High-resolution computed tomography of the chest for the screening, re-screening and follow-up of systemic sclerosis-associated interstitial lung disease: a EUSTAR-SCTC survey

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Abstract

Objective

High-resolution computed tomography (HRCT) of the chest is the gold standard to diagnose interstitial lung disease (ILD). A prior survey reported that fewer than 60% of SSc-treating rheumatologists order an HRCT for ILD screening in newly diagnosed SSc patients. Since then, efforts were initiated to increase awareness of HRCT as a screening tool. The aim of the present study was to assess efficacy of these awareness programmes.

Methods

European Scleroderma Trials and Research (EUSTAR) and Scleroderma Clinical Trials Consortium (SCTC) members answered a survey about the use of HRCT at diagnosis, the re-screening of patients with a negative baseline HRCT, and the follow-up of HRCT positive SSc-ILD patients. When HRCT was not routinely requested, additional details were collected.

Results

Among 205 physician responders, 95.6% would perform an HRCT at SSc diagnosis: 64.9% as routine screening for ILD (65.4% of SSc referral and 63.6% of non-referral physicians) and 30.7% upon clinical suspicion (95.2% in case of crackles on auscultation). Among non-screening physicians, clinical and ethical concerns were major driving factors for not ordering HRCTs. During follow-up, 79.0% of responders would repeat HRCTs in baseline negative cases: 14.1% as routine screening and 64.9% for diagnostic purposes. Finally, 93.2% of responders would repeat a chest HRCT after SSc-ILD diagnosis: 36.6% as yearly routine and 56.6% according to clinical evaluation.

Conclusion

The use of baseline HRCT for the screening of SSc-ILD has slightly increased, but awareness programmes should be adapted for further improvement. HRCT use in re-screening and follow-up may benefit from validated algorithms.

Key words

systemic sclerosis, interstitial lung disease, computed tomography, screening, follow-up

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Received on November 22, 2021; accepted in revise form on February 14, 2022.

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These results are reported on behalf of the EUSTAR and SCTC communities. We thank all the participants in the survey and the EUSTAR/SCTC collaborators. The list of EUSTAR and SCTC collaborators is reported in the Supplementary material.

Competing interets: page 1954.

Introduction

Interstitial lung disease (ILD) is the most frequent pulmonary manifestation of systemic sclerosis (SSc) and is a significant cause of morbidity and mortality (1, 2). High-resolution computed tomography (HRCT) of the chest is the gold standard diagnostic test for ILD. Alternative screening tests are insensitive or not fully validated (3-5); for example, pulmonary function tests (PFTs) including forced vital capacity (FVC) and diffusing capacity of the lung for carbon monoxide (DLCO) showed inadequate power to detect SSc-ILD (6, 7).

For these reasons, interdisciplinary expert consensus panels recommended that HRCT should be obtained in all SSc patients at baseline to screen for ILD (8). Early detection of SSc-ILD has become important given the recent availability of approved treatments for SSc-ILD (*i.e.* nintedanib and tocilizumab) (9, 10). However, a previous survey from 2017 reported that only 51% of general rheumatologists and 66% of SSc experts at referral centers ordered chest HRCTs for ILD screening in newly diagnosed SSc patients; moreover, only 10% of responders reported repeating HRCTs at follow up visits (11). Since then, major efforts have been undertaken – via primary research publications, educational presentations, and review articles – to promote the use of HRCT for the screening of ILD in all patients with SSc (12).

The aims of the present study were: 1) to analyse whether these awareness programmes have changed screening patterns for SSc-ILD; and 2) to better understand reasons for not adhering to screening guidelines. The results of this study would enable adaptation of the current awareness programmes to improve their efficacy.

Methods

A Google Modules survey was sent to European Scleroderma Trials and Research (EUSTAR) and Scleroderma Clinical Trials Consortium (SCTC) members, with additional advertisement through the EUSTAR twitter account. The survey was administered between Nov 25th and Dec 31st, 2020. Questions were asked about the use of chest HRCT at baseline, the re-screening of patients with a negative baseline HRCT, and the follow-up of HRCT positive SSc-ILD patients. When HRCTs were not routinely requested, we collected additional details about the indications for its prescription and the reasons for non-screening (Supplementary file 1). The results of the survey were analysed with IBM SPSS software v. 26. Differences according to geographical region, medical specialty, working environment, self-reported SSc referral centre, and EUSTAR/SCTC membership were analysed by Chi-squared test.

Results

A total of 205 out of 630 physicians replied to the survey (32.5% response rate). The participants were widely distributed in terms of geographic region (130 from Europe, 23 from Asia, 23 from North America, 9 from South America, 7 from Australia, 4 from Africa, 9 unspecified), medical specialty (156 rheumatology, 21 internal medicine, 14 clinical immunology, 14 other), working environment (176 University Hospital, 12 community hospital, 17 other), SSc dedicated-referral centres (179 referral and 26 non-referral), and scientific society membership (98 EUSTAR, 42 SCTC, 42 EUSTAR and SCTC, 23 not declared).

Of the 205 responders, 64.9% reported performing a chest HRCT in all newly diagnosed SSc patients as routine screening (65.4% of the physicians working in SSc referral centres and 63.6% of the physicians from non-referral centres). Conversely, 30.7% percent ordered HRCTs only when there was other evidence of ILD (Fig. 1). Among those, the presence of crackles on auscultation (95.2%), FVC<80% predicted (87.3%), FVC±DLCO relative decline reaching the current definition of ILD progression (87.0%), or dyspnoea at rest/exercise (82.0/84.1%) represented the main indications for ordering HRCTs (Fig. 2). When questioned about the reasons for not performing a screening chest HRCT at baseline, 60.3% of "non-screeners" reported the preference to rely on clinical suspicion as the main explanation, followed by ethical concerns (includ-

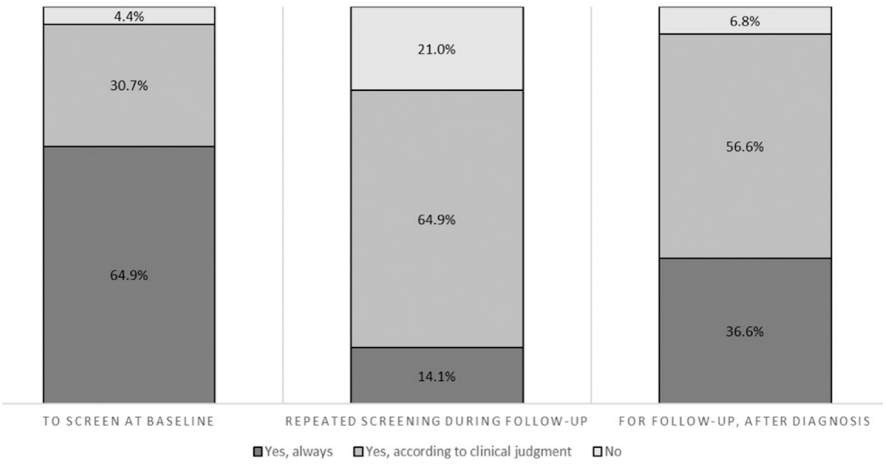

Fig. 1. Performance of chest HRCT in SSc patients at baseline (left panel), at re-screening of baseline HRCT negative cases (central panel) and in the follow-up SSc-ILD patients after diagnosis (right panel).

ing radiation exposure) in 46.0%, the need for further scientific support of the guidelines in 23.8%, and cost and administrative reasons in 17.5% and 8.0% of cases, respectively.

During follow-up, 79.0% of responders would repeat chest HRCTs in baseline negative cases: 14.1% as yearly routine screening and 64.9% upon clinical suspicion of a newly developed ILD (Fig. 1). The decision of the latter group was most frequently driven by FVC±DLCO relative decline indicative of ILD progression (91.0%), new onset or worsening of dyspnea at rest/exercise (81.2/85.7%), and new onset or worsening of crackles on auscultation of the lungs (83.5%) (Fig. 2).

Finally, 93.2% of the responders would repeat chest HRCTs after SSc-ILD diagnosis: 36.6% as a yearly routine to detect progression and 56.6% upon certain indications (Fig. 1) including new FVC±DLCO relative decline (91.4%), new onset or worsening of dyspnoea at rest/exercise (83.6/80.2%), or to evaluate treatment effects (4.5%; Fig. 2).

When comparing responses by geographical origin, medical specialty, working environment, SSc referral institute, and EUSTAR/SCTC membership, we found no differences.

Discussion

Our survey showed that the use of baseline HRCT for the screening of SSc-ILD has slightly increased at non-referral centres and remained stable at referral centres, compared to a previous survey. In addition, we provide new data on use of HRCT in re-screening for SSc-ILD in patients with negative baseline HRCTs, and for the follow-up of SSc-ILD.

Screening for SSc-ILD is supported by both expert opinion and consensus-based advice (8, 13). Compared to previous results, we noticed an increase in this practice among physicians at non-SSc referral centres, which might represent the first contact of patients in the early disease phase, before the patient is sent to an expert referral centre. However, there is still a third of physicians from referral centres who do not routinely screen for SSc-ILD with chest HRCT at time of SSc diagnosis and prefer, instead, to perform a diagnostic HRCT only in case of clinical suspicion. In comparison to the previous survey, our data showed a meaningful decline in hypoxaemia at rest as a driver for SSc experts to perform baseline HRCT (from 91% to 65%) (11). Conversely, a meaningful increase in reasons to order a baseline HRCT was noted for DLCO<80% (from 52% to 73%), anti-topoisomerase I antibody positivity (from 33% to 57%), and diffuse cutaneous subset (from 38% to 68%) (11). This increase could be possibly related to further improvement in the knowledge about predictors of SSc-ILD presence (14), which were also reported in the recent European consensus (8). The remaining variables showed slight changes, possibly related to geographic variation. For exam-

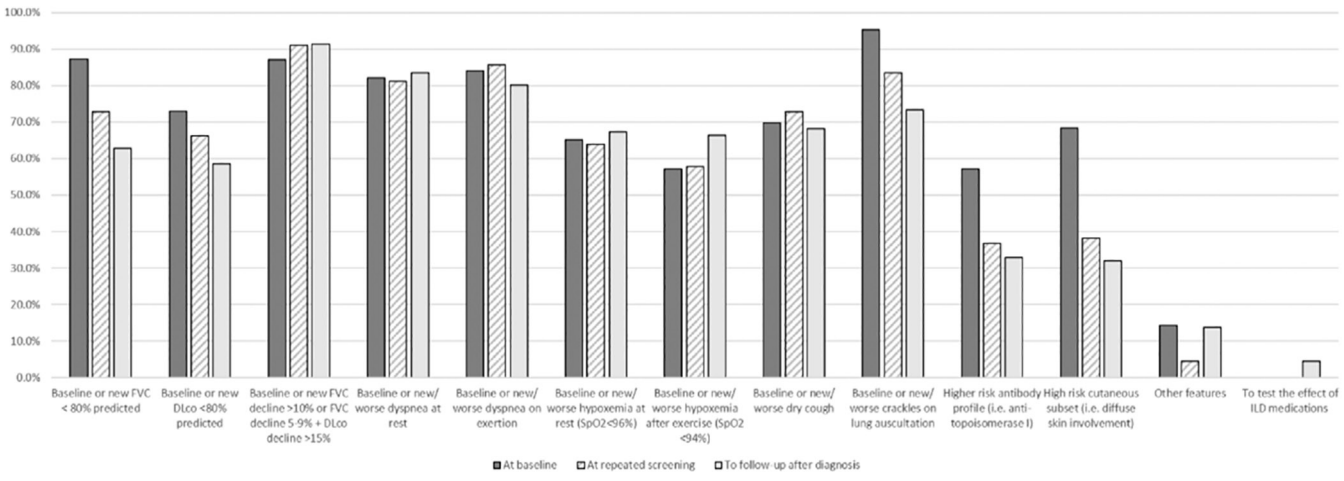

Fig. 2. Clinical drivers to ordering a diagnostic HRCT in the suspicion of SSc-ILD, among all responders (dark grey bars represent baseline, striped bars re-screening and light grey bars follow-up after diagnosis).

ple, two thirds of our responders were practicing in Europe, while there was a similar number of European and North American participants in the previous survey (11).

When questioned about reasons for not performing screening HRCTs, responders often mentioned lack of supporting scientific evidence. Indeed, it is currently unknown whether routine HRCTs lead to a better long-term prognosis of SSc-ILD. Still, recent data have shown that more than 60% of inflammatory diffuse SSc patients show evidence of SSc-ILD on HRCT and that its early treatment represents an effective strategy to prevent ILD progression (15). In addition, data from the observational EUSTAR cohort show that approximately 27% of SSc-ILD patients have functional decline already in the first year (16) and data from two SSc-ILD clinical trial cohorts demonstrate that a functional decline over 2 years is associated with worse prognosis (17). Moreover, healthcare utilisation and costs are meaningfully higher in patients with more severe, advanced forms of SSc-ILD (18).

In the follow-up of SSc patients with baseline HRCTs that are negative for SSc-ILD, experts primarily rely on the use of PFTs to detect ILD onset. The application of HRCT in this context is more controversial and is in line with the results of our survey, which showed that HRCT re-screening of SSc patients with negative baseline HRCTs is regularly performed only by 14% of physicians. However, the use of PFTs has been shown to be insufficient for the early detection of ILD. Other strategies have been proposed to overcome this limitation, including the low radiation dose of HRCT protocols (19) and the use of CT protocols with reduced number of slices (20).

Our survey showed interesting results regarding the use of HRCT in patients with confirmed SSc-ILD. More than a third of the responders would use HRCTs to follow-up SSc-ILD patients routinely, while the remaining would obtain an HRCT to confirm functional or clinically significant changes or to assess treatment response. The use of follow-up HRCT represents another grey area for physicians treating patients with SSc-ILD. The recent European consensus suggested that the decision regarding whether to repeat an HRCT should be based on a combination of current disease status and speed of progression, agreeing that repeat HRCT should be used as a diagnostic rather than a routine follow up test.

In conclusion, the results of our survey provide important guidance for the further implementation of awareness programmes for HRCTs as a key screening tool for SSc-ILD. We found that the implementation of guidelines into clinical practice has slightly improved but major efforts need to be undertaken to implement them further. In addition, our data confirm the need to develop validated screening and follow-up algorithms for SSc-ILD in order to support physicians' decision making about when to perform HRCTs in clinical practice.

Take home messages

- What is already known about this subject?
  Although high resolution computed tomography (HRCT) is the gold standard for the diagnosis of systemic sclerosis associated interstitial lung disease (SSc-ILD), its application in a screening context is variable.
- What does this study add?
  This study confirms the effect of awareness campaigns in promoting the use of HRCT for the screening of SSc-ILD and raises the point of using it in re-screening of initially negative patients and in the follow-up of SSc-ILD patients.
- How might this impact on clinical practice or future developments?
  Our study has stressed the importance of developing algorithms to support the screening, re-screening and follow-up of SSc-ILD, as already available for pulmonary arterial hypertension.

Competing interests

C. Bruni received consulting fees and/or honoraria from Actelion, Eli-Lilly, Boehringer Ingelheim; research grants from Gruppo Italiano Lotta alla Sclerodermia (GILS), European Scleroderma Trials and Research Group (EUSTAR), Scleroderma Clinical Trials Consortium (SCTC), and educational grants from AbbVie.

L. Chung received consulting fees and/or served on Advisory Board for Boehringer Ingelheim, Eicos, Mitsubishi Tanabe; served on Data Safety Monitoring Board for Reata.

A.M. Hoffmann-Vold received consulting fees and/or served on advisory boards for Actelion, ARXX therapeutics, Bayer, Boehringer-Ingelheim, Janssen, Medscape, MSD, Lilly, Roche.

S. Assassi received consulting fees from Boehringer Ingelheim, Novartis, AstraZeneca, Abbvie, and Corbus; received grants from Momenta, Janssen, and Boehringer Ingelheim, and speaking fees from Integrity Continuing Education.

D. Khanna received grant support from NIH, Immune Tolerance Network, Bayer, BMS, Horizon, Pfizer; has been a consultant for Acceleron, Actelion, Abbvie, Amgen, Bayer, Boehringer Ingelheim, Chemomab, CSL Behring, Genentech/Roche, Horizon, Merck, Mitsubishi Tanabe Pharma, Prometheus Leadership/Equity position - Chief Medical Officer, Eicos Sciences, Inc.

O. Distler has/had consultancy relationship with and/or has received research funding from or has served as a speaker for the following companies in the area of potential treatments for systemic sclerosis and its complications in the last three years: Abbvie, Acceleron, Alcimed, Amgen, AnaMar, Arxx, AstraZeneca, Baecon, Blade, Bayer, Boehringer Ingelheim, ChemomAb, Corbus, CSL Behring, Galapagos, Glenmark, GSK, Horizon (Curzion), Inventiva, iQvia, Kymera, Lupin, Medac, Medscape, Mitsubishi Tanabe, Novartis, Roche, Roivant, Sanofi, Serodapharm, Topadur and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143).

The other authors have declared no competing interests.

Acknowledgements

We thank Adara Borys and Esmeralda Recalde Leon for their help in sending the invitations to the Survey.

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