Evidence-based consensus statements for the identification and management of interstitial lung disease in systemic sclerosis

Anna-Maria Hoffmann-Vold,[1] Toby M. Maher,[2,3] Ali Ashrafzadeh,[4] Oliver Distler[5]

[1]Department of Rheumatology, Oslo University Hospital, Oslo, Norway; [2]National Heart and Lung Institute, Imperial College London, London, UK; [3]Interstitial Lung Disease Unit, Royal Brompton Hospital, London, UK; [4]Rheumatology Center of Excellence, IQVIA, San Diego, CA, USA; [5]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland

MODIFIED DELPHI PROCESS[1] TO DEVELOP EVIDENCE-BASED CONSENSUS STATEMENTS

AIM

- To establish the first European evidence-based expert consensus statement for SSc-ILD management in six key domains, applying well-established methodologies
- Develop a management algorithm providing a framework for future decision-making in SSc-ILD

EXPERT PANEL

- 27/31 participants completed all study rounds
  - 16 rheumatologists
  - 7 pulmonologists
  - 4 internists

Systematic literature review:
280 articles on SSc-ILD published January 1992–April 2018 used to generate 95 draft statements

- Three rounds of online surveys
- A face-to-face discussion
- A WebEx meeting

Consensus statements established → **Initial management algorithm proposed**

Publication of Phase III data for nintedanib[2] and tocilizumab[3] in SSc-ILD:
Further 14 draft statements generated

- Supplemental Delphi process with further round of online review

Additional consensus statements established → **Management algorithm defined**

STATEMENTS IN SIX KEY DOMAINS

1. Risk factors that affect the likelihood of developing SSc-ILD[4–9]

Respiratory symptoms	More likelihood of ILD
Smoking history	
Ethnicity (Native American; African heritage)	
Male gender	
Diffuse cutaneous SSc	
Anti-topoisomerase I antibodies	
Anti-centromere antibodies	Less likelihood of ILD

2. Screening for SSc-ILD[10–14]

All patients should be screened at baseline using HRCT

Pulmonary function testing provides baseline parameters
- FVC
- DL_{CO}
- Auscultation

3. SSc diagnosis[15,16] and severity assessment[17,18]

The primary tool for diagnosing ILD in patients with SSc is HRCT

Supporting diagnostic tools
Pulmonary function tests and clinical assessment of respiratory symptoms[18]

More than one measure should be used to determine severity

HRCT findings	Respiratory symptoms	Exercise-induced oxygen desaturation	Quality of life

MANAGEMENT ALGORITHM

Screen all patients with SSc for ILD using HRCT
FVC and DL_{CO} at baseline and at regular intervals:
every patient should receive an ILD-related physical examination

Diagnose ILD using HRCT
Assess ILD severity using multiple methods
HRCT, FVC, DL_{CO}, exercise-induced blood O_2 desaturation, clinical symptoms, QoL

Continue monitoring for ILD
Guided by risk of ILD, lung function, symptoms

Decide whether pharmacological therapy is required
Factors to consider include disease severity, QoL, available clinical guidelines

Pharmacological therapy
Mycophenolate mofetil, cyclophosphamide, nintedanib
No consensus with regard to tocilizumab

No pharmacological therapy
Follow up closely

Assess ILD progression using multiple methods

Inadequate treatment response or disease progression

Escalate therapy
- Modify dose or choice of pharmacological treatment:
  - Mycophenolate mofetil, cyclophosphamide, nintedanib
  - Consider rituximab
- Evaluate for lung transplant
- Consider autologous haemopoietic stem-cell transplantation for selected patients

4. SSc-ILD treatment initiation[19] and options[2,20–22]

Drivers of treatment initiation
- QoL
- Clinical guidelines/ experience
- Patient's symptoms
- Efficacy
- Safety/tolerability

Pharmacological treatment options
"No pharmacological treatment" is an option for some
- Patients should be followed up regularly and treatment initiated in case of progression

All cases of severe ILD should be offered treatment
- Mycophenolate mofetil, cyclophosphamide and nintedanib are effective

5. SSc-ILD disease progression assessment[18,23]

More than one measure should be used to assess progression
Changes in extent of fibrosis or pattern on HRCT
Pulmonary function tests (FVC and DL_{CO} absolute value, or FVC decline)
Exercise-induced oxygen desaturation
Worsening of clinical symptoms

6. SSc-ILD treatment escalation and options[2, 24–29]

Drivers of escalation
- Pace of progression
- Disease severity

Available treatment options
- All patients with severe or progressive SSc-ILD should be offered pharmacological treatment
  - Available options include: mycophenolate mofetil, cyclophosphamide, nintedanib, combination nintedanib and mycophenolate mofetil, rituximab
- Autologous haemopoietic stem-cell transplant
- Lung transplant (evaluate suitability early)

CONCLUSIONS

- **This multidisciplinary modified Delphi study provides evidence-based expert consensus statements for SSc-ILD management across six key domains**
- **An SSc-ILD management algorithm for use in clinical practice is also provided**
- **These consensus statements and the clinical management algorithm provide important clinical guidance for the early identification and medical management of SSc-ILD, and offer a framework for future treatment decision-making**

Acknowledgements

The steering committee extend their thanks to the 31 expert panellists, without whom this modified Delphi study would not have been possible: Jérôme Avouac (France), Gianluca Bagnato (Italy), Rafic Barake (France), Simone Barsotti (Italy), Cosimo Bruni (Italy), Paolo Carducci (Italy), Patricia E Carreira (Spain), Ivan Castellví (Spain), Francesco Del Galdo (UK), Jörg HW Distler (Germany), Ivan Foeldvari (Germany), Paolo Fraticelli (Italy), Peter M George (UK), Bridget Griffiths (UK), Alfredo Guillén-Del-Castillo (Spain), Abdul Monem Hamid (France), Bernhard Hellmich (Germany), Rudolf Horváth (Czech Republic), Michael Hughes (UK), Michael Kreuter (Germany), Belén López-Muñiz (Spain), Florentine Moazedi-Fuerst (Austria), Jacek Olas (Poland), Suman Paul (UK), Cinzia Rotondo (Italy), Manuel Rubio-Rivas (Spain), Andrei Seferian (France), Michal Tomčík (Czech Republic), Yurdagül Uzunhan (France), Ulrich A Walker (Switzerland), and Ewa Więsik-Szewczyk (Poland).

The steering committee was chaired by John Cole from IQVIA (London, UK). The modified Delphi process was managed by Laura Wilson from IQVIA (Reading, UK). Medical writing support was provided by John Carron, PhD, of Nucleus Global (Manchester, UK), funded by Boehringer Ingelheim International GmbH (BI), under the authors' conceptual direction and based on feedback from the authors. The study was funded by BI. BI had no influence on data generation and interpretation in this study and had no influence on the steering committee discussions and decisions nor the panellists' discussions and voting. BI had no influence on design or implementation of the Delphi process, including selection of the panellists; the concept for the study and study initiation came from the steering committee. BI was given the opportunity to review the poster for medical and scientific accuracy as well as intellectual property considerations, but no changes were made after this review. The authors take full responsibility for the scope, direction, content of, and editorial decisions related to the poster.

Disclosures

AMH-V received research funding and/or consulting fees or other remuneration from Actelion, Boehringer Ingelheim, Roche and GSK. TMM received research funding and/or consulting fees or other remuneration from GSK, UCB, Boehringer Ingelheim, AstraZeneca, Roche, Bayer, Biogen Idec, Cipla, Prometic, and Sanumed, and has stock options or bond holdings in a for-profit corporation in Apellis. AA is a current employee of IQVIA. OD had a consultancy relationship and/or has received research funding from A. Menarini, Acceleron Pharma, Amgen, AnaMar, Bayer, Boehringer Ingelheim, Catenion, CSL Behring, ChemomAb, Ergonex, GSK, Inventiva, Italfarmaco, iQone, iQvia, Lilly, medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Blade Therapeutics, Glenmark Pharmaceuticals, Target BioScience and UCB in the area of potential treatments of scleroderma and its complications. In addition, OD has a patent mir-29 for the treatment of systemic sclerosis issued (US8247389, EP2331143). The authors did not receive payment for the development of the poster.

The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). AMH-V (ORCID ID 0000-0001-6467-7422), TMM (ORCID ID 0000-0001-7192-9149), AA and OD provided input into the conception and design of the study; were involved in interpretation of the study data; all authors reviewed and revised the poster critically for important intellectual content; and approved the final version of the poster. While the study was funded by Boehringer Ingelheim, the company had no influence on the steering committee discussions and decisions, nor the panellists' discussions and voting. Treatment statements are reflective of the authors' opinions.

References

1. Hohmann E, et al. Arthroscopy 2018; 34:3278–3282;
2. Distler O, et al. N Engl J Med 2019; 380:2518–2528;
3. Khanna D, et al. ACR 2018 abstract 898;
4. Wangkaew S, et al. Mod Rheumatol 2016; 26:588–593;
5. Liaskos C, et al. Autoimmunity 2017;50:414–21;
6. Ashmore P, et al. Rheumatol Int 2018; 38:657–662;
7. Steen V, et al. Arthritis Rheum 2012; 64:2986–2994;
8. Nihtyanova S, et al. Arthritis Rheumatol 2014; 66:1625–1635;
9. Sanchez-Cano D, et al. Rheumatol Int 2018; 38:363–374;
10. Hoffmann-Vold AM, et al. Am J Respir Crit Care Med 2019; 200:1258–1266;
11. Wangkaew S, et al. Quant Imaging Med Surg 2016; 6:381–390;
12. Showalter K, et al. J Rheumatol 2018; 45:1572–1576;
13. Le Gouellec N, et al. PLoS One 2017; 12:e0181692;
14. Tashkin DP, et al. Ann Rheum Dis 2016; 75:374–381;
15. Chowaniec M, et al. Reumatologia 2018; 56:249–254;
16. Caron M, et al. Eur Respir Rev 2018; 27:170102;
17. Salaffi F, et al. PLoS One 2016; 11:e0149240;
18. Wu W, et al. Ann Rheum Dis 2018; 77:1326–1332;
19. Hoffmann-Vold AM, et al. RMD Open 2019; 5:e000826;
20. Tashkin DP, et al. N Engl J Med 2006; 354:2655–2666;
21. Tashkin DP, et al. Lancet Respir Med 2016; 4:708–719;
22. Volkmann ER, et al. Arthritis Rheumatol 2017; 69:1451–1460;
23. Goh NS, et al. Arthritis Rheumatol 2017; 69:1670–1678;
24. Daoussis D, et al. Semin Arthritis Rheum 2017; 46:625–631;
25. Jordan S, et al. Ann Rheum Dis 2015; 74:1188–1194;
26. Burt RK, et al. Lancet 2011; 378:498–506;
27. van Laar JM, et al. JAMA 2014; 311:2490–2498;
28. Sullivan KM, et al. N Engl J Med 2018; 378:1066–1067;
29. Jablonski R, et al. Curr Opin Rheumatol 2018; 30:562–569.

Abbreviations

DL_{CO}, diffusing capacity of the lungs for carbon monoxide; FVC, forced vital capacity; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; QoL, quality of life; SSc, systemic sclerosis.

INTERACTIVE

https://www.globalmedcomms.com/respiratory/SSWC2020/ https://www.globalmedcomms.com/respiratory/SSWC2020/Hoffmann-Vold_1/

Poster presented at the 6th Systemic Sclerosis World E-Congress, 2020.