Biologic treatment for rheumatic disease: real-world big data analysis from the Greek country-wide prescription database

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Abstract

Objective

To directly assess the prevalence of inflammatory rheumatic disease under treatment with biologic disease-modifying anti-rheumatic drugs (b-DMARDs) and compare treatment patterns between rheumatoid arthritis (RA) and spondyloarthropathy (SpA), including psoriatic arthritis.

Methods

The obligatory country-wide prescription electronic database covering 10.223.000 Greek citizens (95.1% of the population, 99.5% Caucasian), all of whom with fully reinbursed access to b-DMARDs, was used to retrospectively capture all patients under b-DMARDs for RA/SpA between June 2014-May 2015. Age, gender and medications for RA/SpA and co-morbid classical cardiovascular risk factors (hypertension, dyslipidaemia, diabetes) were retrieved and analysed.

Results

A total of 9.824 RA (61.2±14.0 years, 79% women) and 9.279 SpA patients (51.4±13.1 years, 41% women) using pharmacy-dispensed prescriptions for b-DMARDs were identified (overall prevalence 0.19%). Tumour necrosis factor inhibitors were used in 73% and 99% of RA and SpA patients, respectively. B-DMARD monotherapy (RA: 18.71%, SpA: 52.11%), b-DMARD switching during 12 months (RA: 7.73%, SpA: 6.26%), and use of methotrexate (RA: 50.25%, SpA: 27.35%) and corticosteroids (RA: 55.8%, SpA: 23.63%) differed between the two patient subgroups. In both subgroups, women received more often than men methotrexate, leflunomide, hydroxychloroquine and corticosteroids, and less often b-DMARD monotherapy. After adjustments for age, gender and concomitant drugs, the probability for anti-hypertensive and lipid-lowering drug prescription was higher in SpA than RA [OR=1.41 (95%CI: 1.29-1.54) and 1.24 (1.14-1.36), respectively, p<0.001], whereas for anti-diabetics it was similar.

Conclusion

In the first country-wide study that examines the characteristics of rheumatic disease patients under b-DMARD we show that their exact prevalence is 0.19%, with RA patients being older by 10 years, only slightly more numerous, and less likely to receive treatment for hypertension and dyslipidaemia than their demographically matched SpA counterparts. Longitudinal studies should assess the implications of these novel findings on the differential financial burden of rheumatic diseases, as well as on cardiovascular morbidity and mortality of these patients.

Key words

rheumatoid arthritis, spondyloarthritis, DMARDs (biologics), hypertension, diabetes, dyslipidaemia

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Introduction

During the last two decades, different biologic disease-modifying antirheumatic agents (b-DMARDs) are increasingly used for the treatment of chronic inflammatory rheumatic disease (1, 2). In addition to randomised controlled trials that have assessed the short term clinical efficacy and safety of these medications by employing a strict experimental design, longitudinal or cross-sectional observational studies based on large, high quality patient registries have also provided valuable information (3), which can be used both for clinical decision-making and health services planning (4).

To our knowledge, very few countries have a complete countrywide obligatory prescription system that covers their entire population. In Greece, during the last 5 years the Greek National Organisation for Provision of Healthcare Services (EOPYY) has implemented an obligatory electronic prescription platform for all prescribing physicians. Within the third year of its function, this electronic database has expanded to include more than 95% of the permanent Greek population, estimated to be 10.816.286 (2011 census).

Since the exact prevalence and characteristics of rheumatic disease patients under b-DMARDs have not been studied, we performed a retrospective analysis of country-wide data regarding prescription patterns of antirheumatic medication and captured all b-DMARD-treated patients with rheumatoid arthritis (RA) and spondyloarthropathies (SpA) in Greece. Due to the high prevalence of cardiovascular morbidity in these patients, prescription patterns for common cardiovascular risk factors, such as arterial hypertension, diabetes mellitus and dyslipidaemia, were also retrieved and analysed.

Methods

In this retrospective study, the EOPYY database covering 10.223.000 citizens was used to identify all patients with chronic inflammatory rheumatic disease who used at least one pharmacy-dispensed prescription of b-DMARD during a 12-month period (from June 1st 2014 to May 31st 2015). According to national laws, all Greek citizens have fully reimbursed access to b-DMARDs when prescribed trough the EOPPY database. The following predefined ICD-10 codes were used to capture all b-DMARD treated patients: M05, M05.0, M05.1, M05.2, M05.3, M05.8, M05.9, M06, M06.0, M06.4, M06.8 and M06.9 for RA and M45, M46, M46.0, M46.1, M46.8, M46.9, M07.2, M07.4, M07.5, M07.6, M76.6, M76.9, M77, M77.8, M07, M07.0, M07.1, M07.3 and L40.5 for SpA, including psoriatic arthritis. Permission for use of anonymised data was obtained by the EOPYY administration in accordance to the national legislation on Personal Data Protection.

For all patients under b-DMARDs (tumour necrosis factor inhibitors/TNFi, other bDMARDs) we retrieved data on age, gender, disease-related medication use, such as conventional synthetic DMARDs (cs-DMARDs) (methotrexate, leflunomide, hydroxychloroquine, other) and corticosteroid use. Medications for hypertension (centrally and peripherally acting anti-adrenergic agents, diuretics, b-blockers, calcium channel antagonists, agents acting on the renin-angiotensin system), diabetes mellitus (insulin and oral anti-diabetic agents), and dyslipidaemia (statins, fibrates, bile acid sequestrants, ezetimibe) were also recorded.

Student's *t*-test and chi-square test were used for descriptive statistics and simple comparisons, while binary logistic regression was applied for multivariate analysis, where appropriate, using the Stata/SE v. 12 statistical package software. Statistical significance was set at the level of $p<0.05$.

Results

Among 10.223.000 Greek citizens listed in the National prescription database, we identified 9.824 (79% women) and 9.279 (41% women) b-DMARD users with RA or SpA, respectively, during this one-year period (Table I). Therefore, the exact prevalence of chronic inflammatory rheumatic disease under treatment with b-DMARDs in Greece during the study period was 0.19%, being almost equal in RA and SpA.

Biologic-DMARD-treated RA patients

Table I. Patient demographics and medication use in the study population.

Disease		Rheumatoid arthritis (n=9824)		Spondyloarthropathy (n=9279)		
		n	%	n	%	*p*-value*
Gender (men)		2074	21.11	5479	59.05	**<0.00001**
Age groups						
≤45 years		1361	13.85	3082	33.21	**<0.00001**
>45-65 years		4332	44.09	4818	51.92	**<0.00001**
>65 years		4131	42.05	1379	14.86	**<0.00001**
bDMARDs						
TNF inhibitors		7211	73.40	9231	99.48	**<0.00001**
Other bDMARDs		2947	30.00	72	0.78	**<0.00001**
bDMARD monotherapy		1838	18.70	4835	52.11	**<0.00001**
Number of bDMARD switches	1	692	7.04	535	5.76	**0.000277**
	2	64	0.65	45	0.48	0.109
	3	3	0.03	1	0.01	0.625
csDMARDs						
Methotrexate		4937	50.25	2538	27.35	**<0.00001**
Leflunomide		1714	17.45	483	5.21	**<0.00001**
Hydroxychloroquine		973	9.90	103	1.11	**<0.00001**
Other csDMARDs		611	6.22	977	10.53	**<0.00001**
Corticosteroids		5482	55.8	2193	23.63	**<0.00001**
Anti-hypertensive drug use		4119	41.93	3075	33.14	**<0.00001**
Lipid-lowering drug use		2575	26.21	2085	22.47	**<0.00001**
Anti-diabetic drug use		1177	11.98	937	10.10	**0.000034**

*Student's *t*-test or chi-square test where appropriate.
bDMARDs: Biologic disease-modifying anti-rheumatic drugs, csDMARDs: conventional synthetic DMARDs, TNF: tumour necrosis factor. In bold, statistically significant differences ($p<0.05$) are shown.

were approximately 10 years older compared to SpA patients (61.21±13.99 *vs*. 51.39±13.08 years. $p=0.0001$). Almost all SpA patients were treated with TNFi (99.48%) compared to 73.4% of RA patients ($p<0.00001$). During this 12-month period, bDMARDs were far more commonly given as monotherapy in SpA compared to RA patients (52.11% *vs*. 18.71%, $p<0.00001$), while bDMARD switching was more frequent in RA compared to SpA patients (7.73% *vs*. 6.26%, $p<0.0001$). As expected, corticosteroid and cs-DMARD use was much lower in the SpA compared to the RA group (23.63% *vs*. 55.8%, $p<0.00001$ and 38.74% *vs*. 70.12%, respectively, $p<0.00001$). Methotrexate was the most commonly administered cs-DMARD (SpA: 27.35%, RA: 50.25%, $p<0.00001$). Other csDMARDs, such as leflunomide (5.21% in SpA *vs*.17.45% in RA) and hydroxychloroquine (1.11% in SpA *vs*. 9.90% in RA), were used less frequently.

As shown in Table II, the distribution of age groups (younger or equal to 45 years, >45–65 years, older than 65 years) was comparable between women and men, although in both RA and SpA men were somewhat younger than women, having a larger representation in the younger than 45 years patient subgroup (mean age ± SD: 61.50±13.74 years for women *vs*. 60.14±14.84 years for men in RA, $p<0.0001$ and 52.31±13.28 years for women *vs*. 50.76±12.90 years for men in SpA, $p<0.0001$, respectively). Notably, in both subgroups, b-DMARD treatment was used as monotherapy by far more frequently in men than women (27.77% *vs*. 16.28% in RA, $p<0.0001$ and 61.87% *vs*. 38.03% in SpA, $p<0.0001$), since women received more often than men methotrexate, leflunomide, hydroxychloroquine and corticosteroids. In the RA subgroup, the number of men and women under treatment with anti-hypertensive (40.60% men *vs*. 42.28% women, $p=0.167$) and lipid lowering agents (24.98% men *vs*. 26.54% women, $p=0.150$) was comparable, but there were slightly more men receiving anti-diabetics (14.08% men *vs*. 11.42% women, $p=0.001$). On the other hand, in the SpA subgroup, there were more women than men under anti-hypertensive (31.61% men *vs*. 35.34% women, $p<0.0001$) and lipid-lowering agents (21.26% men *vs*. 24.21% women, $p=0.001$), while the percents for anti-diabetics were comparable between genders (10.42% men *vs*. 9.63% women, $p=0.214$).

Anti-hypertensives, lipid-lowering agents and anti-diabetics were prescribed less often in SpA compared to RA patients (33.14% *vs*. 41.93%, 22.47% *vs*. 26.21% and 10.1% vs 11.98%, respectively, $p<0.0001$, Table I). Notably, however, in multivariate analysis after adjusting for age, gender, use of csDMARDs (methotrexate leflunomide, hydroxychloroquine) and corticosteroids, as well as for anti-diabetics, lipid lowering agents or anti-hypertensives in the appropriate comparisons, patients with SpA had a statistically significant higher probability to be prescribed anti-hypertensives (odds ratio-OR 1.41, 95% confidence intervals-CI: 1.29–1.54, $p<0.001$) and lipid lowering agents (OR 1.24, 95% CI: 1.14–1.36, $p<0.001$). No such difference was seen for anti-diabetics (OR=1.01, 95% CI: 0.90–1.13, $p=0.897$, Table III).

Further subgroup analysis by age and gender revealed that SpA patients older than 45 years had a statistically significant higher probability, regardless of gender, for using anti-hypertensives than RA patients, after adjusting for all available possible confounders. This was also the case for lipid-lowering agents, with the exception of men older than 65 years. Regarding anti-diabetics, only men older than 65 years with SpA were more likely to receive them compared to their RA counterparts (Table IV).

Discussion

Collection and monitoring of data is of primary importance both for epidemiology and for planning of health care policies. An increasing number of studies are nowadays being conducted using "routinely collected health data"(5), also known as "real-world data"(6), derived from health administration databanks, electronic medical records, primary care surveillance systems and disease registries. These real-world data may provide new incentive for efficient and cost-effective epidemiological research, capable of assisting health care administration authorities in stra-

Table II. Medication use in men and women with rheumatoid arthritis and spondylarthropathy.

Disease status		Rheumatoid arthritis n=9.824				Spondylarthropathy n=9.279			
Mean Age (years ± SD)*§		Women (n=7750) 61.50±13.74		Men (n=2074) 60.14±14.84		Women (n=3800) 52.31±13.28		Men (n=5479) 50.76±12.90	
		n	%	n	%	n	%	n	%
Age Subgroups*§	≤45 years	1001	12.92	360	17.36	1172	30.84	1910	34.86
	>45-65 years	3478	44.88	854	41.18	1989	52.34	2829	51.63
	>65 years	3271	42.21	860	41.47	639	16.82	740	13.51
Anti-TNF-α§	yes	5654	72.95	1557	75.07	3764	99.05	5467	99.78
	no	2096	27.05	517	24.93	36	0.95	12	0.22
Other bDMARDs*§	yes	2374	30.63	573	27.63	51	1.34	21	0.38
	no	5376	69.37	1501	72.37	3749	98.66	5458	99.62
bDMARD monotherapy*§		1262	16.28	576	27.77	1445	38.03	3390	61.87
Number of bDMARD switches*§	1	578	7.46	114	5.50	274	7.21	261	4.76
	2	47	0.61	17	0.82	27	0.71	18	0.33
	3	2	0.03	1	0.05	0	0.00	1	0.02
Methotrexate*§	yes	4004	51.66	933	44.99	1363	35.87	1175	21.45
	no	3746	48.34	1141	55.01	2437	64.13	4304	78.55
Leflunomide*§	yes	1414	18.25	300	14.46	297	7.82	186	3.39
	no	6336	81.75	1774	85.54	3503	92.18	5293	96.61
HCQ*§	yes	866	11.17	107	5.16	74	1.95	29	0.53
	no	6884	88.83	1967	94.84	3726	98.05	5450	99.47
Other csDMARDs§	yes	478	6.17	133	6.41	519	13.66	458	8.36
	no	7272	93.83	1941	93.59	3281	86.34	5021	91.64
Corticosteroids*§	yes	4494	57.99	988	47.64	1236	32.53	957	17.47
	no	3256	42.01	1086	52.36	2564	67.47	4522	82.53
Hypertension Drugs§	yes	3277	42.28	842	40.60	1343	35.34	1732	31.61
	no	4473	57.72	1232	59.40	2457	64.66	3747	68.39
Diabetes Mellitus drugs*	yes	885	11.42	292	14.08	366	9.63	571	10.42
	no	6865	88.58	1782	85.92	3434	90.37	4908	89.58
Dyslipidaemia drugs§	yes	2057	26.54	518	24.98	920	24.21	1165	21.26
	no	5693	73.46	1556	75.02	2880	75.79	4314	78.74

*Denotes significant differences between men and women in rheumatoid arthritis.
§Denotes significant differences between men and women in spondylarthritis

Table III. Prevalence of concomitantly prescribed anti-hypertensives, anti-diabetics, or lipid lowering agents in patients on biologics and adjusted probabilities for drug prescription in spondyloarthropathy versus rheumatoid arthritis (used as the reference group) by logistic regression applied for multivariate analysis.

	Rheumatoid arthritis (n=9824)		Spondyloarthropathy (n=9279)				
Drug use	n	%	n	%	OR	95% CI	*p*-value
Anti-hypertensives	4119	41.93	3075	33.14	**1.41***	**1.29-1.54**	**<0.001**
Anti-diabetics	1177	11.98	937	10.10	1.01§	0.90-1.13	0.897
Lipid lowering agents	2575	26.21	2085	22.47	**1.24§**	**1.14-1.36**	**<0.001**

*Adjusted for age, gender, use of methotrexate, corticosteroids, leflunomide, hydroxychloroquine, antidiabetics and lipid lowering agents.
§Adjusted for age, gender, use of methotrexate, corticosteroids, leflunomide, hydroxychloroquine, antihypertensives and lipid lowering agents.
§ Adjusted for age, gender, use of methotrexate, corticosteroids, leflunomide, hydroxychloroquine, antihypertensives and antidiabetics.
In bold, statistical significant differences ($p<0.05$) are shown.

tegic planning, decision-making and resources' allocation.

Inflammatory rheumatic disease registries have contributed significant knowledge, however, an enormous amount of relevant data is spread among health insurers, primary care providers, hospitals and researchers, preventing their effective use. To the best of our knowledge this is the first and largest study using such real-world, big data in the field of Rheumatology. Since Greece is among the first countries that developed an extensive electronic prescription system, we aimed to identify all patients

Table IV. Subgroup analysis by gender and age group comparing the probability to be using antihypertensive medications, antidiabetic medications and lipid lowering agents between rheumatoid arthritis and spondylarthropathy patients.

Disease status	Rheumatoid arthritis (n=9824)		Spondylarthropathy (n=9279)			
	n	%	n	%	OR	95% CI
Antihypertensive use						
Men						
age ≤45 years	29	0.30	98	1.06	0.81*	0.50-1.32
45 < age ≤65 years	291	2.96	1093	11.78	***1.30****	***0.08-1.58***
age >65 years	522	5.31	541	5.83	***1.69****	***1.32-2.18***
Women						
age ≤45 years	63	0.64	58	0.63	1.18*	0.78-1.80
45 <age ≤65 years	1192	12.13	791	8.52	***1.37****	***1.20-1.57***
age >65 years	2022	20.58	494	5.32	***1.77****	***1.42-2.20***
Antidiabetic use						
Men						
age ≤45 years	10	0.10	32	0.34	0.65§	0.30-1.41
45 <age ≤65 years	107	1.09	339	3.65	0.89§	0.68-1.16
age >65 years	175	1.78	200	2.16	***1.32§***	***1.01-1.71***
Women						
age ≤45years	22	0.22	16	0.17	0.56§	0.27-1.16
45 <age ≤65 years	316	3.22	201	2.17	0.92§	0.75-1.13
age >65 years	547	5.57	149	1.61	1.13§	0.91-1.40
Use of lipid lowering agents						
Men						
age ≤45 years	21	0.21	96	1.03	1.04§	0.60-1.80
45 <age ≤65 years	193	1.96	757	8.16	***1.33§***	***1.08-1.64***
age >65 years	304	3.09	312	3.36	1.02§	0.81-1.30
Women						
age ≤45 years	33	0.34	35	0.38	***1.08§***	***0.63-1.84***
45 <age ≤65 years	830	8.45	545	5.87	***1.19§***	***1.03-1.38***
age >65 years	1194	12.15	340	3.66	***1.60§***	***1.32-1.92***

*Adjusted for use of methotrexate, corticosteroids, leflunomide, hydroxychloroquine, antidiabetics and lipid lowering agents. §Adjusted for use of methotrexate, corticosteroids, leflunomide, hydroxychloroquine, antihypertensives and lipid lowering agents. §Adjusted for use of methotrexate, corticosteroids, leflunomide, hydroxychloroquine, antihypertensives and antidiabetics.

with prescribed biological treatment for RA and SpA in our country. The Health Care system in Greece fully covers financially the whole population for b-DMARD use, but also, virtually none can afford the b-DMARD high cost outside the system. As it has been previously shown incorporation of data on the use of prescription medications allowed for enhanced accuracy in the detection of RA prevalence in a large-scale population study performed among non-institutionalised elderly adults in the US (7).

At the time of this study the obligatory electronic prescription platform of the National Organization for Provision of Health Care Services addressed the needs of 10.223.000 citizens, practically achieving nearly complete coverage of the population (96.0%). The opportunity to collect data from almost the entire Greek population, which is essentially of a homogeneous Caucasian origin, constitutes the main strength of our study. Moreover, the use of pharmacy-dispensed prescriptions over those issued by physicians, further enhanced the accuracy of our findings. In addition, limiting our data to only fully reimbursed prescriptions, such as for biologic expensive drugs, permitted a more precise identification of the total number of patients under treatment. Therefore, since biologic therapy outside the electronic prescription platform does not exist, the exact prevalence of patients with chronic inflammatory rheumatic diseases under biological therapy in Greece is 0.19%, being equal between RA and SpA. The almost equal absolute number of bDMARD treated RA and SpA patients essentially confirms the findings of a smaller Norwegian study, which included about 1.400.000 citizens. Among them there were 1,035 and 1,039 first-time prescriptions of b-DMARDs for RA and SpA patients, respectively, that were recorded from 2002 through 2011 (total prevalence of 0.15%) (3).

Limitations of our study include the possibility of misclassification of some RA patients who were receiving b-DMARDs to SpA or vice-versa, the lack of separate statistical analysis for the different forms of SpA (AS, PsA, enteropathic etc.) and the estimation of co-morbidities based on drug usage and not on recorded diagnoses.

Regarding the exact penetration of b-DMARDs in Greece, there are also some limitations in our data presented herein. Based on the number of patients registered in the Greek EOPYY database during the period of the present study with at least one prescribed pharmacological treatment for RA (n=35,878), the estimated penetration rate of b-DMARDs is 27% for RA. However, this is an overestimate because a good proportion of patients with RA treated with cs-DMARDs avoid the electronic prescription that carries a 5 Euro prescription charge (instituted by the end of 2014), when it concerns cheap medications, such as corticosteroids, methotrexate, non-steroidal anti-inflammatory drugs or hydroxychloroquine, which cost less than 5 Euro per month. Also, other patients prefer to skip the time-consuming procedure of having cheap medications electronically prescribed. Again, based on the total number of patients registered in the EOPYY database during the period of the present study with at least one prescribed pharmacological treatment for SpA (n=25,585), the estimated penetration rate of bDMARDs is 36% for SpA. However, the total number of patients with SpA in our country could be substantially higher because, in addition to the reasons mentioned above (*i.e.* many patients would prefer to pay themselves for cheap NSAIDS), misclassification of patients with less severe forms of SpA to other ICD-10 codes, for instance "inflammatory polyarthritis" (M13), by prescribing physicians cannot be ruled out. Therefore,

the percentage of bDMARD treated patients among the whole population of RA and SpA in Greece is certainly lower than 27% and 36%, respectively. Importantly, patient registries from USA and Europe provide almost always higher rates of biologic agent usage for inflammatory rheumatic disease, estimated to be 47.4% for SpA (8) and 27-28.8% for RA (8, 9), which, in our view, are overestimates.

Analysis of demographic data revealed a 10-year age difference between SpA and RA patients. Reports from registries have also shown a similar pattern, with b-DMARD-treated RA patients (8-12) having a mean age ranging between 53–70 years, compared to 43-45 years (8, 13) in SpA patients. Women comprised 79% of RA and 41% of SpA patients in our study, compared to 73-88% (9-12) and 25–35% (8, 13), respectively in the literature.

Biologic agents were given as monotherapy to 19% of RA patients and 52% of SpA, compared to 33% of RA (9) patients and 37% of SpA (13) in large registries from USA and Sweden, respectively. In our biologic treated RA patients the rate of methotrexate usage (50.25%) was lower, while that of concomitant glucocorticoid usage (55.8%) was higher, compared to the Danish Registry of Biologics (76.4% methotrexate, 45.4% glucocorticoids) (10). Similarly, concomitant administration of methotrexate among SpA patients was considerably lower in our study (27.35%), compared to other cohorts (42%) (13). Notably, within either the RA or the SpA patient subgroup, women received more often than men methotrexate, leflunomide, hydroxychloroquine and corticosteroids, a difference that has not been previously reported. This finding possibly reflects an earlier observation that men with RA (14), ankylosing spondylitis (15) and psoriatic arthritis (16, 17) are more likely to respond to and achieve remission under treatment with TNF-α inhibitors than their female counterparts. Therefore, the need for combination therapy in the case of male patients under biologics could be less pronounced.

Another novel finding of our study was the higher probability of SpA patients to use anti-hypertensives or lipid-lowering agents, in comparison to RA patients, after correcting for potential confounders. Although an elevated cardiovascular risk and a higher probability for traditional cardiovascular disease risk factors, such as hypertension, has long been established in RA patients (18), growing evidence suggests that SpA patients are also at increased risk for cardiovascular morbidity, mortality and presence of cardiovascular disease risk factors, compared to controls (19-24).

Only few cohort studies have directly compared cardiovascular risk between SpA and RA patients. Jamnitski *et al*. found a similar prevalence of cardiovascular disease between psoriatic arthritis (PsA) and RA (25), whereas Mok *et al*., showed that PsA patients had a 2.44 odds ratio of having metabolic syndrome compared to RA and ankylosing spondylitis patients (26). In a 10-year prospective study from Spain including 2,234 patients seen at rheumatology outpatient clinics, classic risk factors for cardiovascular disease and features of metabolic syndrome were more common among PsA patients in comparison to RA and AS patients. However, the prevalence of cardiovascular disease was higher in RA (10.5%), followed by AS (7.6%), PsA (7.2%), and controls (6.4%). Multivariate analysis adjusted for cardiovascular risk factors and disease duration revealed a stronger trend for cardiovascular disease in AS (OR=1.77; 95% CI: 0.96–3.27; p=0.07), compared to RA (OR=1.58; 95% CI: 0.90–2.76; p=0.10) (27). Finally, in another study, the prevalence ratio of ischaemic heart disease, atherosclerosis, peripheral vascular disease, congestive heart failure, cerebrovascular disease, type II diabetes, hyperlipidaemia, and hypertension were higher in SpA and RA patients than in controls, but this difference seemed to be more pronounced for RA than for SpA patients (19).

In conclusion, these real-world, big data analysis based on a country-wide obligatory prescription database covering more than 10 million Greek citizens showed that the number of SpA patients treated with bDMARDS was almost equal to RA patients, despite the significant difference in the prevalence of these diseases (probably reflecting patients' therapeutic needs) and also that SpA patient, despite being younger by 10 years compared to RA patients possess a higher cardiovascular disease classical risk factor burden, evidenced by their increased adjusted prescription rate for hypertension and dyslipidaemia. Longitudinal studies are needed to assess the implications of these novel findings on the differential financial burden of chronic inflammatory rheumatic disease, as well as on morbidity and mortality of these patients.

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