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**BRIEF REPORT**

# Performance of the DETECT Algorithm for Pulmonary Hypertension Screening in a Systemic Sclerosis Cohort

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**Objective.** Pulmonary arterial hypertension (PAH) is one of the leading causes of mortality in systemic sclerosis (SSc). This study was undertaken to assess predictive accuracies of the DETECT algorithm and the 2015 European Society of Cardiology/European Respiratory Society (ESC/ERS) guidelines in SSc patients who underwent right-sided heart catheterization (RHC) for pulmonary hypertension (PH) evaluation.

**Methods.** Patients with SSc who had diagnostic RHC, had no PH or had PAH, and had available data on variables to allow application of the DETECT and 2015 ESC/ERS guidelines were included for analysis. PH classification was based on hemodynamics using the 2018 revised criteria and extent of lung fibrosis shown on high-resolution computed tomography. Sensitivity and predictive accuracies of the DETECT algorithm and 2015 ESC/ERS guidelines were calculated, including analysis of subjects with a diffusing capacity for carbon monoxide (DLco) of ≥60% predicted.

**Results.** Sixty-eight patients with SSc had RHC, of whom 58 had no PH and 10 had PAH. The mean age was 60.0 years, and 58.8% had limited cutaneous SSc. The DETECT algorithm had a sensitivity of 1.00 (95% confidence interval [95% CI] 0.69–1.00) and a negative predictive value (NPV) of 1.00 (95% CI 0.80–1.00), whereas the 2015 ESC/ERS guidelines had a sensitivity of 0.80 (95% CI 0.44–0.97) and an NPV of 0.94 (95% CI 0.81–0.99). In patients with a DLco of ≥60% (n = 27), the DETECT algorithm had a sensitivity of 1.00 (95% CI 0.29–1.00) and an NPV of 1.00 (95% CI 0.59–1.00), whereas the 2015 ESC/ERS guidelines had a sensitivity of 0.67 (95% CI 0.09–0.99) and an NPV of 0.94 (95% CI 0.71–1.00).

**Conclusion.** The DETECT algorithm has high sensitivity and NPV for diagnosis of PAH, including among individuals with a DLco of ≥60%.

## INTRODUCTION

Systemic sclerosis (SSc) is an autoimmune disease affecting multiple organ systems and characterized by fibrosis, inflammation, and vascular damage (1,2). Pulmonary arterial hypertension (PAH) is one of the leading causes of mortality in SSc, and in the past, SSc-associated PAH (SSc-PAH) had a significantly worse prognosis compared to other forms of PAH. PAH may go unrecognized in SSc patients until the disease has reached advanced stages, due to lack of or mild symptoms or attribution of symptoms to other comorbidities, such as interstitial lung disease (ILD) and/or myopathy.

PAH is present in 10–12% of patients with SSc and in 19% of those with a diffusing capacity for carbon monoxide (DLco) of <60% predicted (1,2). Over the last decade, treatment for PAH has evolved dramatically due to the addition of new therapies and

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the transition from sequential to initial combination therapy. Outcomes have recently improved in SSc-PAH and are now similar to those with idiopathic PAH (2,3).

Previous observational studies have shown that screening for PAH may lead to better outcomes. Among patients in a French SSc-PAH registry, application of an active PAH screening program identified patients at a lower functional class with SSc-PAH, and patients had better survival (4). The PHAROS (Pulmonary Hypertension Assessment and Recognition of Outcomes in Scleroderma) registry, a large North American registry of SSc patients at risk for or with incident PAH that incorporated PAH screening, showed improved survival compared to historical cohorts (5).

There are various screening algorithms and guidelines for early detection of SSc-PAH. The European Society of Cardiology/European Respiratory Society (ESC/ERS) guidelines for identification of PAH on echocardiography were published in 2009 and were revised in 2015 to improve sensitivity during screening for PAH (6). These revisions included a combination of tricuspid regurgitation velocity (TRV), additional echocardiographic variables with assessment of the right ventricle (RV) size and pressure overload, the pattern of blood flow velocity out of the RV, the diameter of the pulmonary artery, and an estimate of right atrial pressure. The DETECT algorithm is an evidence-based screening algorithm created in 2013 as the result of a multicenter cross-sectional study that compared multiple clinical variables to the gold standard of right-sided heart catheterization (RHC), which resulted in the development of a 2-step PAH detection algorithm (7). Step 1 includes the combination of 6 clinical variables and step 2 includes echocardiographic variables. The DETECT algorithm has been recommended by a number of different societies, including the 2013 recommendations for screening and detection of connective tissue disease (CTD)–associated PAH (8), the 2015 ESC/ERS guidelines, and the 2018 6th World Symposium on Pulmonary Hypertension (WSPH) (9).

In the present study, we compared the predictive accuracies of the DETECT algorithm and the 2015 ESC/ERS guidelines in a cohort of SSc patients who underwent RHC for pulmonary hypertension (PH) evaluation. In this analysis, we applied the 2018 6th WSPH Task Force revised hemodynamic definition of group I PH (PAH) (9).

## PATIENTS AND METHODS

**Study design and subjects.** This was a cross-sectional study of a cohort of SSc patients at the University of Michigan (UM) who had a diagnostic RHC prior to March 14, 2019. All patients were at least 18 years of age and met the 2013 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for SSc (10). The study was approved by the UM Institutional Review Board, and a waiver of consent was approved as this was a retrospective analysis. The study was carried out in compliance with the Declaration of Helsinki.

The initial cohort included 261 patients who underwent RHC between December 2004 and March 2019. One hundred fourteen of these patients did not have PH, 63 had PAH, 30 had group II PH, 35 had group III PH, and 19 had group IV PH based on the 2018 hemodynamic classification (9). One hundred nine subjects were excluded as they did not have available data on variables required to calculate a DETECT score and/or did not have a transthoracic echocardiogram (TTE) available for review at UM to apply the 2015 ESC/ERS guidelines. Of the remaining subjects, we focused on the 68 who had PAH or no PH and had data available for application of the DETECT algorithm and the 2015 ESC/ERS guidelines. Data on demographic characteristics and additional clinical variables were obtained for each of the 68 subjects. Additional analyses were performed by applying the DETECT algorithm and the 2015 ESC/ERS guidelines to the 2009 hemodynamic definition of PAH (mean pulmonary arterial pressure [mPAP] ≥25 mm Hg and pulmonary arterial wedge pressure [PAWP] ≤15 mm Hg with no-to-minimal ILD), as incorporated in the original DETECT publication (7,11). We also explored the performance of the DETECT algorithm for screening of group II and group III PH.

**PAH screening.** All SSc patients at UM undergo PAH screening at the time of SSc diagnosis and annually thereafter, based on the 2013 CTD-PAH recommendations, which include clinical signs/symptoms, N-terminal pro–brain natriuretic peptide (NT-proBNP), pulmonary function tests (PFTs), TTE variables, and the DETECT algorithm (8). In clinical practice, we routinely apply the DETECT algorithm to patients with SSc regardless of their $DL_{CO}$. Patients who had a diagnostic RHC with variables available for application of the DETECT algorithm and had TTE imaging at UM prior to RHC were included for analysis. Every TTE was reanalyzed by a cardiologist (VMM) using the TTE variables included in the 2015 ESC/ERS guidelines (6). The data for this study were primarily derived after the 2013 e-publication of the DETECT algorithm and the 2013 CTD-PAH recommendations.

**PAH classification.** PAH classification was based on the 2018 WSPH Task Force revised hemodynamic definition of group I PH (PAH), i.e., mPAP >20 mm Hg, PAWP ≤15 mm Hg, pulmonary vascular resistance (PVR) ≥3 Wood units (WU) (9), and extent of ILD <20% on high-resolution computed tomography (HRCT). Patients classified as having postcapillary PH or group II PH had an mPAP of >20 mm Hg, PAWP of >15 mm Hg, and PVR of <3 WU. Those classified as having group III PH had precapillary PH due to chronic lung disease, i.e., 1) HRCT demonstrating >20% total lung involvement due to ILD, or 2) total lung involvement due to ILD 10–20% with concomitant moderate-to-severe emphysema, or 3) if HRCT was not available, then forced vital capacity (FVC) of <70% predicted within a median of 2 months of the RHC.

**Statistical analysis.** Descriptive statistics for demographic and clinical characteristics of SSc patients without PH and those with PAH were calculated using the mean and SD for continuous variables and the percentage for categorical variables. For continuous variables, the significance of the differences between groups was assessed by Student's *t*-test for normally distributed variables and by Wilcoxon's rank sum test for non-normally distributed variables. For categorical variables, Fisher's exact test was used due to small, expected counts. Predictive accuracies were calculated, and 95% confidence intervals (95% CIs) were obtained via a binomial method for comparisons between non-PH and groups I, II, and III PH. *P* values less than 0.05 were considered significant. Missing data, if any, were not imputed. Analyses were conducted with SAS 9.4 (SAS Institute).

## RESULTS

**Baseline demographic characteristics of the patients.** Of the 261 patients in this cohort who had undergone RHC, 63 had PAH and 114 had no PH. Of these 177 patients, 68 had available data on variables needed to calculate a DETECT score and TTE data available to apply the 2015 ESC/ERS guidelines; these

**Table 1.** Characteristics of the study patients*

| Characteristic† | Total (n = 68) | No PH (n = 58) | PAH (n = 10) | *P*‡ |
|---|---|---|---|---|
| Age at RHC, years | 60.0 ± 11.7 | 59.4 ± 12.0 | 63.2 ± 9.6 | 0.39 |
| Age at initial non-RP sign/symptom, years | 50.5 ± 12.8 | 49.8 ± 13.1 | 54.4 ± 10.7 | 0.34 |
| Female sex, no. (%) | 58 (85.3) | 49 (84.5) | 9 (90.0) | 1.00 |
| Race, no. (%) | | | | 1.00 |
| White | 58 (85.3) | 49 (84.5) | 9 (90.0) | |
| African American | 5 (7.4) | 4 (6.9) | 1 (10.0) | |
| Asian | 2 (2.9) | 2 (3.4) | 0 (0.0) | |
| Other | 3 (4.4) | 3 (5.2) | 0 (0.0) | |
| SSc subtype, no. (%) | | | | 0.77 |
| Limited cutaneous SSc | 40 (58.8) | 33 (56.9) | 7 (70.0) | |
| Diffuse cutaneous SSc | 27 (39.7) | 24 (41.4) | 3 (30.0) | |
| Sine scleroderma | 1 (1.5) | 1 (1.7) | 0 (0.0) | |
| Disease duration, years | 9.5 ± 7.6 | 9.6 ± 7.8 | 8.8 ± 6.8 | 0.87 |
| Autoantibodies, no. (%) | | | | |
| ANA (n = 64) | 59 (92.2) | 50 (90.9) | 9 (100.0) | 1.00 |
| ANA pattern (n = 59) | | | | 0.0355 |
| Nucleolar | 13 (22.0) | 10 (20.0) | 3 (33.3) | |
| Centromere | 12 (20.3) | 8 (16.0) | 4 (44.4) | |
| Other | 34 (57.6) | 32 (64.0) | 2 (22.2) | |
| Anti–Scl-70 (n = 60) | 11 (18.3) | 11 (21.2) | 0 (0.0) | 0.33 |
| Anti–RNA polymerase III (n = 31) | 6 (19.4) | 6 (21.4) | 0 (0.0) | 1.00 |
| Anticentromere (n = 54) | 10 (18.5) | 7 (14.9) | 3 (42.9) | 0.11 |
| HRCT with ILD near time of RHC, no. (%) (n = 59) | 43 (72.9) | 40 (76.9) | 3 (42.9) | 0.078 |
| PFTs near time of RHC | | | | |
| Time from PFT to RHC, months | 4.5 ± 7.3 | 4.0 ± 5.4 | 7.4 ± 14.1 | 0.82 |
| FVC, % predicted | 79.8 ± 19.5 | 78.6 ± 19.4 | 86.5 ± 19.5 | 0.26 |
| DLco, % predicted (n = 67) | 53.6 ± 18.8 | 54.6 ± 18.6 | 47.8 ± 20.2 | 0.29 |
| FVC % predicted:DLco % predicted (n = 67) | 1.6 ± 0.6 | 1.6 ± 0.6 | 2.0 ± 0.7 | 0.03 |
| TTE near time of RHC | | | | |
| Time from TTE to RHC, months | 4.0 ± 7.8 | 3.6 ± 6.9 | 6.1 ± 12.0 | 0.76 |
| RA area, $cm^2$ | 15.7 ± 4.3 | 15.3 ± 4.2 | 17.7 ± 4.5 | 0.10 |
| TRV, meters/second (n = 54) | 2.8 ± 0.5 | 2.7 ± 0.4 | 3.3 ± 0.4 | <0.0001 |
| RVSP, mm Hg (n = 54) | 37.3 ± 11.8 | 34.4 ± 9.0 | 52.0 ± 13.7 | 0.0006 |
| RHC | | | | |
| mPAP, mm Hg | 23.5 ± 7.0 | 21.6 ± 5.4 | 34.2 ± 6.1 | <0.0001 |
| mPAWP, mm Hg | 10.9 ± 3.0 | 10.8 ± 3.2 | 11.2 ± 2.1 | 0.81 |
| CO (TD), liters/minute | 5.7 ± 1.5 | 5.8 ± 1.5 | 5.1 ± 1.3 | 0.0999 |
| PVR, Wood units | 2.3 ± 1.4 | 1.9 ± 0.6 | 4.8 ± 2.0 | <0.0001 |

* Except where indicated otherwise, values are the mean ± SD. PH = pulmonary hypertension; PAH = pulmonary arterial hypertension; RHC = right-sided heart catheterization; RP = Raynaud's phenomenon; SSc = systemic sclerosis; ANA = antinuclear antibody; HRCT = high-resolution computed tomography; ILD = interstitial lung disease; PFTs = pulmonary function tests; FVC = forced vital capacity; DLco = diffusing capacity for carbon monoxide; TTE = transthoracic echocardiography; RA = right atrial; TRV = tricuspid regurgitation velocity; RVSP = right ventricular systolic pressure; mPAP = mean pulmonary arterial pressure; mPAWP = mean pulmonary arterial wedge pressure; CO (TD) = cardiac output (thermodilution); PVR = pulmonary vascular resistance.
† For some characteristics, data were not available for all 68 patients; n values represent the total number with available data.
‡ By Wilcoxon's rank sum test; Fisher's exact test, or Student's *t*-test as appropriate.

**Table 2.** Predictive accuracies of the DETECT algorithm and the 2015 ESC/ERS guidelines in screening for PAH as classified using the 2018 revised hemodynamic definition*

| | DETECT (95% CI) | 2015 ESC/ERS guidelines (95% CI) |
|---|---|---|
| 2018 revised hemodynamic PAH definition and all DLco values (n = 68) | | |
| Sensitivity | 1.00 (0.69–1.00) | 0.80 (0.44–0.97) |
| Specificity | 0.29 (0.18–0.43) | 0.57 (0.43–0.70) |
| PPV | 0.20 (0.10–0.33) | 0.24 (0.11–0.42) |
| NPV | 1.00 (0.80–1.00) | 0.94 (0.81–0.99) |
| 2018 revised hemodynamic PAH definition and DLco ≥60% predicted (n = 27) | | |
| Sensitivity | 1.00 (0.29–1.00) | 0.67 (0.09–0.99) |
| Specificity | 0.29 (0.13–0.51) | 0.67 (0.45–0.84) |
| PPV | 0.15 (0.03–0.38) | 0.2 (0.03–0.56) |
| NPV | 1.00 (0.59–1.00) | 0.94 (0.71–1.00) |

* ESC/ERS = European Society of Cardiology/European Respiratory Society; PAH = pulmonary arterial hypertension; 95% CI = 95% confidence interval; DLco = diffusing capacity for carbon monoxide; PPV = positive predictive value; NPV = negative predictive value.

individuals were the subjects of the present study. When comparing these 68 patients to the 109 patients who had missing data, we found that patients with missing data were more likely to have limited cutaneous SSc (lcSSc) (70.6% versus 58.8%) and to have higher TRV (3.2 meters/second versus 2.8 meters/second), mPAP (31.7 mm Hg versus 23.5 mm Hg), and PVR (4.4 WU versus 2.3 WU) (all $P < 0.05$).

Of the 68 patients included in the study, 58 did not have PH and 10 had PAH. The mean ± SD age in the overall cohort was 60.0 ± 11.7 years, age at initial non–Raynaud's phenomenon sign/symptom was 50.5 ± 12.8 years, and disease duration was 9.5 ± 7.6 years. The cohort was mainly composed of patients who were female (85.3%), White (85.3%), and had lcSSc (58.8%) (Table 1).

**Cardiopulmonary characteristics of the patients.** Among the patients with PAH, 42.9% were anticentromere antibody positive. Compared to the patients without PH, the prevalence of ILD in those with PAH was lower, though the difference was not statistically significant (42.9% versus 76.9%; $P = 0.08$), and the patients with PAH had a lower mean DLco % predicted (47.8 versus 54.6; $P = 0.29$) and a significantly higher FVC % predicted:DLco % predicted (2.0 versus 1.6; $P = 0.03$) (Table 1).

TTE variables in the patients with PAH compared to those without PH indicated a higher mean TRV (3.3 meters/second versus 2.7 meters/second; $P < 0.0001$) and estimated right ventricular systolic pressure (52.0 mm Hg versus 34.4 mm Hg; $P = 0.0006$). On RHC, the mPAP in the PAH group was 34.2 mm Hg, cardiac output was 5.1 liters/minute, and PVR was 4.8 WU (Table 1).

**Predictive accuracies of the DETECT algorithm and 2015 ESC/ERS guidelines for diagnosing SSc-PAH.** Using the 2018 revised hemodynamic definition of group I PH (PAH), the DETECT algorithm performed better as a PAH screening tool compared to the 2015 ESC/ERS guidelines. The sensitivity of the DETECT algorithm was 1.00 (95% CI 0.69–1.00) and its negative predictive value (NPV) was 1.00 (95% CI 0.80–1.00), whereas the 2015 ESC/ERS guidelines yielded false-negative results in 2 patients (sensitivity 0.80 [95% CI 0.44–0.97], NPV 0.94 [95% CI 0.81–0.99]) (Table 2). As expected for a screening tool, specificity and positive predictive value (PPV) of the DETECT algorithm were low at 0.29 (95% CI 0.18–0.43) and 0.20 (95% CI 0.10–0.33),

**Table 3.** Predictive accuracies of the DETECT algorithm and 2015 ESC/ERS guidelines in screening for PAH as classified using the 2009 hemodynamic definition*

| | DETECT (95% CI) | 2015 ESC/ERS guidelines (95% CI) |
|---|---|---|
| 2009 hemodynamic PAH definition from original DETECT study and all DLco values (n = 70) | | |
| Sensitivity | 1.00 (0.82–1.00) | 0.74 (0.49–0.91) |
| Specificity | 0.33 (0.21–0.48) | 0.61 (0.46–0.74) |
| PPV | 0.36 (0.23–0.50) | 0.41 (0.25–0.59) |
| NPV | 1.00 (0.80– 1.00) | 0.86 (0.71–0.95) |
| 2009 hemodynamic PAH definition from original DETECT study and DLco ≥60% predicted (n = 28) | | |
| Sensitivity | 1.00 (0.48–1.00) | 0.60 (0.15–0.95) |
| Specificity | 0.30 (0.13–0.53) | 0.70 (0.47–0.87) |
| PPV | 0.24 (0.08–0.47) | 0.30 (0.07–0.65) |
| NPV | 1.00 (0.59–1.00) | 0.89 (0.65–0.99) |

* ESC/ERS = European Society of Cardiology/European Respiratory Society; PAH = pulmonary arterial hypertension; 95% CI = 95% confidence interval; DLco = diffusing capacity for carbon monoxide; PPV = positive predictive value; NPV = negative predictive value.

respectively, and specificity and PPV of the 2015 ESC/ERS guidelines were 0.57 (95% CI 0.43–0.70) and 0.24 (95% CI 0.11–0.42), respectively (Table 2). The 2009 hemodynamic definition of PAH (mPAP ≥25 mm Hg and PAWP ≤15mm Hg with no-to-minimal ILD), as incorporated in the original DETECT publication, was also evaluated in 70 subjects in the cohort who had no PH or PAH and had available data on variables needed to apply the DETECT algorithm and 2015 ESC/ERS guidelines, with the DETECT algorithm showing higher sensitivity and NPV compared to the 2015 ESC/ERS guidelines (Table 3).

At our institution, we apply the DETECT algorithm to all patients with SSc including those with a DLCO of ≥60% predicted. Within this cohort, there were 27 patients with a DLCO of ≥60% predicted who had no PH (n = 24) or had PAH (n = 3) according to the 2018 revised hemodynamic definition of PAH and had both DETECT scores and a TTE to review for the 2015 ESC/ERS guidelines. The DETECT algorithm had a sensitivity of 1.00 (95% CI 0.29–1.00) and an NPV of 1.00 (95% CI 0.59–1.00), whereas the 2015 ESC/ERS guidelines had a sensitivity of 0.67 (95% CI 0.09–0.99) and an NPV of 0.94 (95% CI 0.71–1.00) (Table 2). The results were similar in patients with a DLCO of ≥60% predicted who had PAH or no PH when using the 2009 hemodynamic definition of PAH described in the original DETECT publication (Table 3).

**Application of the DETECT algorithm and 2015 ESC/ERS guidelines for group II PH and group III PH screening.** Additionally, we evaluated the performance of the DETECT algorithm and the 2015 ESC/ERS guidelines in patients with group II PH (n = 12) and group III PH (n = 12), using the 2018 revised hemodynamic definitions. The performance of the DETECT algorithm was overall similar to that of the 2015 ESC/ERS guidelines in patients with group II PH (NPV 0.94 [95% CI 0.71–1.00] and NPV 0.92 [95% CI 0.76–0.98], respectively) and in patients with group III PH (NPV 0.94 [95% CI 0.71–1.00] and NPV 0.97 [95% CI 0.85–1.00], respectively).

## DISCUSSION

We compared predictive accuracies of the DETECT algorithm and the 2015 ESC/ERS guidelines in a cohort of SSc patients who underwent RHC for PH evaluation, using the 2018 WSPH Task Force revised hemodynamic definition of group I PH (PAH). Our results demonstrate that the DETECT algorithm works well as a screening tool for PAH with 100% NPV and 100% sensitivity, and it was effective in patients with a DLCO of ≥60% predicted. We also evaluated the DETECT algorithm using the 2009 PAH definition that was used in the original DETECT study, and again found high sensitivity and NPV.

The performance of the DETECT algorithm in the present study using both the 2009 and 2018 revised hemodynamic definitions of PAH was similar to that in previous studies using the 2009 hemodynamic definition of PAH. In the original DETECT derivation study by Coghlan et al, the DETECT algorithm had a sensitivity of 96%, NPV of 98%, specificity of 48%, and PPV of 35% (7). Guillén-Del Castillo and colleagues studied 63 SSc patients who had PAH or no PH and found that the sensitivity of the DETECT algorithm was 100%, NPV was 100%, specificity was 42.9%, and PPV was 68.6% (12). In a study by Hao et al in a prospective cohort of 61 SSc patients with PAH or no PH, the DETECT algorithm had a sensitivity and NPV of 100%, specificity of 35.3%, and PPV of 55.1% (13). In a prospective SSc cohort studied by Vandecasteele and colleagues, the DETECT algorithm demonstrated a PPV of 6% (95% CI 2–17%); sensitivity and NPV were not reported (14).

The World Health Organization defines a screening test as the presumptive identification of an unrecognized disease in a patient who is asymptomatic (https://apps.who.int/iris/bitstream/handle/10665/330829/9789289054782-eng.pdf). TTE has been advocated by different societies and is included as part of screening and diagnostic algorithms. In the original DETECT study, TTE (according to the 2009 ESC/ERS guidelines) missed 29% of patients who had PAH on RHC (7). Most published studies regarding the detection of PAH through routine screening of SSc patients based on TTE used the 2009 ESC/ERS guidelines, which are based on symptoms and TRV (15). In the previously published studies by Guillén-Del Castillo et al, Hao et al, and Coghlan et al, the 2009 ESC/ERS guidelines had lower sensitivity (ranging from 71.0% to 96.3%) and NPV (ranging from 88.9% to 90.9%) (7,12,13). One report discussed the application of the 2015 ESC/ERS guidelines for detection of asymptomatic SSc-PAH, but data on sensitivity and NPV were not provided (14).

During the development of the DETECT algorithm, the key inclusion criteria included a disease duration of >3 years and a DLCO of <60% predicted, largely to account for patients at higher risk of PAH. However, this should not be interpreted to mean that SSc patients whose DLCO is ≥60% predicted are not at risk for development of PAH. Previously published data from the UK showed that ~10% of SSc patients with PH had a DLCO of ≥60% (16), and in the study by Hao and colleagues, DLCO was >60% in 6.5% of patients (n = 4) with PAH (13). If a strict criterion of DLCO <60% predicted was enforced to apply the DETECT algorithm, 3 patients with PAH would have been missed in our current analysis using the 2018 revised hemodynamic definition, and 5 patients with PAH would have been missed using the 2009 PAH hemodynamic definition. Our data using DLCO ≥60% predicted provide evidence in support of the 2018 WSPH recommendations that proposed the DETECT algorithm, along with the 2015 ESC/ERS guidelines or an FVC:DLCO ratio of >1.6 (assuming no-to-mild ILD) and an NT-proBNP level >2 times the upper limit of normal among those with an uncorrected DLCO of <80% predicted.

The DETECT algorithm is being increasingly incorporated into clinical practice and was developed to discriminate between PAH and non-PH. In our cohort, the performance of the DETECT algorithm was similar to that of the 2015 ESC/ERS guidelines in

patients with group II and group III PH, and we do not advocate incorporating DETECT into clinical practice to distinguish between group II or III PH and non-PH.

It should also be kept in mind that the DETECT algorithm is a screening tool with high sensitivity and NPV that provides guidance regarding whether a patient should undergo RHC. High sensitivity is preferred in a screening tool, but the tradeoffs include an increased number of RHCs to exclude PAH, as seen in the original DETECT cohort (7). Since PAH is the leading cause of mortality in SSc and a recent meta-analysis suggests better outcomes with utilization of screening algorithms and early initiation of combination therapy (2), we believe a higher rate of RHC to rule out PAH is justified. In patients who do not meet the criteria for RHC at a single time point according to the DETECT algorithm (i.e., the DETECT score does not indicate that the patient should be referred for RHC), we continue to incorporate the DETECT algorithm on an annual basis during clinic visits, with spirometry with DLco to assess the FVC:DLco ratio and with measurement of serum uric acid and NT-proBNP levels. If TTE is recommended, it is performed as part of the screening algorithm. In patients for whom RHC is recommended based on the DETECT score but are not found to have PH on RHC (53% of patients in our cohort), DETECT is no longer a valid tool in screening for PH. In this scenario, we follow the 6th WSPH recommendations with annual screening with TTE, incorporate the 2015 ESC/ERS guidelines, and assess for worsening of DLco and an FVC:DLco ratio of >1.6 (assuming no-to-mild ILD) and for an NT-proBNP level >2 times the upper limit of normal. In addition, new signs/symptoms suggestive of PH should lead to a clinical evaluation for PH.

We uniformly screen SSc patients according to published recommendations for CTD-PAH (8). Although our cohort included 261 patients who had RHC, of whom 114 did not have PH and 63 had PAH, our analysis focused on only 68 patients, in whom a screening algorithm was largely applied prospectively and TTE was available for reassessment using 2015 ESC/ERS guidelines highlighting an inherent limitation of cohort studies. The more severe hemodynamic findings in members of the cohort with missing data may reflect a lack of uniform screening in the patient population prior to 2013–2014, which was when DETECT and the CTD-PAH recommendations were published (7,8). This was a single-center study with small numbers of patients, and the findings need to be validated in a prospective study in the future. In addition, we did not exclude patients in the non-PH group with moderate-to-severe ILD, which may impact the diagnostic accuracy of our analysis.

In conclusion, early detection of PAH in SSc is necessary to implement early treatment, which can improve outcomes (2). To our knowledge, this is the first cohort study to assess the performance of the DETECT algorithm and 2015 ESC/ERS guidelines using the 2018 revised hemodynamic definition of PAH. The DETECT algorithm is a better screening tool for SSc-PAH than TTE. Although the original derivation study for the DETECT excluded patients with higher DLco values, our present results suggest that those whose DLco is ≥60% predicted can have PAH, and the DETECT algorithm performs well in this group.

## AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Khanna had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study conception and design.** Young, Jaafar, Huang, Nagaraja, McLaughlin, Khanna.

**Acquisition of data.** Young, Moles, Jaafar, Visovatti, Vummidi, Nagaraja, McLaughlin, Khanna.

**Analysis and interpretation of data.** Young, Jaafar, Huang, Nagaraja, McLaughlin, Khanna.

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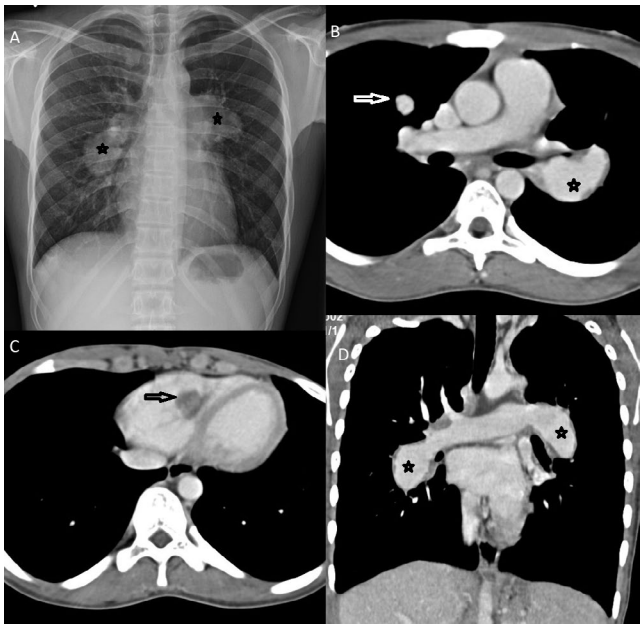
## Clinical Images: Multiple pulmonary artery aneurysms in Hughes-Stovin syndrome




The patient, an 18-year-old man, presented with fever of 1 month's duration and intermittent hemoptysis, dry cough, joint pain, and myalgia. There were no oral or genital ulcers. His erythrocyte sedimentation rate was elevated (117 mm/hour) a with microcytic, hypochromic anemia. Results of a complete blood cell count with differential cell count and laboratory test results were otherwise normal. Plain posteroanterior radiography of the chest showed enlarged hila (**asterisks** in **A**). Contrast-enhanced computed tomography (CE-CT) of the chest showed saccular and fusiform pulmonary artery aneurysms involving the main pulmonary arteries, extending into lobar and segmental branches. CE-CT (**B** and **C**) and imaging of coronal reformation (**D**) showed pulmonary artery aneurysms (**asterisks** in **B** and **D**) involving main, lobar, and segmental branches (**arrow** in **B**) along with a right ventricular thrombus (**arrow** in **C**). The CT window showed normal findings in all lung fields. The right ventricle showed a mural thrombus close to the interventricular septum, consistent with a diagnosis of Hughes-Stovin syndrome. Hughes and Stovin described the syndrome as being characterized by multiple pulmonary artery aneurysms and systemic venous thromboses, including thromboses in the right side of the heart (1). Cases of Hughes-Stovin syndrome have been found predominantly in male patients with Behçet's syndrome. With routine use of CT pulmonary angiography, the need for catheter pulmonary angiography is reduced (2,3). Treatment approaches involving immunomodulator therapy have been shown to reverse many of the changes occurring in Hughes-Stovin syndrome.

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