

**Rheumatologists' and Pulmonologists' attitudes and regarding Rheumatoid Arthritis-  
associated interstitial lung disease: national survey**

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Short title: Portuguese survey about interstitial lung disease in Rheumatoid Arthritis

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Dear Editor,

Rheumatoid Arthritis' interstitial lung disease (RA-ILD) compounds great morbimortality - the quality of life is comparable to that of idiopathic pulmonary fibrosis<sup>1</sup>. Yet, we lack consensual guidelines on its practical approach, and rheumatologists might undervalue RA-ILD's impact and need for a specialized evaluation<sup>2</sup>.

To compare rheumatologists' and pulmonologists' opinion/knowledge regarding RA-ILD's risk factors, screening, diagnosis, and treatment, an online survey was conducted, consisting of 25 questions for rheumatologists and 20 questions for pulmonologists. It was emailed to the Portuguese Rheumatology Society and the Portuguese Pulmonology Society associates following ULSAM's Ethics Committee approval. It covered sociodemographic data, RA-ILD's epidemiology, screening methods, medications (effective and ineffective), management, and follow-up. Rheumatologists also had 3 case vignettes regarding patients with: (1) increased ILD risk without respiratory symptoms, (2) increased ILD risk with respiratory symptoms and normal chest X-ray (CXR), (3) increased ILD risk without respiratory symptoms but having crackles on auscultation. Statistical analysis was performed using SPSSv23, and t-test, chi-square, Mann-Whitney, and Fisher exact tests, as appropriate.

We amounted 112 respondents. Response rates were 27% (81/297) for rheumatologists and 2.6% (31/1200) for pulmonologists. Table I depicts both groups' features. Fifty-eight (71.6%) rheumatologists had an interest/differentiation in RA; 25 (80.6%) pulmonologists felt similarly about ILD. Overall, 64.3% (50 rheumatologists and 22 pulmonologists) of respondents participated in a multidisciplinary rheumatology-pulmonology consultation; 80.6% of pulmonologists had a pulmonology-radiology one. Most pulmonologists (64.5%) found usual interstitial pneumonia as the main computed tomography (CT) pattern. Seventy-eight (96.3%) rheumatologists routinely screen respiratory symptoms, 79 (97.5%) screen smoking habits, and 63 (77.8%) request screening CXR in newly diagnosed RA. Twenty-nine (93.5%) pulmonologists request a screening chest CT for newly diagnosed RA-ILD, and 29 (93.5%) request pulmonary function tests (PFT). More than 90% of respondents estimated RA-ILD's prevalence to be 2-30%; all respondents agreed ILD increased RA's mortality. More rheumatologists found high titers of rheumatoid factor/anti-citrullinated protein antibodies to be a risk factor (97.5% vs 61.3%,  $p < 0.001$ ), as well as smoking (96.3% vs 77.4%,  $p = 0.004$ ). Although not statistically significant, 61 rheumatologists (75.3%) and 20 pulmonologists (64.5%) considered male gender a risk factor, whereas 54 rheumatologists (66.7%) and 23 pulmonologists (74.2%) identified advanced age as a risk factor. More pulmonologists found methotrexate (MTX) to be harmful (22.6% vs 6.2%,

p=0.019). Thirty-six percent of rheumatologists and 48% of pulmonologists avoid MTX in RA-ILD. For inflammatory RA-ILD (inf-RA-ILD), more rheumatologists found rituximab (91.4% vs 71.0%, p=0.013) to be effective; and for non-inflammatory RA-ILD (Ninf-RA-ILD), more pulmonologists found mycophenolate mofetil (29.0% vs 9.9%, p=0.018) and azathioprine (22.6% vs 3.7%, p=0.004) effective. Compared to younger practicing doctors (0-5 years of practice, as well as 6-10, 11-15, and 15-30 years), physicians working >30 years more commonly selected the 2% RA-ILD's prevalence response (44.4%, p=0.015, adjusted residues 2.6). Physicians working for 15-30 and >30 years more commonly considered nintedanib ineffective in Ninf-RA-ILD (p=0.005, 26.3% and 33.3% vs 4.8% – adjusted residues 2.4 and 2.3). For inf-RA-ILD, those working for <15 years more commonly found rituximab effective (p=0.006, 90.5% vs 84.2% and 44.4%, adj residues 2.5). Rheumatologists' main attitudes regarding the case vignettes were: (A) 64.5% requested CXR and 22.2% took no action; (B) 86.4% requested chest CT and 93.8% PFT; (C) 97.5% requested chest CT and 80.2% PFT. Respectively, 0%, 17.3%, and 23.5% referred to Pulmonology in cases (A), (B) and (C).

This survey revealed variability among Portuguese physicians caring for RA-ILD, including risk factors, screening methods, and medications. It helped to identify unmet needs, research priorities, disease state education, and traits of our current medical structure. Recent data, such as the INBUILD trial showing nintedanib's positive role in ILD including RA's<sup>3</sup>, seem to be more impregnated than MTX's misconception on RA-ILD<sup>4</sup> (potentially denying/underutilizing this effective medication). Closer rheumatologists-pulmonologists cooperation enhances diagnosis and treatment accuracy<sup>5</sup>. Thus, greater education/multidisciplinarity might increase evidence-based knowledge and align strategies to minimize this condition's impact. Study limitations include a small sample size, low and unequal response rate (which may unbalance the statistical power between groups, and in this case, not capture the real variability amongst pulmonologists), and uneven geographical variability. Follow-up electronic reminders might have been useful in increasing the number of participants, especially in the pulmonologists' group. Furthermore, we did not provide a clear definition for inf-RA-ILD and Ninf-RA-ILD, did not ask about their correlation with joint disease activity or disease duration, nor did we inquire about the reasons some clinicians avoid using MTX. Moreover, to simplify and shorten the questionnaires, we excluded topics such as combination therapies (including corticosteroids with immunosuppressants) and patient hospitalization.

**Tables and Figures**

**Table I – Demographic of respondents**

|  | <b>Rheumatologists</b><br>(n=81) | <b>Pulmonologists</b><br>(n=31) | <b>Total (n=112)</b> | <b>P value<sup>a</sup></b> |
|--|----------------------------------|---------------------------------|----------------------|----------------------------|
| <b>Gender, male</b>                    | 21 (25.9%)                       | 13 (41.9%)                      | 34 (30.4%)           | 0.099                      |
| <b>Age, median (IQR)</b>               | 35 (12)                          | 38 (18)                         | 36 (13)              | 0.225                      |
| <b>Professional status, specialist</b> | 59 (72.8%)                       | 23 (74.2%)                      | 82 (73.2%)           | 0.885                      |
| <b>Years in practice</b>               |                                  |                                 |                      | 0.727                      |
| 0-5                                    | 28 (34.6%)                       | 9 (29.0%)                       | 37 (33.0%)           |                            |
| 6-10                                   | 23 (28.4%)                       | 7 (22.6%)                       | 30 (26.8%)           |                            |
| 11-15                                  | 12 (14.8%)                       | 5 (16.1%)                       | 17 (15.2%)           |                            |
| 15-30                                  | 13 (16.0%)                       | 6 (19.4%)                       | 19 (17.0%)           |                            |
| >30                                    | 5 (6.2%)                         | 4 (12.9%)                       | 9 (8.0%)             |                            |
| <b>Practice location</b>               |                                  |                                 |                      | <b>0.038</b>               |
| Aveiro                                 | 6 (7.4%)                         | 3 (9.7%)                        | 9 (8.0%)             |                            |
| Braga                                  | 6 (7.4%)                         | 2 (6.5%)                        | 8 (7.1%)             |                            |
| Bragança                               | 1 (1.2%)                         | 0                               | 1 (0.9%)             |                            |
| Castelo Branco                         | 2 (2.5%)                         | 1 (3.2%)                        | 2 (2.7%)             |                            |
| Coimbra                                | 7 (8.6%)                         | 2 (6.5%)                        | 9 (8.0%)             |                            |
| Faro                                   | 3 (3.7%)                         | 3 (9.7%)                        | 6 (5.4%)             |                            |
| Guarda                                 | 0                                | 3 (9.7%)*                       | 3 (2.7%)             | <b>*adj res 2.8</b>        |
| Leiria                                 | 2 (2.5%)                         | 0                               | 2 (1.8%)             |                            |
| Lisboa                                 | 27 (33.3%)                       | 8 (25.8%)                       | 35 (31.3%)           |                            |
| Porto                                  | 5 (6.2%)                         | 6 (19.4%)*                      | 11 (9.8%)            | <b>*adj res 2.1</b>        |
| Açores                                 | 4 (4.9%)                         | 0                               | 4 (3.6%)             |                            |
| Setúbal                                | 8 (9.9%)                         | 2 (6.5%)                        | 10 (8.9%)            |                            |
| Viana do Castelo                       | 7 (8.6%)                         | 0                               | 7 (6.3%)             |                            |
| Vila Real                              | 0                                | 1 (3.2%)                        | 1 (0.9%)             |                            |
| Viseu                                  | 3 (3.7%)                         | 0                               | 3 (2.7%)             |                            |
| <b>Hospital setting, tertiary</b>      | 44 (54.3%)                       | 12 (38.7%)                      | 56 (50.0%)           | 0.139                      |

<sup>a</sup>P-value compares rheumatologists to pulmonologists using Qui<sup>2</sup>/Fisher's exact testing as appropriate. IQR – interquartile range.

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