPD = chronic obstructive pulmonary disease, CPD = cardiopulmonary disease, CT = computed tomography, CTD = connective tissue disease, CTPA = compu-computer tomography pulmonary angiography, ECG = echocardiography, HRCT = high resolution computed tomography, ILD = interstitial lung disease, mPAP = mean pulmonary arterial pressure, N = no, NA = Not available, P = prospective, PLD = parenchymal lung disease, PPH = precapillary pulmonary hypertension, PVD = pulmonary vascular disease, QUADAS = quality assessment of diagnostic accuracy studies, R = resprospective, RHC = right heart catheterization, sPAP = systolic pulmonary arterial pressure, SS = systemic sclerosis, Y = yes.

*This study was designed to detected border pulmonary hypertension.a,b means 2 studies in one publication.Mean time interval means the time between RHC and CT examination.

**TABLE 2.** Patients Distribution and Correlation With mPAP and PVR

| First Author (Ref) | Year | PH | non-PH | Cut-Off Value | TP | FP | FN | TN | Correlation With mPAP | Correlation With PVR |
|---|---|---|---|---|---|---|---|---|---|---|
| mPAD | | | | | | | | | | |
| Kuriyama K (19) | 1984 | 16 | 11 | 28.6 mm | 11 | 0 | 5 | 11 | r = 0.83 | r = 0.72 |
| Edwards PD (20) | 1998 | 12 | 100 | 33.2 mm | 7 | 5 | 5 | 95 | NA | NA |
| Tan RT (21) | 1998 | 36 | 9 | 29 mm | 31 | 1 | 5 | 8 | r = 0.124* | NA |
| Ng CS (22) | 1999 | 37 | 13 | 30 mm | 25 | 0 | 12 | 13 | r = 0.74 | r = 0.55 |
| Pérez-Enguix D (23) | 2007 | 35 | 24 | 29 mm | 23 | 10 | 11 | 15 | NA | NA |
| Alhamad EH (24)a | 2011 | 37 | 63 | 25 mm | 32 | 37 | 5 | 26 | r = 0.301 | NA |
| Alhamad EH (24)b | 2011 | 19 | 15 | 31.6 mm | 9 | 1 | 10 | 14 | r = 0.701 | NA |
| Burger IA (25) | 2011 | 37 | 63 | 30 mm | 29 | 6 | 8 | 57 | NA | NA |
| Chan AL (26) | 2011 | 53 | 48 | 29 mm | 41 | 5 | 12 | 43 | NA | NA |
| Davarpanah AH (28) | 2011 | 67 | 34 | 27.6 mm | 59 | 7 | 8 | 27 | NA | NA |
| Dornia C (29) | 2012 | 114 | 58 | 29 mm | 107 | 22 | 7 | 36 | NA | NA |
| Rajaram S (30) | 2012 | 55 | 22 | 29 mm | 32 | 6 | 23 | 16 | r = 0.37 | r = 0.28 |
| Kam JC (31) | 2013 | 25 | 15 | 33.3 mm | 20 | 0 | 5 | 15 | NA | NA |
| Lange TJ (32) | 2013 | 26 | 52 | 29 mm | 20 | 20 | 6 | 32 | r = 0.496 | r = 0.445 |
| Mahammedi A (33) | 2013 | 298 | 102 | 29.5 mm | 211 | 21 | 87 | 81 | r = 0.51 | NA |
| Corson N (34) | 2014 | 175 | 114 | 29 mm | 156 | 19 | 19 | 95 | r = 0.34 | NA |
| McCall RK (36) | 2014 | 32 | 16 | 30.8 mm | 26 | 2 | 6 | 14 | NA | NA |
| Sertogullarindan B (37) | 2014 | 96 | 28 | 29 mm | 87 | 6 | 9 | 22 | NA | NA |
| Siegel Y (38) | 2014 | 26 | 24 | 29 mm | 18 | 7 | 8 | 17 | NA | NA |
| PA:A ratio | | | | | | | | | | |
| Ng CS (22) | 1999 | 37 | 13 | 1 | 26 | 1 | 11 | 12 | r = 0.74 | r = 0.59 |
| Alhamad EH (24)a | 2011 | 37 | 63 | 0.94 | 24 | 25 | 13 | 38 | r = 0.434 | NA |
| Alhamad EH (24)b | 2011 | 19 | 15 | 0.94 | 13 | 3 | 6 | 12 | r = 0.626 | NA |
| Chan AL (26) | 2011 | 53 | 48 | 1 | 46 | 10 | 7 | 38 | NA | NA |
| Condliffe R (27) | 2011 | 50 | 17 | 1 | 40 | 2 | 10 | 15 | NA | NA |
| Dornia C (29) | 2012 | 114 | 58 | 1 | 72 | 4 | 42 | 54 | NA | NA |
| Rajaram S (30) | 2012 | 55 | 22 | 1 | 30 | 6 | 25 | 16 | r = 0.43 | r = 0.36 |
| Mahammedi A (33) | 2013 | 298 | 102 | 1 | 211 | 24 | 87 | 78 | r = 0.54 | NA |
| Corson N (34) | 2014 | 175 | 114 | 1 | 156 | 21 | 19 | 93 | r = 0.40 | NA |
| Iyer AS (35) | 2014 | 22 | 38 | 1 | 16 | 6 | 6 | 32 | r = 0.56 | r = 0.45 |

FN = false negative, FP = false positive, mPAD = main pulmonary artery diameter, mPAP = mean pulmonary arterial pressure, PA:A ratio = pulmonary artery to aorta ratio, PH = pulmonary hypertension, PVR = pulmonary vascular resistance, TN = true negative, TP = true positive.

* The *P* value>0.05, the others were all less than 0.05.

summarized the clinical characteristics of the studies, patient distribution in each study as well as the QUADAS scores for each publication.

## Diagnostic Accuracy of mPAD Measurement

The following pooled parameters were calculated over all 19 studies examining mPAD measurement for diagnosing PH: sensitivity, 0.79 (95% CI: 0.72–0.84); specificity, 0.83 (95% CI: 0.75–0.89); PLR, 4.68 (95% CI: 3.13–6.99) (Figure 2); NLR, 0.26 (95% CI: 0.20–0.33) (Figure 2); and DOR, 18.13 (95% CI: 10.87–30.24). All 5 performance indices showed high $I^2$ values: SEN, 80.43%; SPE, 84.73%; PLR, 76.18%; NLR, 77.35%; and DOR, 99.81% (all with $P < 0.05$). This suggests substantial heterogeneity among included studies.

The SROC curve was shown in Figure 3, which shows a plot of the rate of true positives as a function of the rate of false positives for individual studies. We plotted the observed and predicted ellipses at a 95% CI. The AUC was 0.87 (95% CI: 0.84–0.90), indicating a good discriminatory ability of mPAD measurement. Fagan's nomogram for likelihood ratios indicated that using mPAD to detect PH increased the post-probability to 54% when the results were positive and reduced the post-probability to 6% when the results were negative (Figure 4).

Significant heterogeneity was identified among included studies, so we performed a meta-regression analysis to explore the possible sources of heterogeneity. We used several covariates in the present meta-regression: (1) publication year (before 2000 vs after 2000); (2) sample size (<100 subjects vs ≥100 subjects); (3) contrast use (yes vs no/not reported); (4) procedure interval (<3 months vs ≥3 months); (5) QUADAS score (<10 vs ≥10); (6) design (prospective vs retrospective);(7) blinding (yes vs no/not reported); and (8) sampling method (consecutive vs nonconsecutive/random/not reported). The outcomes of the meta-regression are shown in supplementary Table 1, http://links.lww.com/MD/A99. In the present study, except sample size ($P < 0.05$), the other of the above covariates were not found to be the significant source of heterogeneity($P > 0.05$), suggesting the heterogeneity may be from sample size or other un-defined covariates.

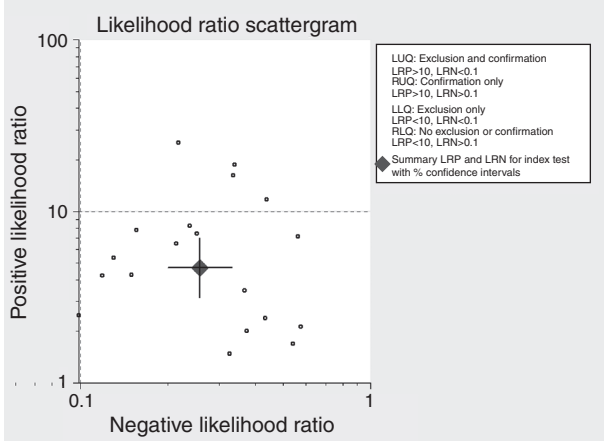


**FIGURE 2.** Scatterplot of the positive likelihood ratio (PLR) and negative likelihood ratio (NLR) when using mPAD measurements to diagnose PH.

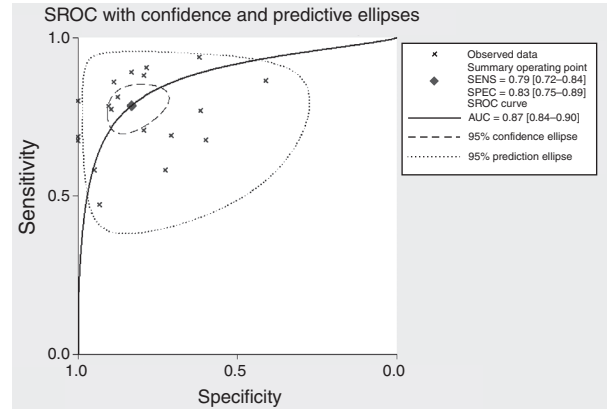


**FIGURE 3.** Summary receiver operating characteristic (SROC) curve for mPAD measurements to diagnose PH.

## Diagnostic Accuracy of the PA:A Ratio

A total of 10 studies with 1350 subjects examined the ability of the PA:A ratio to distinguish PH from non-PH subjects. Table 3 summarized the sensitivity, specificity,

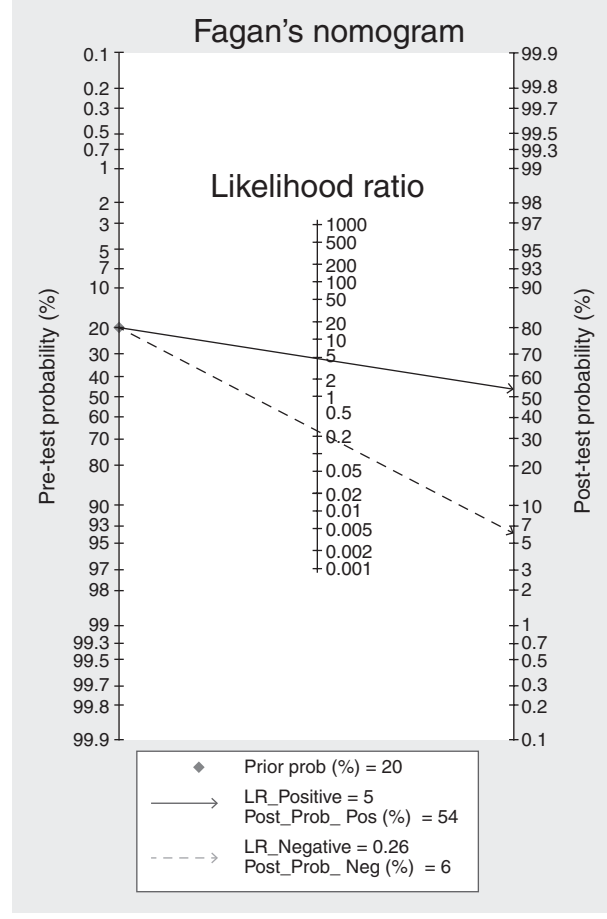


**FIGURE 4.** Fagan's nomogram for likelihood ratios and pre- and post-test probabilities for using mPAD measurements to diagnose PH.

**TABLE 3.** Diagnostic Summary of mPAD and PA:A Ratio

| Diagnostic Index | mPAD | PA:A Ratio |
|---|---|---|
| Sensitivity | 0.79 (95% CI: 0.72–0.84) | 0.74 (95% CI: 0.66–0.80) |
| Specificity | 0.83 (95% CI: 0.75–0.89) | 0.81 (95% CI: 0.74–0.86) |
| PLR | 4.68 (95% CI: 3.13–6.99) | 3.83 (95% CI: 2.70–5.43) |
| NLR | 0.26 (95% CI: 0.20–0.33) | 0.33 (95% CI: 0.24–0.44) |
| DOR | 18.13 (95% CI: 10.87–30.24) | 11.77 (95% CI: 6.60–21.00) |
| PPP | 54% | 49% |
| PPN | 6% | 8% |
| AUC | 0.87 (95% CI: 0.84–0.90) | 0.84 (95% CI: 0.81–0.87) |

AUC = area under the curve, DOR = diagnostic odds ratio, mPAD = mean pulmonary arterial pressure, NLR = negative likelihood ratio, PA:A ratio = pulmonary artery to aorta ratio, PLR = positive likelihood ratio, PPN = post-probability-negative, PPP = post-probability-positive.

PLR, NLR, and DOR. The AUC was 0.84 (95% CI: 0.81–0.87), suggesting moderate overall accuracy (Figure 5).

## Publication Bias

Deeks' funnel plot asymmetry test was used to assess likelihood of publication bias in the final set of studies. The slope coefficients for mPAD and PA:A ratio were associated with a *P* value of 0.89 and 0.68, respectively, suggesting symmetry in the data and low likelihood of such bias (Figure 6).

## DISCUSSION

In this study, we summarized the overall diagnostic performance of mPAD and PA:A measurement for PH, and our meta-analysis suggests that both mPAD and PA:A ratio measurement play a role in diagnosing PH, though they probably cannot stand on their own and they should be used in combination with other traditional tests.

Our meta-analysis showed that mPAD measurement was associated with medium sensitivity (0.79, 95% CI: 0.72–0.84) and specificity (0.83, 95% CI: 0.75–0.89), suggesting a relative high rate of missed diagnosis (21%) and misdiagnosis (17%). The SROC curve illustrates overall test performance, our SROC analysis showed an AUC of 0.87, suggesting a good overall accuracy. DOR is another indicator of diagnostic accuracy, with higher values indicating better discriminatory test performance. Pooled DOR in our meta-analysis was 18.13, suggesting that measurement of mPAD should be helpful in the diagnosis of PH. PLR and NLR were also used to determine the diagnostic accuracy, which are easier to understand in clinical practice.[39] The pooled PLR value of 4.68 suggests that PH patients have an approximately 5-fold higher chance of giving a positive mPAD test result than do patients without PH. At the same time, the pooled NLR was 0.26, indicating that a negative mPAD test result is 26% likely to be a false negative, which is not low enough to rule out PH. In addition, our results revealed that PA:A ratio showed lower sensitivity of 0.74 (95% CI: 0.66–0.80), and the AUC was 0.84, suggesting that the PA:A ratio shows medium discriminatory ability.

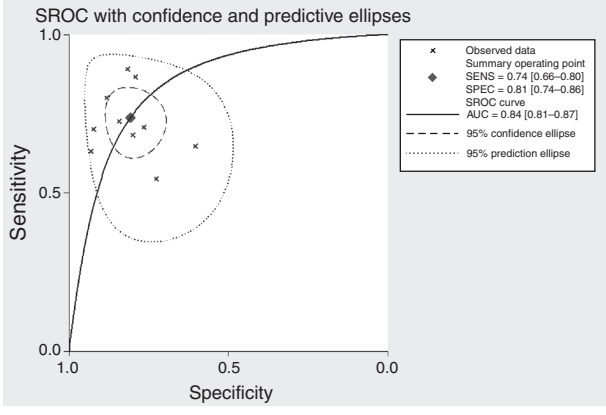


**FIGURE 5.** Summary receiver operating characteristic (SROC) curve for using the pulmonary artery to aorta ratio to diagnose pulmonary hypertension.

In fact, several studies have been published and summarized the overall diagnostic accuracy of echocardiography and cardiovascular magnetic resonance for PH.[8,9,40,41] (Supplementary Table 2, http://links.lww.com/MD/A99). To our best knowledge, our study is the first meta-analysis that evaluated the accuracy of CT-based pulmonary artery measurement for PH. When compared with echocardiography and cardiovascular magnetic resonance, our meta-analysis included the largest population, and showed highest specificity. The SROC curve analysis suggested that the diagnostic performance of CT is even better than echocardiography. However, echocardiography remains the first choice for suspected PH patients, it can provide a comprehensive functional assessment comparable with that of invasive hemodynamic measurements in patients who undergo RHC and it can be used to rule in and rule out PH and increased PVR, and echocardiography-derived new technique is helpful for assessing right ventricular function, which is associated with mortality in PH paitients.[42–44] Echocardiography also plays an important role in assessing outcomes, monitoring the efficacy of specific therapeutic interventions for PH.[7] What should be point out is that, echocardiography plays the starring role and current CT examination is not the first imaging technique to diagnose PH. In our meta-analysis, many of the patients included in studies were referred to CT for specific reasons, particularly chronic obstructive pulmonary disease, cardiovascular disorders, or other diseases where CT plays an important role and the mPAD and PA:A ratio will come for free. Although CT examination is a routine used technique for patients suspected with lung diseases, for PH diagnosis, echocardiography remains the first choice, this comprehensive analysis of the diagnostic accuracy of CT-based pulmonary artery measurement suggests that this indicator may not be reliable enough on its own but should instead be used in

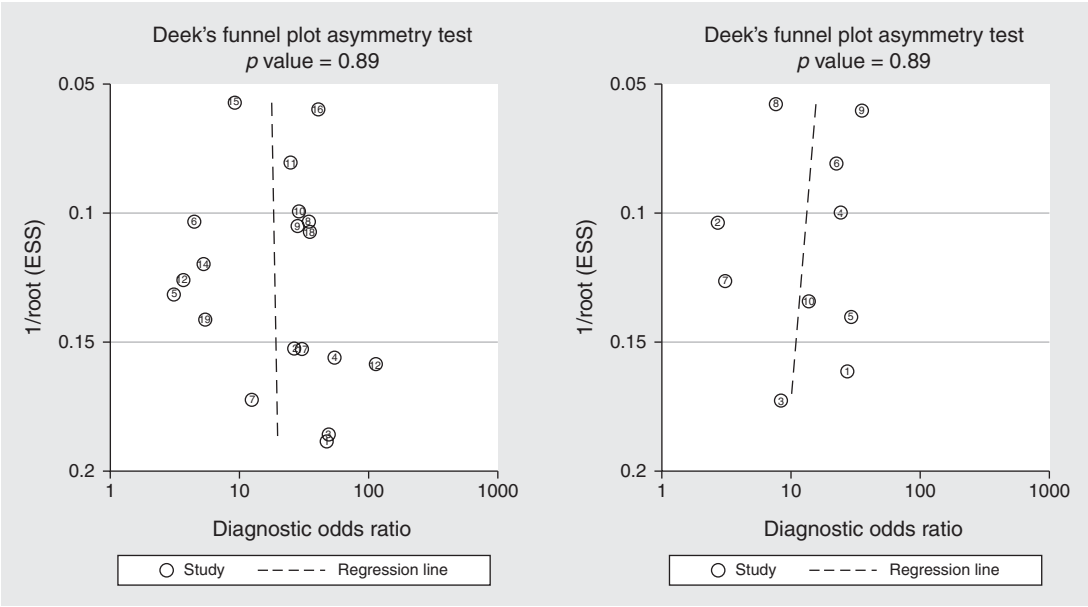


**FIGURE 6.** Deek's funnel plot to assess the likelihood of publication bias.

conjunction with other conventional tests, such as echocardiography, rather than to replace echocardiography.

Growing studies pay attention to the clinical significance of measurement of mPAD and PA:A ratio other than their diagnostic performance. Devaraj et al[45] reported that pulmonary arterial enlargement on CT scans is a highly significant prognostic indicator in the evaluation of patients with bronchiectasis. In 2012, Żyłkowska et al[46] also reported that pulmonary artery dilatation emerges as an independent risk factor for death unexplained by right ventricular failure or comorbidities in patients with pulmonary arterial hypertension and chronic thromboembolic PH, which may be caused by pulmonary artery compression of the left main coronary artery, pulmonary artery rupture, or dissection with cardiac tamponade. Wells et al[47] reported that CT-detected pulmonary artery enlargement (defined as PA:A ratio of $>1$) was associated with severe exacerbations of chronic obstructive pulmonary disease, it was related to prognosticate chronic obstructive pulmonary disease progression, acute exacerbations, and hospitalizations. All these studies suggest that pulmonary artery measurement may be an important tool for non-invasive clinical surveillance and supply more information for the comprehensive management of PH patients. Based on this, detection of pulmonary artery dilation may be used to guide treatment decision-making and identify patients whom will get the most clinical benefits from therapy.[48]

For clinical utility, there are several points that should be addressed. First of all, CT examination's sensitivity is not that high as expected, it should be function as a surrogate diagnostic method for PH, rather than to replace RHC, or echocardiography. Secondly, in Table 2, we summarized the available correlation of mPAP and CT determined mPAD and PA:A ratio, these studies suggested that CT determined mPAD or PA:A ratio has good correlation with mean pulmonary arterial pressure, we propose that CT scanning can serve as a qualitative rather than as a quantitative tool in the assessment of PH. Thirdly, the clinical utility of CT to detect PH should pay attention to the etiology of patients, Devaraj et al[49] reported that pulmonary artery dilatation occurs in the absence of PH in patients with pulmonary fibrosis and is therefore an unreliable sign of PH in these patients. The lack of reliability of pulmonary artery dilation in PH detection in pulmonary fibrosis patients also raises the question as whether it is applicable in other pulmonary diseases conditions, since the mPAD is not absolutely affected by pulmonary arterial pressure in these diseases.[50] Last but not least, the standard of CT measurement to diagnose PH in has not been founded, for mPAD measurement, the cut-off value ranges from 25 to 33.2 mm, this variation in cut-off value partly reflects differences in clinical context, but, further work should aim to identify the cut-off value that provides optimal diagnostic accuracy.

For interpretation the findings of this meta-analysis, several limitations should be addressed. Our strict inclusion and exclusion criteria may have helped reduce selection bias, but they led to a relatively small final set of studies for which statistical power may be inadequate for drawing definitive conclusions about the ability of pulmonary artery determination to discriminate between PH and non-PH subjects. We also detected substantial heterogeneity across the included studies, and subgroup analyses suggest that differences in sample size may account for the possible heterogeneity, and future studies should aim for greater rigor in order to decrease the risk of bias. In addition, our results may be biased by our omission of unpublished studies, studies published in other languages, and studies published in journals not indexed in the databases we searched.[16]

## CONCLUSION

Taken together, our meta-analysis suggests that CT-based mPAD and PA:A ratio measurement may play an important role in aiding diagnosis of PH. In the near future, CT-based pulmonary artery measurement may prove useful as a non-invasive confirmatory test to complement current diagnosing procedures for PH.

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