Quantitative Computed Tomography in Systemic Sclerosis–Interstitial Lung Disease: Are We Ready to Go beyond Standard Assessment?

To the Editor:

I read with great attention the paper by Saldana and colleagues entitled “Association of Computed Tomography Densitometry with Disease Severity, Functional Decline, and Survival in SSc–ILD” (1). The study is very interesting because it further explores chest quantitative computed tomographic (QCT) imaging possibilities in to stratifying patients with systemic sclerosis (SSc) according to severity to establish the prognosis. As the authors point out, many of the elements useful for establishing the SSc–ILD prognosis (i.e., forced vital capacity, diffusing capacity of the lung for carbon monoxide, and fibrosis visual score) are subject to significant variability, whereas QCT imaging is operator independent (2).

Conversely, the paper indirectly leads to considering some issues as relevant limitations for QCT imaging implementation in trial or clinical practice. For example, patients with emphysema were excluded. However observational data suggest that in the SSc, emphysema is

| SUBJECT | GENO | AGE | PRE | YR1 | YR2 | YR3 | YR4 | YR5 | YR6 | YR7 | YR8+ |
|---------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| A       | GG   | 1   | 22  | 101 | 384 |
| B       | GF   | 1   | 346 | 500 |
| C       | GM   | 2   | 46  | 373 |
| D       | GF   | 2   | <15 | 60  | 253 |
| E       | GR   | 2.1 | 124 | 287 | 500 |
| F       | GF   | 5.8 | <15 | <15 | 135 | 120 |
| G       | GG   | 5.8 | 165 | 169 | 414 |
| H       | GF   | 5.9 | <15 |     | 27  |
| I       | GG   | 6   | <15 |     | 96  | 285 | 165 |
| J       | GG   | 6   | 19  |     | 204 | 206 |
| K       | GG   | 6.1 | <15 |     | 214 | 88  | 258 | 105 |
| L       | GR   | 6.1 | 131 | 110 | 381 | 419 |
| M       | GR   | 6.5 | 38  | 25  | 118 | 206 |
| N       | GF   | 8.7 | <15 |     |     |     |     | 190 |
| O       | GF   | 9.3 | <15 |     |     |     |     | 195 |
| P       | GG   | 9.5 | <15 |     |     | <15 |     |     |
| Q       | GF   | 9.7 | <15 | <15 | 21  | 25  |
| R       | GF   | 11.4| <15 |     |     |     |     | 28  |

Figure 1. Genotype groups, age at initiation, and fecal elastase levels in children before (PRE) and after (by year) ivacaftor initiation. The last result entered is the latest result available for the subject. Shaded boxes represent children who have discontinued pancreatic enzyme replacement therapy. The chart is organized by age at initiation. GENO = genotype; GF = heterozygous for a gating mutation and F508del; GG = homozygous for gating mutations; GM = heterozygous for a gating mutation and a minimum function mutation; GR = heterozygous for a gating and a residual function mutation; PRE = before ivacaftor initiation.

References

1 Davies JC, Cunningham S, Harris WT, Lapey A, Regelmann WE, Sawicki GS, et al.; KIWI Study Group. Safety, pharmacokinetics, and pharmacodynamics of ivacaftor in patients aged 2-5 years with cystic fibrosis and a CFTR gating mutation (KIWI): an open-label, single-arm study. Lancet Respir Med 2016;4:107-115.

2 Hamilton JL, Zobell JT, Robson J. Pancreatic insufficiency converted to pancreatic sufficiency with ivacaftor. Pediatr Pulmonol 2019;54:1654.

3 Megalaa R, GopalaReddy V, Champion E, Goralski JL. Time for a gut check: pancreatic sufficiency resulting from CFTR modulator use. Pediatr Pulmonol 2019;54:E16–E18.

4 Rosenfield M, Cunningham S, Harris WT, Lapey A, Regelmann WE, Sawicki GS, et al.; KLIMB Study Group. An open-label extension study of ivacaftor in children with CF and a CFTR gating mutation initiating treatment at age 2-5 years (KLIMB). J Cyst Fibros 2019;18:838–843.

5 Howlett C, Ronan NJ, NiChroinin M, Mullane D, Plant BJ. Partial restoration of pancreatic function in a child with cystic fibrosis. Lancet Respir Med 2016;4:e21–e22.

6 Nichols AL, Davies JC, Jones D, Carr SB. Restoration of exocrine pancreatic function in older children with cystic fibrosis on ivacaftor. Paediatr Respir Rev 2020;35:99–102.

Copyright © 2021 by the American Thoracic Society
associated with ILD, appearing as a combined pulmonary fibrosis and emphysema syndrome (3). Having excluded these patients who have a poor prognosis could have depleted the cohort of patients at a high risk of mortality (4). A second limitation that Saldana and colleagues report is the scarce possibility of using QCT in clinical routine for the following two reasons: inability to process computed tomographic (CT) scans of all patients (38% of all CT scans performed) and the significant time required to evaluate each CT scan. Fortunately, these two issues can be overcome, as already described in the literature, by using an independent operator algorithm based on a free and open-source program that provides QCT indexes in a few seconds (5).

For this reason, we urge the authors to look with more optimism at their results, which support the possibility of easily establishing SSc-ILD prognosis, providing rheumatologists with new tools for tailoring treatments (in particular antibiotics).

Author disclosures are available with the text of this letter at www.atsjournals.org.

Alarico Ariani, M.D.*
Azienda Ospedaliero Universitaria di Parma
Parma, Italy

ORCID ID: 0000-0003-1428-6102 (A.A.),
*Corresponding author (e-mail: dottalaricoariani@libero.it).

1. Saldana DC, Hague CJ, Murphy D, Coxson HO, Tschiren J, Peterson S, et al. Association of computed tomography densitometry with disease severity, functional decline, and survival in systemic sclerosis-associated interstitial lung disease. Ann Am Thorac Soc 2020;17:813–820.

2. Ariani A, Silva M, Bravi E, Saracco M, Parisi S, De Gennaro F, et al. Operator-independent quantitative chest computed tomography versus standard assessment of interstitial lung disease related to systemic sclerosis: a multi-centric study. Mod Rheumatol 2015;25:724–730.

3. Cottin V, Nunes H, Mouthon L, Gamondes D, Lazor R, Hachulla E, et al.; Groupe d’Eudes et de Recherche sur les Maladies “Orphelines” Pulmonaires. Combined pulmonary fibrosis and emphysema syndrome in connective tissue disease. Arthritis Rheum 2011;63:295–304.

4. Ariani A, Silva M, Bravi E, Parisi S, Saracco M, De Gennaro F, et al. Overall mortality in combined pulmonary fibrosis and emphysema related to systemic sclerosis. RMD Open 2019;5:e000820.

5. Ariani A, Lumetti F, Silva M, Santilli D, Mozzani F, Lucchini G, et al. Systemic sclerosis interstitial lung disease evaluation: comparison between semiquantitative and quantitative computed tomography assessments. J Biol Regul Homeost Agents 2014;28:507–513.

Copyright © 2021 by the American Thoracic Society