Figure 1:Participants Flow chart



Table 1**: Patients demographics and anthropometric measurements**

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| **Variable** | | **Summary Statistics** |
| **Sex** | Female | 230 (68.9%) |
|  | Male | 104 (31.1%) |
| **Occupations** | Roof worker | 1 (0.3%) |
|  | Metal worker | 3 (0.9%) |
|  | Other | 128 (38.3%) |
|  | Unknown | 202 (60.5%) |
| **Smoking** | Never Smoked | 153 (45.8%) |
|  | Quit Smoking | 64 (19.2%) |
|  | Active Smoker | 24 (7.2%) |
|  | Unknown | 93 (27.8%) |
| **Weight (in kg)** | mean ± sd | 70.9 ± 12.9 |
| **nmissing =153** | Median (Q1 - Q3) | 70 (63 - 80) |
|  | Min - Max | 40 - 113 |
| **Height (in cm)** | mean ± sd | 163.1 ± 9.2 |
| **nmissing =178** | Median (Q1 - Q3) | 162 (155 - 170) |
|  | Min - Max | 142 - 184 |
| **BMI (kg/m2)** | mean ± sd | 26.7 ± 4.8 |
| **nmissing =177** | Median (Q1 - Q3) | 26.1 (23.8 - 28.7) |
|  | Min - Max | 16.2 - 44.6 |

Table 2**: Patients' Comorbidities**

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| **Variable** | | **Summary Statistics** |
| **Comorbidities** | Yes | 220 (65.9%) |
|  | No | 114 (34.1%) |
| **Comorbidities (among those with comorbidities n=220)** | 1 | 122 (55.5%) |
| >1 | 98 (44.5%) |
| **Comorbidity types (among those with comorbidities n=220)** | Arterial Hypertension | 112 (50.9%) |
| Diabetes Mellitus | 58 (26.4%) |
| Ischemic Heart Disease | 33 (15.0%) |
| Gastroesophageal reflux disease | 20 (9.1%) |
| Pulmonary hypertension | 14 (6.4%) |
| Hypothyroidy | 13 (5.9%) |
| Malignancy | 13 (5.9%) |
| Congestive Heart Failure | 10 (4.5%) |
| Neurological disease | 6 (2.7%) |
| Long Term Proton Pump Inhibitor Usage | 6 (2.7%) |
| Liver disease | 4 (1.8%) |
| Other comorbidities | 83 (37.7%) |

Table 3**: Characteristics of CTD Diagnosis**

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| **Variable** | | **Summary Statistics** |
| **CTD Type Diagnosis** | Single | 312 (93.4%) |
|  | Multiple | 22 (6.6%) |
| **CTD Diagnosis \*** | Systemic Sclerosis | 149 (44.6%) |
|  | Sjogren's syndrome | 92 (27.5%) |
|  | Rheumatoid Arthritis | 84 (25.1%) |
|  | Myositis | 11 (3.3%) |
|  | Mix Connected tissue | 10 (3.0%) |
|  | Systemic lupus erythema | 7 (2.1%) |
|  | ANCA-associated vasculitis | 3 (0.9%) |
| **Age at CTD Diagnosis** | mean ± sd | 52.4 ± 14.0 |
| Median (Q1 - Q3) | 54.0 (41.8 - 63.0) |
| Min - Max | 13.0 - 86.0 |
| **CTD First Symptom (n=234)** | Arthralgia | 114 (48.7%) |
| Raynaud phenomenon | 61 (26.1%) |
| Dry mouth/skin/eyes | 36 (15.4%) |
| Skin rash | 7 (3.0%) |
| Edema of the hands | 6 (2.6%) |
| Dactylitis | 4 (1.7%) |
| Weakness | 4 (1.7%) |
| Digital ulcer | 1 (0.4%) |
| Telangiectasias | 1 (0.4%) |
| **Time to CTD Diagnosis from Symptom (Month) (n=209)** | mean ± sd | 7.6 ± 11.6 |
| Median (Q1 - Q3) | 2.0 (0.0 - 11.6) |
| Min - Max | 0.0 - 56.1 |
| **Rheumatoid arthritis joint involvement (among n=84 patients with RH)** | 4-10 small joints (large joints not counted) | 33 (40.7%) |
| 1-3 small joints (large joints not counted) | 28 (34.6%) |
| >10 joints including at least one small joint | 11 (13.6%) |
| 2-10 large joints | 9 (11.1%) |
| Missing | 3 |
| **Rheumatoid arthritis Serology (among n=84 patients with RH)** | High positive RF or high positive ACPA | 51 (68.9%) |
| Negative RF and negative ACPA | 14 (18.9%) |
| Low positive RF or low positive ACPA | 9 (12.2%) |
| Missing | 10 |
| **Rheumatoid arthritis Acute Phase reaction (among n=84 patients with RH)** | Abnormal CRP or abnormal ESR | 61 (80.3%) |
| Normal CRP and normal ESR | 15 (19.7%) |
| Missing | 8 |
| **Rheumatoid arthritis Duration of symptoms (among n=84 patients with RH)** | >=6 weeks | 75 (98.7%) |
| <6 weeks | 1 (1.3%) |
| Missing | 8 |

Table 4: **ILD Diagnosis and characteristics**

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| **Variable** | | **Summary Statistics** |
| **ILD diagnosis year** | <2000 | 2 (0.6%) |
|  | 2000-2004 | 7 (2.1%) |
|  | 2005-2009 | 16 (4.8%) |
|  | 2010-2014 | 53 (15.9%) |
|  | 2015-2019 | 256 (76.6%) |
| **ILD Symptomatic** | Asymptomatic | 58 (17.4%) |
|  | Symptomatic | 276 (82.6%) |
| **ILD Symptoms** | Dyspnea | 221 (80.1%) |
|  | Cough | 181 (65.6%) |
|  | Fatigue | 57 (20.7%) |
|  | Weight Loss | 23 (8.3%) |
|  | Other | 5 (1.8%) |
| **Age at ILD Diagnosis** | mean ± sd | 54.8 ± 13.7 |
|  | Median (Q1 - Q3) | 56.0 (44.8 - 65.0) |
|  | Min - Max | 19.0 - 86.0 |
| **Time to ILD Diagnosis from Symptom (Month) (n=279)** | mean ± sd | 4.1± 6.4 |
| Median (Q1 - Q3) | 1.9 (0.0 - 5.0) |
| Min - Max | 0.0 - 36.9 |
| **Lung Biopsy** | Yes | 17 (5.1%) |
|  | No | 297 (88.9%) |
|  | unknown | 20 (6.0%) |
| **Antinuclear Antibody (ANA) (N=220)** | Positive | 180 (81.8%) |
|  | Negative | 40 (18.2%) |
| **Rheumatoid Factor (RF) (N=255)** | Positive | 79 (31.0%) |
|  | Negative | 176 (69.0%) |
| **DLCO (N=21)** | mean ± sd | 523.2 ± 2125.8 |
| Median (Q1 - Q3) | 58 (34 - 89) |
| Min - Max | 4 - 9800 |
| **DLCO VA (N=55)** | mean ± sd | 75.1 ± 21.3 |
| Median (Q1 - Q3) | 75 (58 - 89) |
| Min - Max | 24 - 130 |
| **Six Minute Walking Test at Diagnosis** | Completed | 115 (34.4%) |
| Not completed | 22 (6.6%) |
| Not Done | 197 (59%) |
| **Six Minute Walking Test result at Diagnosis in meters (n=114)** | mean ± sd | 428.2 ± 78.5 |
| Median (Q1 - Q3) | 440 (390 - 480) |
| Min - Max | 160 - 620 |
| **SPO % at Initial Six Minute Walking Test (n=90)** | mean ± sd | 95.8 ± 2.2 |
| Median (Q1 - Q3) | 96 (95 - 97) |
| Min - Max | 85 - 99 |
| **SPO % at the end Six Minute Walking Test (n=90)** | mean ± sd | 91.7 ± 6 |
| Median (Q1 - Q3) | 94 (90 - 96) |
| Min - Max | 65 - 99 |

Table 5**: Laboratory results**

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| **Variable** | | **Summary Statistics** |
| **Creatinine Kinase (CK) (N=81)** | mean ± sd | 85.6 ± 82.3 |
| Median (Q1 - Q3) | 61 (36.5 - 94.5) |
| Min - Max | 13 - 528 |
| **C-Reactive Protein (CRP) (N=230)** | mean ± sd | 13.4 ± 27.1 |
| Median (Q1 - Q3) | 5.1 (2.1 - 15) |
| Min - Max | 0.1 - 281 |
| **Sedimentation Rate (n=334)** | mean ± sd | 26.0 ± 24.8 |
| Median (Q1 - Q3) | 20 (0 - 42) |
| Min - Max | 0 - 135 |
| **Anti RO (N=154)** | Positive | 29 (18.8%) |
|  | Negative | 125 (81.2%) |
| **Anti RO 52 (N=180)** | Positive | 31 (17.2%) |
|  | Negative | 149 (82.8%) |
| **Anti LA (N=181)** | Positive | 8 (4.4%) |
|  | Negative | 173 (95.6%) |
| **Anti SCL70 (N=196)** | Positive | 82 (41.8%) |
|  | Negative | 114 (58.2%) |
| **Anti Smith Antibody (N=170)** | Positive | 3 (1.8%) |
|  | Negative | 167 (98.2%) |
| **Anti RNP (N=184)** | Positive | 8 (4.3%) |
|  | Negative | 176 (95.7%) |
| **c ANCA (N=159)** | Positive | 0 (0%) |
|  | Negative | 159 (100%) |
| **p ANCA (N=161)** | Positive | 3 (1.9%) |
|  | Negative | 158 (98.1%) |
| **Anti PR3 (N=151)** | Positive | 1 (0.7%) |
|  | Negative | 150 (99.3%) |
| **Anti MPO (N=155)** | Positive | 1 (0.6%) |
|  | Negative | 154 (99.4%) |

Table 6**: Treatments and End of Study Patients' Status**

|  |  |  |
| --- | --- | --- |
| **Variable** | | **Summary Statistics** |
| **Time from CTD Diagnosis to Treatment Start (Days) (N=331)** | mean ± sd | 40.6 ± 50.9 |
| Median (Q1 - Q3) | 27 (2 - 54) |
| Min - Max | 0 - 250 |
| **Time from ILD Diagnosis to Treatment Start (Days) (N=331)** | mean ± sd | 31.8 ± 41.7 |
| Median (Q1 - Q3) | 18 (0 - 44) |
| Min - Max | 0 - 209 |
| **CTD Initial Treatment** | CS-DMARD | 168 (50.3%) |
|  | Low-Dose Steroid | 86 (25.7%) |
|  | hydroxychloroquine | 21 (6.3%) |
|  | High Dose Steroid | 14 (4.2%) |
|  | Rituximab | 11 (3.3%) |
|  | Azathioprine | 9 (2.7%) |
|  | Cyclophosphamide | 8 (2.4%) |
|  | Biological DMARD | 6 (1.8%) |
|  | TS-DMARD | 3 (0.9%) |
|  | Azathioprine, Mycophenolate mofetil | 2 (0.6%) |
|  | Mycophenolate mofetil | 2 (0.6%) |
|  | Colchicine | 1 (0.3%) |
|  | D-PENICILLAMINE | 1 (0.3%) |
|  | Methotrexate | 1 (0.3%) |
|  | Mycophenolate mofetil, Hydroxychloroquine | 1 (0.3%) |
| **ILD Initial Treatment** | Low-Dose Steroid | 136 (40.7%) |
|  | Low Dose Steroid + CS-DMARD | 67 (20.1%) |
|  | CS-DMARD | 30 (9%) |
|  | Azathioprine | 22 (6.6%) |
|  | Cyclophosphamide | 19 (5.7%) |
|  | High Dose Steroid | 15 (4.5%) |
|  | Rituximab | 11 (3.3%) |
|  | High Dose Steroid + CS-DMARD | 10 (3%) |
|  | Mycophenolate mofetil | 8 (2.4%) |
|  | Hydroxychloroquine | 5 (1.5%) |
|  | Biological DMARD | 4 (1.2%) |
|  | Azathioprine, Mycophenolate mofetil | 2 (0.6%) |
|  | Hydroxychloroquine, Azathioprine, Mycophenolate mofetil | 1 (0.3%) |
|  | Methotrexate | 1 (0.3%) |
|  | Mycophenolate mofetil, Hydroxychloroquine | 1 (0.3%) |
|  | NINTEDANIB | 1 (0.3%) |
|  | TS-DMARD | 1 (0.3%) |
| **Patient Status at End of Study** | Alive | 263 (78.7%) |
| Dead | 34 (10.2%) |
| Lost to follow up | 37 (11.1%) |
| **Age (at last visit/death)** | mean ± sd | 61.3 ± 12.3 |
|  | Median (Q1 - Q3) | 62.8 (52.8 - 70.0) |
|  | Min - Max | 23.8 – 89.4 |

Figure 2**: ILD Diagnosis per year**