Supplementary Table 1. Diagnostic criteria for malignant rheumatoid arthritis

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| --- | --- |
| **1.** | **Clinical manifestations** |
| (1) | Peripheral neuropathy: sensory or motor disorder. |
| (2) | Skin ulcer, skin embolism, or digital necrosis without infection or trauma. |
| (3) | Skin nodule: subcutaneous nodules on bony protrusions, extensor surfaces, or near joints. |
| (4) | Episcleritis or iritis: ophthalmologist confirmed and other causes excluded. |
| (5) | Pleuritis or pericarditis: other causes (e.g. infection) excluded. Adhesions alone are not positive. |
| (6) | Myocarditis: diagnosis based on clinical findings, inflammatory reactions, myogenic enzyme levels, electrocardiograms, echocardiograms, etc. |
| (7) | Interstitial pneumonia or pulmonary fibrosis: confirmed with physical findings, chest X-rays, and pulmonary function tests. The extent of the lesions does not matter. |
| (8) | Organ infarction: caused by ischemia and necrosis due to vasculitis in organs such as the intestines, myocardium, and lung. |
| (9) | High titers of rheumatoid factor: RAHA or RAPA 1:2,560 or higher (RF: ≥960 IU/ml) on ≥2 tests. |
| (10) | Hypocomplementemia or presence of immune complexes: hypocomplementemia (low levels of C3, C4, or CH50 on ≥2 tests or presence of C1q reactive immune complexes on ≥2 tests. |
|  |  |
| **2.** | **Histological findings**: Biopsy of skin, muscles, nerves, and other organs reveals small-to medium –sized vessel necrotizing vasculitis, granulomatous vasculitis, or obstructive vasculitis. |
|  |  |
| **Diagnostic category** | |
| Fulfills the 2010 ACR/EULAR criteria for rheumatoid arthritis and (I) or (II) below. | |
| (I) | Positive for ≥3 clinical manifestations. |
| (II) | Positive for ≥1 clinical manifestation and histological findings. |

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ACR, American College of Rheumatology; EULAR, European League Against Rheumatic Diseases; MHLW, Ministry of Health, Labour and Welfare; RF, rheumatoid factor.

Supplementary Table 2. Number of data from each year and each prefecture.

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 |
| Hokkaido | 0 | 0 | 212 | 0 | 0 | 172 | 132 | 0 | 201 | 8 | 20 |
| Aomori | 22 | 40 | 46 | 70 | 47 | 87 | 112 | 89 | 120 | 114 | 116 |
| Iwate | 13 | 64 | 7 | 42 | 43 | 47 | 44 | 46 | 41 | 42 | 4 |
| Miyagi | 76 | 162 | 84 | 92 | 98 | 77 | 94 | 15 | 91 | 85 | 91 |
| Akita | 32 | 74 | 31 | 37 | 29 | 42 | 44 | 40 | 37 | 0 | 0 |
| Yamagata | 21 | 44 | 25 | 33 | 37 | 35 | 28 | 26 | 26 | 14 | 38 |
| Fukushima | 109 | 216 | 103 | 13 | 15 | 5 | 125 | 71 | 7 | 118 | 115 |
| Ibaraki | 75 | 103 | 95 | 0 | 3 | 99 | 110 | 118 | 119 | 118 | 119 |
| Tochigi | 41 | 100 | 45 | 49 | 41 | 40 | 41 | 47 | 42 | 41 | 44 |
| Gunma | 89 | 162 | 74 | 72 | 74 | 78 | 68 | 72 | 68 | 71 | 69 |
| Saitama | 110 | 571 | 60 | 64 | 28 | 32 | 369 | 325 | 371 | 379 | 338 |
| Chiba | 147 | 486 | 279 | 163 | 385 | 454 | 477 | 383 | 456 | 440 | 312 |
| Tokyo | 172 | 599 | 46 | 54 | 38 | 512 | 532 | 531 | 619 | 287 | 0 |
| Kanagawa | 358 | 697 | 387 | 365 | 515 | 478 | 117 | 400 | 566 | 467 | 0 |
| Niigata | 42 | 72 | 26 | 31 | 0 | 29 | 32 | 0 | 44 | 47 | 0 |
| Toyama | 76 | 140 | 67 | 63 | 61 | 54 | 61 | 59 | 61 | 59 | 56 |
| Ishikawa | 51 | 97 | 64 | 60 | 82 | 75 | 72 | 69 | 49 | 67 | 62 |
| Fukui | 30 | 54 | 33 | 29 | 30 | 30 | 45 | 39 | 42 | 40 | 42 |
| Yamanashi | 13 | 22 | 11 | 8 | 9 | 9 | 14 | 16 | 18 | 16 | 15 |
| Nagano | 56 | 10 | 17 | 7 | 18 | 14 | 27 | 26 | 42 | 81 | 97 |
| Gifu | 21 | 38 | 30 | 32 | 34 | 1 | 33 | 32 | 28 | 4 | 0 |
| Shizuoka | 191 | 0 | 204 | 0 | 219 | 0 | 263 | 248 | 287 | 227 | 0 |
| Aichi | 77 | 128 | 16 | 0 | 0 | 0 | 88 | 74 | 7 | 51 | 90 |
| Mie | 0 | 73 | 0 | 85 | 40 | 104 | 81 | 54 | 48 | 103 | 100 |
| Shiga | 10 | 0 | 2 | 41 | 49 | 53 | 56 | 0 | 0 | 0 | 1 |
| Kyoto | 0 | 262 | 149 | 144 | 17 | 1 | 201 | 222 | 222 | 239 | 264 |
| Osaka | 369 | 754 | 462 | 383 | 431 | 441 | 46 | 446 | 435 | 52 | 16 |
| Hyogo | 176 | 387 | 233 | 246 | 0 | 227 | 236 | 242 | 233 | 259 | 250 |
| Nara | 62 | 112 | 1 | 2 | 0 | 0 | 0 | 52 | 0 | 11 | 0 |
| Wakayama | 31 | 13 | 38 | 40 | 10 | 28 | 25 | 36 | 32 | 40 | 40 |
| Tottori | 1 | 10 | 6 | 10 | 8 | 4 | 9 | 8 | 6 | 4 | 5 |
| Shimane | 23 | 0 | 40 | 0 | 0 | 0 | 21 | 23 | 26 | 21 | 25 |
| Okayama | 66 | 9 | 56 | 62 | 67 | 66 | 68 | 12 | 67 | 65 | 62 |
| Hiroshima | 167 | 285 | 9 | 153 | 171 | 210 | 59 | 17 | 18 | 119 | 7 |
| Yamaguchi | 45 | 52 | 50 | 57 | 52 | 57 | 52 | 57 | 65 | 70 | 75 |
| Tokushima | 0 | 113 | 60 | 65 | 1 | 8 | 61 | 63 | 0 | 0 | 0 |
| Kagawa | 84 | 170 | 97 | 85 | 88 | 88 | 87 | 84 | 5 | 86 | 89 |
| Ehime | 32 | 68 | 40 | 39 | 30 | 33 | 47 | 49 | 45 | 48 | 53 |
| Kochi | 22 | 47 | 29 | 26 | 0 | 42 | 31 | 45 | 45 | 52 | 50 |
| Fukuoka | 0 | 0 | 0 | 14 | 39 | 36 | 214 | 22 | 0 | 7 | 0 |
| Saga | 15 | 49 | 0 | 22 | 0 | 0 | 0 | 9 | 0 | 0 | 13 |
| Nagasaki | 128 | 271 | 185 | 215 | 0 | 254 | 264 | 266 | 295 | 0 | 0 |
| Kumamoto | 44 | 134 | 67 | 62 | 0 | 76 | 79 | 94 | 89 | 72 | 73 |
| Oita | 81 | 0 | 0 | 0 | 48 | 134 | 152 | 170 | 185 | 183 | 19 |
| Miyazaki | 0 | 68 | 33 | 0 | 30 | 0 | 5 | 18 | 41 | 43 | 47 |
| Kagoshima | 106 | 0 | 0 | 131 | 113 | 0 | 115 | 110 | 49 | 39 | 0 |
| Okinawa | 19 | 0 | 0 | 7 | 31 | 47 | 48 | 39 | 42 | 40 | 42 |
| Total | 3303 | 6756 | 3519 | 3173 | 3031 | 4279 | 4885 | 4864 | 5290 | 4329 | 2859 |

Supplementary Table 3. The Patient characteristics, therapy details, and social activities over time for each year.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Overall | 2003 | 2004 | 2005 | 2006 | 2007 |
| Age at survey, median (IQR) |  | 65 (57-72) | 63 (56-70) | 63 (56-70) | 63 (56-70) | 64 (56-71) | 64 (56-71) |
| Sex, female, n (%) |  | 31088 (71.0) | 2362 (72.2) | 2574 (72.0) | 2527 (71.8) | 2295 (72.4) | 2153 (71.0) |
| Stage, n (%) | I | 1701 (4.0) | 79 (2.4) | 118 (3.4) | 111 (3.2) | 109 (3.5) | 96 (3.2) |
|  | II | 7285 (17.1) | 408 (12.6) | 456 (13.0) | 511 (14.8) | 473 (15.1) | 516 (17.3) |
|  | III | 14417 (33.9) | 1109 (34.4) | 1192 (34.0) | 1201 (34.7) | 1072 (34.3) | 1020 (34.2) |
|  | IV | 19081 (44.9) | 1632 (50.6) | 1741 (49.6) | 1635 (47.3) | 1471 (47.1) | 1351 (45.3) |
| Class, n (%) | 1 | 1346 (3.2) | 81 (2.5) | 82 (2.4) | 87 (2.6) | 72 (2.4) | 67 (2.3) |
|  | 2 | 17524 (42.2) | 1190 (37.1) | 1310 (37.9) | 1303 (38.5) | 1205 (39.6) | 1146 (39.2) |
|  | 3 | 16864 (40.6) | 1379 (43.0) | 1501 (43.4) | 1456 (43.1) | 1299 (42.7) | 1250 (42.8) |
|  | 4 | 5832 (14.0) | 559 (17.4) | 568 (16.4) | 535 (15.8) | 469 (15.4) | 459 (15.7) |
| Fever, n (%) |  | 21986 (52.1) | 1727 (54.0) | 1830 (52.4) | 1823 (52.9) | 1675 (53.9) | 1590 (53.8) |
| Skin nodule, n (%) |  | 28063 (66.1) | 2120 (66.1) | 2256 (64.4) | 2231 (64.7) | 2031 (65.1) | 1941 (65.4) |
| Skin ulcer, n (%) |  | 14778 (34.8) | 1194 (37.0) | 1285 (36.5) | 1223 (35.3) | 1116 (35.6) | 1104 (37.0) |
| Skin infarction, n (%) |  | 8467 (20.1) | 637 (20.2) | 705 (20.3) | 717 (20.9) | 652 (21.0) | 688 (23.3) |
| Digital necrosis, n (%) |  | 5890 (13.9) | 535 (16.7) | 567 (16.1) | 483 (14.0) | 421 (13.5) | 425 (14.3) |
| Iritis, n (%) |  | 4656 (12.2) | 399 (14.2) | 422 (13.7) | 404 (13.3) | 357 (13.0) | 324 (12.3) |
| Episcleritis, n (%) |  | 9852 (25.8) | 759 (26.9) | 796 (25.7) | 749 (24.5) | 669 (24.2) | 680 (25.7) |
| Peripheral neuropathy, n (%) |  | 24963 (60.1) | 1881 (60.1) | 2033 (59.5) | 2008 (59.8) | 1822 (59.8) | 1810 (62.4) |
| Pleuritis, n (%) |  | 10378 (25.0) | 693 (22.3) | 747 (22.0) | 779 (23.2) | 758 (24.9) | 760 (26.1) |
| Interstitial pneumonia, n (%) |  | 23883 (56.9) | 1641 (51.9) | 1780 (51.8) | 1818 (53.5) | 1718 (56.0) | 1693 (57.6) |
| Pericarditis, n (%) |  | 4434 (11.1) | 355 (11.8) | 351 (10.7) | 364 (11.2) | 337 (11.6) | 333 (11.9) |
| Myocarditis, n (%) |  | 2163 (5.5) | 204 (6.9) | 196 (6.1) | 181 (5.6) | 168 (5.9) | 164 (5.9) |
| Organ infarction, n (%) |  | 3849 (10.0) | 315 (11.1) | 332 (10.5) | 321 (10.4) | 306 (10.9) | 271 (10.1) |
| Number of clinical manifestations, n (%) |  | 4 (3-5) | 4 (3-5) | 4 (2-5) | 4 (2-5) | 4 (3-5) | 4 (3-5) |
| White blood cell, median (IQR) |  | 8440 (6130-10700) | 9885 (7200-12000) | 9500 (6800-11600) | 7520 (5600-9800) | 7520 (5700-10000) | 7600 (5600-10070) |
| Erythrocyte sedimentation rate, mm, median (IQR) |  | 40 (21-67) | 66 (41-96) | 57 (30-89) | 30 (13-52) | 32 (16-53) | 32 (15-55) |
| C-reactive protein, mg/dl, median (IQR) |  | 1.13 (0.32-3.1) | 3.81 (1.5-7.8) | 2.7 (0.7-6.41) | 0.6 (0.13-1.78) | 0.6 (0.14-1.79) | 0.66 (0.16-1.87) |
| Immunosuppressants, n (%) |  | 23110 (55.1) | 1518 (47.9) | 1639 (47.3) | 1672 (49.1) | 1536 (50.0) | 1581 (53.4) |
| Disease modifying anti-rheumatic drugs, n (%) |  | 30924 (73.4) | 2170 (68.3) | 2425 (69.5) | 2455 (71.8) | 2231 (72.0) | 2162 (72.8) |
| Glucocorticoid dose, mg/day, median (IQR) |  | 7.5 (5-10) | 10 (5-14) | 9 (5-11) | 10 (5-12.5) | 8 (5-11) | 7.5 (5-10) |
| Use of glucocorticoid, n (%) |  | 35972 (86.8) | 2899 (89.5) | 3152 (90.1) | 3102 (90.6) | 2756 (89.0) | 2598 (87.6) |
| Non-steroidal anti-inflammatory drugs, n (%) |  | 31585 (75.3) | 2653 (82.8) | 2817 (80.6) | 2768 (80.9) | 2435 (79.0) | 2330 (78.6) |
| Apheresis therapy, n (%) |  | 195 (6.2) | 207 (6.0) | 150 (6.0) | 154 (5.0) | 130 (4.4) | 151 (3.7) |
| Surgery, n (%) |  | 3147 (7.6) | 353 (11.2) | 368 (10.7) | 306 (9.1) | 287 (9.4) | 257 (8.8) |
| Working, n (%) |  | 5763 (14.2) | 319 (10.5) | 376 (11.3) | 364 (11.1) | 341 (11.5) | 366 (12.9) |
| Working at home, n (%) |  | 10763 (26.5) | 745 (24.5) | 813 (24.3) | 831 (25.4) | 764 (25.8) | 722 (25.4) |
| Student, n (%) |  | 201 (0.5) | 15 (0.5) | 13 (0.4) | 15 (0.5) | 20 (0.7) | 18 (0.6) |
| Recuperating, n (%) |  | 19776 (48.8) | 1632 (53.7) | 1752 (52.4) | 1692 (51.6) | 1498 (50.5) | 1420 (50.1) |
| Hospitalized, n (%) |  | 2957 (7.3) | 250 (8.2) | 296 (8.9) | 288 (8.8) | 266 (9.0) | 226 (8.0) |
| In residential care, n (%) |  | 718 (1.8) | 44 (1.4) | 46 (1.4) | 58 (1.8) | 50 (1.7) | 59 (2.1) |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 |
| Age at survey, median (IQR) |  | 65 (56-72) | 65 (57-72) | 65 (57-72) | 65 (57-73) | 66 (58-73) | 66 (58-73) |
| Sex, female, n (%) |  | 3053 (71.3) | 3408 (69.8) | 3455 (71.0) | 3753 (70.9) | 3012 (69.6) | 1974 (69.0) |
| Stage, n (%) | I | 163 (3.9) | 180 (4.0) | 211 (4.7) | 228 (4.4) | 203 (4.8) | 161 (5.7) |
|  | II | 697 (16.5) | 796 (17.8) | 816 (18.1) | 955 (18.4) | 858 (20.1) | 625 (22.0) |
|  | III | 1472 (34.8) | 1518 (34.0) | 1503 (33.4) | 1702 (32.9) | 1434 (33.6) | 939 (33.1) |
|  | IV | 1898 (44.9) | 1968 (44.1) | 1966 (43.7) | 2295 (44.3) | 1768 (41.5) | 1110 (39.2) |
| Class, n (%) | 1 | 111 (2.7) | 142 (3.2) | 152 (3.5) | 198 (3.9) | 178 (4.3) | 140 (5.1) |
|  | 2 | 1769 (43.0) | 1883 (43.0) | 1934 (44.2) | 2240 (44.4) | 1889 (45.4) | 1323 (47.8) |
|  | 3 | 1658 (40.3) | 1736 (39.7) | 1752 (40.0) | 1979 (39.2) | 1597 (38.4) | 993 (35.8) |
|  | 4 | 578 (14.0) | 613 (14.0) | 541 (12.4) | 630 (12.5) | 499 (12.0) | 314 (11.3) |
| Fever, n (%) |  | 2199 (52.3) | 2294 (51.6) | 2281 (51.1) | 2570 (49.9) | 2220 (52.1) | 1433 (50.9) |
| Skin nodule, n (%) |  | 2837 (67.1) | 3006 (67.1) | 2991 (66.7) | 3467 (66.9) | 2870 (66.9) | 1854 (65.5) |
| Skin ulcer, n (%) |  | 1477 (35.0) | 1479 (33.2) | 1498 (33.5) | 1714 (33.1) | 1450 (33.8) | 982 (34.6) |
| Skin infarction, n (%) |  | 878 (21.0) | 876 (19.7) | 889 (20.0) | 986 (19.1) | 799 (18.7) | 511 (18.1) |
| Digital necrosis, n (%) |  | 604 (14.4) | 607 (13.6) | 568 (12.8) | 627 (12.1) | 558 (13.0) | 405 (14.3) |
| Iritis, n (%) |  | 469 (12.4) | 463 (11.5) | 467 (11.6) | 514 (10.9) | 437 (11.2) | 317 (12.2) |
| Episcleritis, n (%) |  | 945 (24.9) | 1103 (27.2) | 1117 (27.6) | 1190 (25.1) | 1059 (26.9) | 631 (24.2) |
| Peripheral neuropathy, n (%) |  | 2565 (62.2) | 2692 (61.5) | 2697 (61.5) | 3030 (59.5) | 2507 (59.5) | 1560 (56.0) |
| Pleuritis, n (%) |  | 1049 (25.4) | 1130 (25.7) | 1116 (25.4) | 1299 (25.5) | 1131 (26.8) | 693 (24.8) |
| Interstitial pneumonia, n (%) |  | 2398 (57.3) | 2586 (58.3) | 2619 (59.0) | 3029 (58.9) | 2563 (60.1) | 1655 (58.9) |
| Pericarditis, n (%) |  | 462 (11.6) | 465 (11.0) | 471 (11.1) | 545 (11.1) | 435 (10.8) | 258 (9.6) |
| Myocarditis, n (%) |  | 222 (5.6) | 222 (5.3) | 234 (5.6) | 247 (5.0) | 198 (4.9) | 114 (4.2) |
| Organ infarction, n (%) |  | 420 (10.9) | 420 (10.2) | 400 (9.8) | 434 (9.0) | 361 (9.2) | 225 (8.5) |
| Number of clinical manifestations, n (%) |  | 4 (3-5) | 4 (3-5) | 4 (3-5) | 4 (3-5) | 4 (2-5) | 3 (3-5) |
| White blood cell, median (IQR) |  | 7800 (5700-10200) | 8100 (5938-10400) | 8500 (6100-10700) | 8630 (6460-10700) | 8740 (6420-10900) | 9000 (6600-11000) |
| Erythrocyte sedimentation rate, mm, median (IQR) |  | 33.5 (17-58) | 35 (19-58) | 38 (20-61) | 41 (24-65) | 44 (25-68) | 45 (27-70) |
| C-reactive protein, mg/dl, median (IQR) |  | 0.775 (0.2-2.09) | 0.87 (0.27-2.37) | 0.93 (0.3-2.42) | 1.2 (0.41-2.85) | 1.4 (0.49-3.27) | 1.47 (0.57-3.2) |
| Immunosuppressants, n (%) |  | 2298 (55.1) | 2501 (56.9) | 2590 (58.1) | 2986 (58.1) | 2601 (61.1) | 1728 (61.9) |
| Disease modifying anti-rheumatic drugs, n (%) |  | 3126 (74.7) | 3243 (73.5) | 3341 (74.8) | 3886 (75.4) | 3193 (75.0) | 2139 (76.7) |
| Glucocorticoid dose, mg/day, median (IQR) |  | 7.5 (5-10) | 7.5 (5-10) | 6 (5-10) | 6 (5-10) | 6 (5-10) | 6 (5-10) |
| Use of glucocorticoid, n (%) |  | 3747 (89.4) | 3859 (87.9) | 3818 (85.8) | 4251 (83.0) | 3495 (82.1) | 2295 (82.2) |
| Non-steroidal anti-inflammatory drugs, n (%) |  | 3188 (76.5) | 3227 (73.5) | 3241 (73.2) | 3621 (71.0) | 2890 (68.4) | 1917 (69.1) |
| Apheresis therapy, n (%) |  | 112 (2.6) | 80 (1.8) | 86 (1.7) | 79 (1.9) | 27 (1.0) | 6 (0.9) |
| Surgery, n (%) |  | 316 (7.7) | 307 (7.1) | 261 (5.9) | 264 (5.2) | 254 (6.0) | 145 (5.2) |
| Working, n (%) |  | 588 (14.6) | 630 (14.5) | 682 (15.7) | 768 (16.4) | 706 (17.0) | 492 (17.7) |
| Working at home, n (%) |  | 1122 (27.8) | 1129 (26.0) | 1171 (26.9) | 1336 (28.5) | 1107 (26.6) | 786 (28.2) |
| Student, n (%) |  | 25 (0.6) | 28 (0.6) | 20 (0.5) | 18 (0.4) | 15 (0.4) | 11 (0.4) |
| Recuperating, n (%) |  | 1915 (47.5) | 2086 (48.1) | 2065 (47.5) | 2185 (46.5) | 1973 (47.4) | 1265 (45.4) |
| Hospitalized, n (%) |  | 287 (7.1) | 343 (7.9) | 308 (7.1) | 257 (5.5) | 244 (5.9) | 163 (5.8) |
| In residential care, n (%) |  | 70 (1.7) | 76 (1.8) | 70 (1.6) | 95 (2.0) | 84 (2.0) | 50 (1.8) |

Supplementary Table 4. The comparisons between the patients with new and continuous registrations.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | With new registration | With continuous registration | *p* value |
| Basic characteristics |  |  |  |  |
| Age at survey, median (IQR) |  | 64 (55–72) | 65 (57–71) | 0.101 |
| Sex, female, n (%) |  | 3184 (63%) | 27382 (72%) | <0.001 |
| Clinical characteristics |  |  |  |  |
| Stage, n (%) | I | 386 (8%) | 1273 (3%) | <0.001 |
|  | II | 1345 (27%) | 5766 (16%) | <0.001 |
|  | III | 1760 (35%) | 12402 (34%) | 0.161 |
|  | IV | 1514 (30%) | 17321 (47%) | <0.001 |
| Class, n (%) | 1 | 147 (3%) | 1163 (3%) | 0.3288 |
|  | 2 | 2274 (46%) | 14918 (42%) | <0.001 |
|  | 3 | 1884 (38%) | 14716 (41%) | 0.010 |
|  | 4 | 646 (13%) | 5119 (14%) | 0.047 |
| WBC, /μl, median (IQR) |  | 9220 (6830–11140) | 8300 (6040–10600) | <0.001 |
| ESR, mm, median (IQR) |  | 50 (29–74) | 40 (20–65) | <0.001 |
| CRP, mg/dl, median (IQR) |  | 1.80 (0.74–3.92) | 1.04 (0.30–2.95) | <0.001 |
| Manifestations |  |  |  |  |
| Fever, n (%) |  | 2278 (47%) | 19364 (53%) | <0.001 |
| Skin nodule, n (%) |  | 303 (6%) | 24573 (67%) | <0.001 |
| Skin ulcer, n (%) |  | 1524 (31%) | 12998 (35%) | <0.001 |
| Skin infarction, n (%) |  | 842 (17%) | 7496 (21%) | <0.001 |
| Digital necrosis, n (%) |  | 583 (12%) | 5217 (14%) | <0.001 |
| Iritis, n (%) |  | 367 (9%) | 4206 (13%) | <0.001 |
| Episcleritis, n (%) |  | 1004 (25%) | 8694 (26%) | 0.045 |
| Peripheral neuropathy, n (%) |  | 2832 (60%) | 21773 (60%) | 0.813 |
| Pleuritis, n (%) |  | 1279 (27%) | 8876 (25%) | 0.003 |
| Interstitial pneumonia, n (%) |  | 3250 (66%) | 20250 (56%) | <0.001 |
| Pericarditis, n (%) |  | 504 (11%) | 3872 (11%) | 0.706 |
| Myocarditis, n (%) |  | 184 (4%) | 1966 (6%) | <0.001 |
| Organ infarction, n (%) |  | 382 (9%) | 3423 (10%) | 0.057 |
| Number of manifestations, median (IQR) |  | 4 (3-5) | 4 (3-5) | 0.853 |
| Therapy |  |  |  |  |
| Immunosuppressants, n (%) |  | 2990 (61%) | 19660 (54%) | <0.001 |
| DMARDs, n (%) |  | 3876 (78%) | 26495 (73%) | <0.001 |
| GC dose, mg/day, median (IQR) |  | 10 (8-30) | 7 (5-10) | <0.001 |
| NSAIDs, n (%) |  | 3936 (80%) | 27151 (75%) | <0.001 |
| Apheresis therapy, n (%) |  | 183 (4%) | 1188 (3%) | 0.106 |
| Surgery, n (%) |  | 403 (8%) | 2715 (8%) | 0.078 |
| Social productivity levels |  |  |  |  |
| Working, n (%) |  | 819 (17%) | 4813 (14%) | <0.001 |
| Working at home, n (%) |  | 1126 (24%) | 9400 (27%) | <0.001 |
| Student, n (%) |  | 43 (1%) | 155 (0.4%) | <0.001 |
| Recuperating, n (%) |  | 1710 (36%) | 17773 (51%) | <0.001 |
| In residental care, n (%) |  | 51 (1%) | 651 (2%) | <0.001 |
| Hospitalized, n (%) |  | 999 (21%) | 1929 (6%) | <0.001 |

IQR, interquartile; WBC, white blood cell; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; DMARDs, disease modifying anti-rheumatic drugs; GC, glucocorticoid; NSAIDs, non-steroidal anti-inflammatory drugs.