Immunopathologia Persa
DOI:10.34172/ipp.2023.34435
http immunopathol.com

# Evaluation of agreement coefficient between chest computed tomography and echocardiography in the diagnosis of pulmonary artery hypertension in patients with systemic sclerosis; a pilot study

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**Received** 3 July 2022
**Accepted** 9 May 2023
**Published online** 30 July 2023

**Keywords:** Chest CT scan, Echocardiography, Pulmonary arterial hypertension, Systemic sclerosis

## Abstract

**Introduction:** Systemic sclerosis (SSc) is an autoimmune disorder that often presents with skin involvement. SSc affects various organs, and one of the most important of these organs is the cardiovascular system, which is one of the complications of this syndrome, including pulmonary arterial hypertension (PAH). Early diagnosis of this complication is very important due to the importance of the effect of PAH on mortality and morbidity of patients. For diagnosis of PAH, two methods of computed tomography (CT) scan and echocardiography are conducted.
**Objectives:** In this study, we aimed to evaluate the agreement coefficient of chest CT scan in comparison with echocardiography in the diagnosis of PAH in patients with SSc.
**Patients and Methods:** In a diagnostic study, which was conducted in Loghman hospital (Tehran-Iran), patients with a diagnosis of SSc were evaluated for pulmonary artery pressure (PAP) by echocardiography. For patients, a CT scan of the lungs was conducted and PAP was assessed. The results that obtained from the lungs CT scan were compared with the echocardiography results.
**Results:** Fifty patients with SSc were evaluated. Eighty-four percent of patients were female and the mean age of all patients was 48.94 ± 11.02 years. About 16% of all patients had high PAP based on echocardiography and 28% of patients based on CT scan. Kappa's agreement coefficient was 0.428 and Spearman's correlation coefficient was 0.457. In other words, chest CT scan has a partly agreement with the echocardiography method (*P* value = 0.001).
**Conclusion:** Chest CT scan has a high sensitivity, specificity, and accuracy compared to echocardiography as a screening method.

**Citation:** Ahmadzadeh A, Sheibani M, Farsad F, Dehghan P, Gachkar L, Nazarpoor S. Evaluation of agreement coefficient between chest computed tomography and echocardiography in the diagnosis of pulmonary artery hypertension in patients with systemic sclerosis; a pilot study. Immunopathol Persa. 2023;x(x):e34435. DOI:10.34172/ipp.2023.34435.

## Introduction

Pulmonary arterial hypertension (PAH) is a life-threatening disorder that leaves patients disabled and often leads to death. PAH is characterized by proliferative remodeling of the small pulmonary arteries, which raises pulmonary blood flow resistance. This disease is clinically characterized as a rise in mean pulmonary arterial pressure >20 mm Hg during right heart catheterization in the setting of an increased pulmonary vascular resistance >3 Wood units and appropriate left heart pressures (pulmonary artery wedge and/or left ventricular end-diastolic pressure below 15 mm Hg ) (1-3).

At the time of diagnosis, the majority of PAH patients had advanced symptoms and severe hemodynamic abnormalities. Despite recent medical improvements and successful treatments for PAH, yearly mortality in idiopathic PAH remains high, at 10% (4-7). In some subsets, such as PAH accompanied with systemic sclerosis (SSc), the prognosis is much worse (8-10). Given the poor long-term outcomes, it seems sense to try to discover disease signs early, before symptoms appear. The time between the development of symptoms and the identification of PAH is 2-4 years, therefore making its diagnosis as soon as when the symptoms appear (11-14). The prevalence of PAH in SSc varies from 7% to 19%, making it sufficiently prevalent to

**Key point**

Computed tomography (CT) is a good method for screening and diagnosis of high pulmonary artery hypertension in patients with systemic sclerosis. The sensitivity, specificity, PPV, and NPV of CT for diagnosis of pulmonary artery hypertension in patients with systemic sclerosis were 75%, 80.9%, 42.9%, and 94.4%, respectively. The accuracy of this method was 80%.

warrant routine screening (15,16).

Idiopathic pulmonary veno-occlusive disease is an uncommon disorder in which the small pulmonary veins become obstructed in a widespread manner. Pulmonary veno-occlusive disease -like lesions are prevalent in SSc-related pulmonary hypertension (17). According to the study by Dorfmüller et al, 61.5% of SSc-related pulmonary hypertension patients had high-resolution computed tomography (HRCT) symptoms suggestive of pulmonary veno-occlusive disease (18). According to the study by Günther et al, the presence of these symptoms (centrilobular ground-glass opacities, lymph node enlargement, and septal lines) in the HRCT is linked to a lower chance of survival and a higher risk of pulmonary edema following the start of PAH-targeted therapy (19). For patients with SSc-PAH, yearly screening with transthoracic echocardiography (TTE) is recommended and TTE is screening method for SSc-PAH assessment (3,20).

## Objectives

Based on our knowledge, there are very few studies about assessment of agreement between chest HRCT and TTE in the diagnosis of SSc-PAH. In this study, we aimed to evaluate the agreement coefficient of chest CT scan in comparison with echocardiography in the diagnosis of pulmonary artery hypertension in patients with SSc.

## Patients and Methods

### *Study design*

This is a diagnostic study, patients who had SSc who referred to the hospital were assessed. This study was conducted in Loghman hospital (Tehran, Iran).

Inclusion criteria were all patients with SSc involvement and age more than 18 years. Exclusion criteria were age fewer than 18 years, having other disorders that can cause pulmonary hypertension, presence of interstitial lung disease (ILD) in due to other causes except SSc, severe heart failure, existence of overlap syndrome, and reluctance to participate in the study.

After obtaining patient's consent for entering to the study, all patients were evaluated by a rheumatologist and the diagnosis of SSc was conducted according to clinical and laboratory studies based on American College of Rheumatology/European League against Rheumatism (ACR/EULAR) criteria (21). Meanwhile, all patients were evaluated by an expert cardiologist with an echocardiographic device for pulmonary artery pressure (PAP) assessment at rest and patients with pulmonary arterial systolic pressure above 41 mm Hg (22) were considered in this study as high PAH. The definite diagnosis of high PAP is assessed by right heart catheterization and echocardiography while chest CT scan will be conducted for screening. Since right heart catheterization is not available in our hospital and rarity of this disease and while, we were not able to refer patients for right heart catheterization in other centers due to high costs and patient's unconsent, or its complications, we evaluated the coefficient of agreement of chest CT scan with echocardiography in patients with SSc.

The patients therefore underwent a CT scan of the lungs, and the result was reported by an expert radiologist for the diameter of the pulmonary artery at the site of the pulmonary artery bifurcation. The diameter of the site greater than 29 mm was considered as pulmonary hypertension (23).

By selecting the 3% prevalence of SSc reported in Asian race (24) and the 95% confidence level and 89% sensitivity for pulmonary artery diameter (25) and 15% error, the required sample number of 50 people was calculated.

Patient's data including age, gender, type of SSc, lung HRCT findings, electrocardiogram (ECG) findings, and TTE findings were recorded. All data were compared whit TTE findings as best screening method and their relationships with SSc-PAH were evaluated. Finally, agreement coefficient of HRCT with TTE in the diagnosis of SSc-PAH was assessed.

## Statistical analysis

Frequency and percentage were conducted to describe qualitative data and mean, standard deviation, median values. To compare the two diagnostic methods, kappa agreement coefficient indices, Spearman's correlation coefficient, sensitivity, specificity, positive-negative predictive value and accuracy were calculated. The standard method was considered echocardiography as the best screening method. All analyses were performed by SPSS version 25.0 statistical software and *P* value less than 0.05 was considered to be statistically significant.

## Results

The aim of this diagnostic study was to evaluate the agreement coefficient of chest CT scan in comparison with echocardiography in the diagnosis of PAH in patients with SSc. Fifty patients with SSc were included in the study and were divided into two groups of PAH and normal PAP based on the two diagnostic modalities; (a) lung HRCT scan and (b) TTE.

In this study, 8 (16%) patients were male and 42 (84%) were female. The mean age of all patients was 48.94 ± 11.02 with a range of 25 to 71 years.

Based on TTE, 8 (16%) patients had PAH and in chest HRCT, 14 (28%) patients had high PAP. In 42 patients (84.0%) had normal PAP based on TTE and 36 (72.0%) were normal based on HRCT.

Of total patients, 19 (38%) had diffuse cutaneous systemic sclerosis (dcSSc) and 31 (62%) had limited cutaneous systemic sclerosis (lcSSc).

Based on lungs HRCT findings, 47 patients (94%) had ILD, 12 (24%) had pulmonary to aortic diameter ratio (P/A) >1. Additionally, fourteen patients (28%) had pericardial effusion (PE) and diastolic dysfunction grade 1 (DDG1) in TTE. Moreover, in electrocardiography heart blocks were seen in six (14.3%) patients and one patient (2.7%) had narrow QT interval, 26 (70.3%) had normal QT interval, and 10 (27.0%) had prolonged QT interval. In Table 1, the relationships between PAP findings (high or normal) in TTE and ECG, chest HRCT, and the types of disease were evaluated.

In Table 2, we assessed the correlation between chest HRCT results and TTE findings (as a gold standard) in the diagnosis of PAH. Of eight patients who were diagnosed PAH with TTE, chest CT scan correctly identified in six (75%) and incorrectly detected in two of cases (25%), as in the normal range. The kappa agreement coefficient of the two methods was 0.428 and the Spearman's correlation coefficient was 0.457 ($P=0.001$). In other words, chest HRCT is relatively in agreement with the TTE method.

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were assessed for lung HRCT based on TTE. For diagnosis of SSc-PAH, the sensitivity of lung HRCT was 75% (95% confidence interval [CI]: 74%-76%). The specificity, PPV, and NPV of lung HRCT for SSc-PAH diagnosis were 80.9% (95% CI: 74%-76%), 42.9% (95% CI: 28.8%-56.2%), and 94.4% (95% CI: 94.2%-94.6%), respectively. The lung HRCT accuracy for diagnosis of SSc-PAH was 80% (95% CI: 69%-91%). Correlation between lung HRCT and TTE based on P/A ratio result is presented in Table 3.

Of eight patients were diagnosed with high pulmonary arterial pressure by TTE, the P/A correctly identified in five (62.5%) patients by lung HRCT and incorrectly identified in three (37.5%) patients as normal. The kappa agreement coefficient of the two methods was 0.076 and the Spearman's correlation coefficient was 0.443 ($P = 0.002$). In other words, it can be interpreted that the lung HRCT method is relatively in agreement with the TTE method.

**Table 1.** Association of the TTE results with disease factors

| TTE results | | | | | |
|---|---|---|---|---|---|
| | | **Total** | **Normal** | **PAP high** | ***P* value** |
| Type of SSc | dcSSc | 31 (62.0%) | 24 (57.1%) | 7 (87.5%) | 0.197 |
| | LcSSc | 19 (38.0%) | 18 (42.9%) | 1 (12.5%) | |
| ILD | Without ILD | 3 (6.0%) | 3 (7.1%) | 0 (0.0%) | 0.55 |
| | With ILD | 47 (94.0%) | 39 (92.9%) | 8 (100.0%) | |
| P/A | <1 | 36 (75.0%) | 34 (82.9%) | 2 (28.6%) | <0.001 |
| | >1 | 12 (25.0%) | 7 (17.1%) | 5 (71.4%) | |
| DDG1 | Without DDG1 | 31 (62.0%) | 27 (64.3%) | 4 (50.0%) | 0.522 |
| | With DDG1 | 19 (38.0%) | 15 (35.7%) | 4 (50.0%) | |
| PE | Without PE | 36 (72.0%) | 29 (69.0%) | 7 (87.5%) | >0.999 |
| | With PE | 14 (28.0%) | 13 (31.0%) | 1 (12.5%) | |
| QT interval | Short | 1 (2.7%) | 1 (3.2%) | 0 (0.0%) | 0.669 |
| | Normal | 26 (70.3%) | 21 (67.7%) | 5 (83.3%) | |
| | Prolonged | 10 (27.0%) | 9 (29.0%) | 1 (16.7%) | |
| ECG block | Without block | 36 (85.7%) | 32 (91.4%) | 4 (57.1%) | 0.046 |
| | With block | 6 (14.3%) | 3 (8.6%) | 3 (42.9%) | |

ILD, Interstitial lung disease; P/A, Pulmonary to aortic diameter ratio; DDG1, Diastolic dysfunction grade 1; PE, Pericardial effusion; ECG, Electrocardiogram; dcSSc, diffuse cutaneous systemic sclerosis; lcSSc, limited cutaneous systemic sclerosis; TTE, transthoracic echocardiography; PAP, pulmonary artery pressure.

**Table 2.** Correlation between HRCT and TTE in PAH diagnosis

| | | **Echocardiography** | | | | |
|---|---|---|---|---|---|---|
| | | **Normal** | **High PAP (PAH)** | **Measure of agreement (KAPPA)** | **Spearman's correlation coefficient** | ***P* value** |
| Pulmonary high-resolution computed tomography | Normal | 34 (81.0%) | 2 (25.0%) | 0.428 | 0.457 | 0.001 |
| Pulmonary artery diameter | High PAP (PAH) | 8 (19.0%) | 6 (75.0%) | | | |

TTE, transthoracic echocardiography; PAH, pulmonary arterial hypertension; PAP, pulmonary artery pressure; HRCT, high-resolution computed tomography.

**Table 3.** Correlation between lung HRCT and TTE based on P/A results

| | | Echocardiography | | Measure of agreement (KAPPA) | Spearman's correlation coefficient | *P* value |
|---|---|---|---|---|---|---|
| | | Normal | High PAP (PAH) | | | |
| P/A | Normal | 35(83.3%) | 3(23.5%) | 0.076 | 0.443 | 0.002 |
| | Abnormal | 7(16.7%) | 5 (62.5% | | | |

P/A, Pulmonary to aortic diameter ratio; TTE, transthoracic echocardiography; PAH, pulmonary arterial hypertension; PAP, pulmonary artery pressure; HRCT, high-resolution computed tomography.

Additionally, the sensitivity, specificity, PPV, and NPV of P/A of lung HRCT were assessed based on TTE. It was observed that the sensitivity of lung HRCT in assessment of P/A was 62.50% (95% CI: 74%-76%), the specificity was 83.33% (95% CI: 68.64%-93.03%), the positive predictive value was 41.67% (95% CI: 23.15%-62.88%), and NPV was 92.11% (95% CI: 82.52%-96.65%). Therefore, the accuracy of lung HRCT for P/A assessment was 80.00% (95% CI: 66.28%-89.97%).

## Discussion

In this study, the agreement coefficient between CT and echocardiography in the diagnosis of PAH in patients with SSc was evaluated. Fifty patients with SSc-PAH were enrolled to the study. The mean age of patients was 48.94 ± 11.02 and 84% were female. The kappa agreement coefficient of lung HRCT for evaluation of SSc-PAH in comparison with TTE was 0.428 and the Spearman's correlation coefficient was 0.457. The kappa agreement coefficient between these two methods for assessment of P/A> 1 was 0.076 and the Spearman's correlation coefficient was 0.443. These values show that lung HRCT method is partly in agreement with the TTE method.

Systemic sclerosis, commonly known as scleroderma, is a multi-organ disorder characterized by fibrosis and thickening of the skin and internal organs, and vascular abnormalities (26). The ACR/EULAR criteria for SSc diagnosis highlights these immunological, fibrotic, and vascular abnormalities, including PAH (21).

According to the area of skin involvement, SSc is divided into diffuse and limited cutaneous types. Skin involvement is limited distal to the elbows and knees in lcSSc, while in dcSSc, involvement is extended including the trunk (dcSSc) (27). Hoffmann-Vold et al showed that lcSSc had higher prevalence than dcSSc. In their study lcSSc was occurred in 6.9/100 000 and dcSSc in 1.8/100 000 (28). In our study, we observed that dcSSc had higher prevalence than lcSSc. We detected that lcSSc was seen in 38.0% and the rest had dcSSc. Our finding was in contrast with the study by Hoffmann-Vold et al (28). This difference may come from the difference in their study population because in the current study, Iranian population with SSc were evaluated but in the Hoffmann-Vold et al study, southeast Norwegian patients were assessed.

The prevalence of PAH in SSc is predicted to be 6-12% (28). Following idiopathic PAH, it is the second most common cause of PAH in European and US registries (29-32). Likewise, Simonneau et al found that PAH is more common in lcSSc (2). In the current study, it was observed that PAH was more common in dcSSc. We found 7/24 (29.16%) of patients with dcSSc had PAH; however, 1/18 (5.55%) of patients with lcSSc had PAH. Our findings were in contrast with the results of the study by Simonneau et al (2). Similarly, Simonneau et al mentioned that ILD, left side cardiac disease, chronic thromboembolism, and pulmonary venous occlusive disease can all coexist with PAH, making diagnosis and treatment even more difficult (2). In the present study, we found that PAH had no association with ILD or heart disorders, except heart blocks. We found that blocks are associated with PAH.

The best screening method for PAH is TTE. It evaluates right and left ventricular shape and functioning, detects valvular anomalies, and can be conducted to estimate right ventricular pressures (3,31). Lung HRCT is conducted to evaluate ILD or pulmonary veno-occlusive disease. In severe PAH, however, chest HRCT may reveal a dilated pulmonary artery and enlarged right ventricle (3,31). A pulmonary artery that is larger than the surrounding ascending aorta on chest HRCT indicates that pulmonary hypertension is present (26).

Based on our knowledge, there is no study about the assessment of agreement coefficient between lung HRCT and TTE in the diagnosis of SSc-PAH. The main advantage of this study is the evaluation of lung HRCT as a comfort and useful method for PAH-SSc evaluation. As mentioned above, with HRCT, we can evaluate lungs condition in SSc. According to our study, lung HRCT can be used for evaluation of PAH-SSc. In the current study, we observed that lung HRCT could be a good method instead of TTE in patients with SSc-PAH because HRCT accuracy in diagnosis of PAH in these patients, is 80%. However, if lung HRCT is negative and there is high suspicious for existence of PAH, we can use TTE as best screening method. Correspondingly, HRCT accuracy for evaluation of P/A was 80%. This accuracy can show the lung HRCT is an effective method for assessment of condition of pulmonary arterial pressure in patients with SSc.

## Conclusion

It can be concluded that in the field of correct diagnosis of patients with PAH-SSc, there is a good agreement between the results of lung HRCT with echocardiography. Moreover, lung HRCT has high sensitivity (75%), specificity (80.9%) and accuracy (80%) compared to TTE.

Due to the non-invasiveness and availability of CT scans, due to the high rate of lung involvement in SSc, and the need for early detection of pulmonary involvement (effect on prognosis, morbidity and mortality), chest CT scan can be conducted to diagnosis of lung tissue involvement in addition to screen these patients for the diagnosis of PAH.

## Limitations of the study

This study was performed on a limited number of patients. Due to the fact that right heart catheterization is the gold standard method for high PAP diagnosis, it is recommended that future studies performed on larger population of patients with SSc and comparing lung HRCT and echocardiography diagnostic values with right heart catheterization.

### Authors' contribution

Conceptualization: AA and SN.
Methodology: LG.
Validation: RA, SN, PD and MSH.
Formal analysis: LG.
Investigation: RA, SN, PD and MSH.
Resources: RA, SN, PD and MSH.
Data curation: RA and SN.
Visualization: RA, SN, PD and MSH.
Supervision: RA and SN.
Project administration: RA.
Funding acquisition: SN.
Writing–original draft: FF, RA and SN.
Writing–review and editing: RA and SN.

### Ethical issues

The research followed the tents of the Declaration of Helsinki. The Ethics Committee of Shahid Beheshti University of Medical Sciences approved this study. (Ethical code #IR.SBMU.MSP.REC.1400.350). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from rheumatology fellowship thesis of Samad Nazarpoor at this university (Thesis #206609). Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

### Conflicts of interest

The authors declare that they have no competing interests

### Funding/Support

None.

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