# Results from Polish Spondyloarthritis Initiative registry (PolSPI) – methodology and data from – the first year of observation

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Abstract

**Objectives**: Report on one-year results from the Polish Spondyloarthritis Initiative registry (PolSPI), containing the cross-sectional analysis of clinical and imaging data as well as database methodology.
**Material and methods**: The PolSPI registry includes patients with axial (axSpA) and peripheral (perSpA) spondyloarthritis according to ASAS classification criteria, and/or patients with ankylosing spondylitis according to modified New York criteria, psoriatic arthritis according to CASPAR criteria, arthropathy in inflammatory bowel disease, reactive arthritis, juvenile spondyloarthritis or undifferentiated spondyloarthritis. Epidemiologic data and history of signs, symptoms and treatment of spondyloarthritis are collected and assessment of disease activity is performed. Radiographic images of sacroiliac joint, cervical and lumbar spine, and results of bone densitometry are collected. Every 6 months blood samples for inflammatory markers, and for long-term storage are taken.
**Results**: During a one-year period from September 2015 to August 2016, 63 patients were registered on an electronic database; 44 (69.8%) of patients were classified as axial spondyloarthritis (axSpA) and 19 (30.2%) as peripheral spondyloarthritis (perSpA) according to ASAS criteria. Statistically significant differences between axSpA and perSpA were discovered in the percentage of HLA-B27 antigen occurrence (92.6% and 50%, respectively), BASDAI (2.8% and 4.1%, respectively), DAS 28 (2.66% and 4.03%, respectively), percentage of peripheral arthritis (20% and 88.8%, respectively), enthesitis (26.7% and 70.6%, respectively), dactylitis (6.7% and 88.9%, respectively), as well as extra-articular symptoms: acute anterior uveitis (26.7% and 5.6% , respectively) and psoriasis (6.9% and 55.6%, respectively). Patients with axSpA had significantly higher mean grade of sacroiliac involvement according to New York criteria, higher mSASSS score, and lower T-score in femoral neck in bone densitometry.
**Conclusions**: At the early stage of the disease patients with axSpA compared to those with perSpA, have more advanced structural damage of sacroiliac joints and spine, and lower bone mineral

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density in the femoral neck. In the upcoming years the PolSPI registry will prospectively follow-up patients with SpA, recording response to treatment and carrying out research on interaction of inflammation and bone remodelling.

**Key words:** registry, axial spondyloarthritis, peripheral spondyloarthritis.

## Introduction

The research group of academic centers – the Polish Spondyloarthritis Initiative registry (PolSPI), emerged in 2014 as a group of scientists interested in cooperation in the field of spondyloarthritis. The collaboration agreement involved 5 academic centers: Jagiellonian University Medical College in Krakow, Wroclaw Medical University, Pomeranian Medical University in Szczecin, Poznan University of Medical Sciences and Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Torun. The main purpose of PolSPI group is to provide multi-center, comprehensive cooperation in the research on spondyloarthritis. The collaboration involves research on epidemiology and other fields, including response to treatment. The main research tool is PolSPI registry, a prospective database including clinical, imaging and laboratory data and treatment modalities. Registry was approved by the local medical ethics committee of the Jagiellonian University. In September 2015, after accomplishing formal requirements, i.e. protection of personal data and limited access to records, an electronic database has been launched. This article reports on one-year results of Polish Spondyloarthritis Initiative registry (PolSPI).

## Material and methods

The inclusion criteria for PolSPI registry are as follows: age ≤ 45 years, definite diagnosis of axial (axSpA) and/or peripheral (perSpA) spondyloarthritis according to Assessment of SpondyloArthritis International Society (ASAS) classification criteria [1–3], and/or patients with ankylosing spondylitis (AS) according to modified New York criteria [4], also with psoriatic arthritis according to classification criteria for Psoriatic ARthritis (CASPAR) [5]. The registry also includes patients with confirmed diagnosis of diseases such as: arthropathy in inflammatory bowel disease, reactive arthritis, juvenile spondyloarthritis or undifferentiated spondyloarthritis. The exclusion criteria are: age > 45 years, inability to sign informed consent for participation in a study or to follow protocol visit schedule.

Having obtained information about the aim of the registry, patients are asked to sign an informed consent of participation in the study and processing of personal data. Each patient is allotted an individual number in the electronic database for identification of electronic records and micro-tubes with plasma. During the enrolment visit epidemiological and clinical data, including age, gender, weight, height, history of smoking and alcohol use, comorbidities, family history, detailed history of signs, symptoms and pharmacologic treatment of spondyloarthritis are collected. Physical examination of joints (painful and swollen joint count, evidence of dactylitis and enthesitis), assessment of spinal range of motion using BASMI (Bath Ankylosing Spondylitis Metrology Index), assessment of chest wall extension and occipital-wall distance, as well as assessment of disease activity by BASFI (Bath Ankylosing Spondylitis Functional Index), BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), ASDAS (Ankylosing Spondylitis Disease Activity Score), DAS 28 (Disease Activity Score 28) and HAQ (Health Assessment Questionnaire) questionnaires are performed. X-ray images of sacroiliac joints and cervical and lumbar spine for structural damage assessment by mSASSS (modified Stoke Ankylosing Spondylitis Spinal Score), and results of bone densitometry by dual-energy X-ray absorptiometry (DXA) are collected. During enrolment visit and every 6 months thereafter blood samples for inflammatory markers (erythrocyte sedimentation rate – ESR, C-reactive protein – CRP), and for long-term storage are taken. Subsequent visits are scheduled every 6-months – at each visit clinical and laboratory data, and update of current treatment are recorded. According to registry protocol, imaging studies will be collected every 2 years. In 2017 cardiovascular module will be added to the registry. The data analysis was performed with SAS 9.2 version (SAS Institute Inc. Cary, NC, USA). The continuous data are presented as means (SD) and compared with Student's t-test or as percentages and compared with $\chi^2$ test. A $p$ value of $< 0.05$ was considered statistically significant.

## Results

Over one-year period from September 2015 to August 2016, 63 patients were registered on electronic web database; 44 (69.8%) of patients were classified as having axial spondyloarthritis (axSpA) and 19 (30.2%) as peripheral spondyloarthritis (perSpA) according to ASAS criteria (Table I).

**Table I.** Baseline characteristics of patients in PolSPI registry

| | axSpA | perSpA | *p* value |
|---|---|---|---|
| *n*, (%) | 44 (69.8) | 19 (30.2) | NS |
| Age, mean ±SD years | 42 (11.4) | 38,5 (7.7) | NS |
| Gender, % male | 75.6 | 60 | NS |
| HLA B27 positive, % | 92.6 | 50 | 0.002 |
| Duration of symptoms, mean (±SD) months | 7.9 (7.4) | 5.6 (6) | NS |
| Symptoms, % | | | |
| arthritis | 20 | 88.8 | < 0.0001 |
| enthesitis | 26.7 | 70.6 | 0.003 |
| dactylitis | 6.7 | 88.9 | < 0.0001 |
| uveitis | 26.7 | 5.6 | 0.007 |
| IBD | 2,27 | 0 | NA |
| psoriasis | 6.9 | 55.6 | 0.002 |
| CRP, mean (±SD) mg/l | 10.7 (15.3) | 7.8 (6.2) | NS |
| ESR mm/h (±SD) | 25.6 (17.7) | 30.4 (18.9) | NS |
| BASDAI (0–10 scale), mean | 2.8 | 4.1 | *p* = 0.04 |
| ASDAS-CRP, mean (±SD) | 2.4 (1.2) | 2.7 (0.9) | NS |
| DAS 28, mean | 2.66 | 4.03 | 0.0007 |
| SIJ Rx, scale 0–4, SD | | | |
| Right | 2,2 (1.2) | 0.6 (0.8) | 0.0005 |
| Left | 2.4 (1.1) | 0.5 (0.7) | < 0.0001 |
| mSASSS score (SD) | 8.0 (16.2) | 0.7 (0.9) | 0.007 |
| T-score (SD) femoral neck | -0,78 (1,31) | 0.58 (1.16) | 0.02 |
| T-score (SD) L2–L4 | −1.05 (1.37) | −0.07 (0.72) | NS |

*axSpA – axial spondyloarthritis; perSpA – peripheral spondyloarthritis; IBD – inflammatory bowel disease; SIJ Rx – grade of sacroiliac involvement according to New York criteria*

Both groups – with axial and peripheral SpA – were not different with regard to age (years [SD]), 42 (11.4) and 38.5 (7.7), male gender (%), 75.6 and 60% and disease duration (years [SD]), 7.9 (7.4) and 5.6 (6) respectively. No significant differences were found in ESR (mm/h [SD]), 25.6 (17.7) and 30.4 (18.9) and CRP serum concentration (mg/l [SD]), 10.7 (15.3) and 7.8 (6.2), respectively. Statistically significant differences between axSpA and perSpA were discovered in the percentage of HLA-B27 antigen occurrence (92.6% and 50%, *p* = 0.002), and diseases activity assessment scores: BASDAI (2.8 and 4.1, *p* = 0.04) and DAS 28 (2.66 and 4.03, *p* = 0.0007), but not ASDAS-CRP (SD), 2.4 (1.2) and 2.7 (0.9) (*p* = 0.25). Statistically significant differences between axSpA and perSpA were discovered in percentage of peripheral arthritis (20% and 88.8%), enthesitis (26.7% and 70.6%), dactylitis (6.7% and 88.9%), as well as extra-articular symptoms: acute anterior uveitis (26.7% and 5.6%) and psoriasis (6.9% and 55.6%). So far, in the observed cohort there is only one case of SpA associated with Crohn's disease, but the patient also fulfilled the modified New York criteria of ankylosing spondylitis and was allocated to group of axial SpA. Patients with axSpA had significantly higher mean grade of sacroiliac involvement according to New York criteria (SD), 2.2 (1.2) vs. 0.6 (0.8) on the right side and 2.4 (1.1) vs. 0.5 (0.7) on the left side, as well as higher mSASSS score (SD) 8.0 (16.2) vs. 0.7 (0.9). These patients had also significantly lower T-score (SD)

in femoral neck in bone densitometry, –0.78 (1.31) and 0.58 (1.16), respectively. We found no differences in bone mineral density in lumbar spine between these two groups. Among patients with axial SpA, 82.2% fulfilled modified New York classification criteria for ankylosing spondylitis [4], while in the peripheral SpA 30% of patients fulfilled CASPAR classification criteria for psoriatic arthritis [5].

## Discussion

During one year of activity of the registry 63 patients were enrolled in 5 academic centers. Agreement of the consortium enables the linking of other academic and non-academic centers, which gives a good perspective of including more patients in following years. The responsibility of recruitment of other centers lies with the Steering Committee with acceptance of Scientific Board of PolSPI. To limit observation to "early" forms of SpA we implemented the entrance criterion of age ≤ 45 years. This decision was made for three reasons. First, inclusion of patients older than 45 years with disease duration frequently over 20 years leads to overestimation of a number of variables in statistical analysis en block, mainly outcomes of structural damage in sacroiliac joints and spine (mSASSS). It can result in an inadequate picture of the whole population, especially taking into account a small number of patients. Having at one's disposal a small amount of cases, it is difficult to obtain a reliable statistical analysis after dividing patients to groups of short or long disease duration.

Moreover, the exact time-point that divides patients into short or long disease duration subgroups is not obvious. In the literature there are no data about the time point that divides early and late SpA, and for this reason the distinction between early and late SpA was definitely given up a couple years ago. It has instead been agreed to divide patients into low and high disease activity subgroups of SpA, which influences the extent and rate of structural damage. The second reason, is that the most interesting trend area of current research focus on early stages of SpA, because it is speculated that in this stage pathophysiologic changes impact the phenotype of disease (axial or peripheral), as well as response to treatment including inhibition of structural damage progression.

The third reason to exclude patients over 45 years is that it is difficult to follow exact time frames of various pharmacological treatment from the past, including NSAIDs and DMARDs. The most reliable data concerning pharmacological treatment covers the last 10 years, also due to better access to source data from primary care and other specialists. Consequently, in the interest of data reliability and a greater likelihood of providing in-

teresting scientific research, the upper limit of 45 years at the time of enrolment to the registry was implemented. In principle, our registry stores detailed clinical and imaging data (X-rays of sacroiliac joints and spine, and bone densitometry), as well as findings of laboratory tests. Mirroring existing registries in other countries, the possibility of blood samples banking was approved by the Bioethics Committee, and then commenced. This will allow future assessment of different biomarkers and molecules potentially involved in a network of cytokines and proteins of bone remodelling, presumably essential in the pathophysiology and pathogenesis of SpA.

In the recent years, a number of registries of rheumatic diseases, including spondyloarthritis have been initiated all over the world and our registry is largely based on available data of these registries. One of the most important benefits of such databases is the possibility of providing long-term, prospective clinical observation in a "real-life" population, encompassing large and heterogeneous group of patients. Registries, along with clinical trials, are currently main source of data concerning effectiveness and adverse effects of biological treatment, and other data including epidemiological. The registry may also be a tool for both cross-sectional and prospective scientific research, in which patients from the database serve as a study population or control group. The most important European registries of SpA include: the German database GESPIC (German Spondyloarthritis Inception Cohort) [6] – containing mainly patients with axial disease, the French database DESIR (Devenir des spondyloarthropaties recentes) [7] – enrolling patients under 50 years of age with inflammatory back pain, and the Spanish database REGISPONSER (Registro espanol de espondiloartritis de la sociedad espanola de reumatologia) [8]. The PolSPI is the first registry of spondyloarthritis in Poland, aimed primarily at conducting a prospective, comprehensive epidemiological observation, reporting modalities and response to treatment, and providing cutting-edge research in early stages of spondyloarthritis, focusing particularly the interaction between inflammation and bone remodelling. The PolSPI database focus on patients with axial (axSpA) and/or peripheral (perSpA) spondyloarthritis according to Assessment of SpondyloArthritis International Society (ASAS) classification criteria [1–3], and/or patients with ankylosing spondylitis, psoriatic arthritis, arthropathy in inflammatory bowel disease, reactive arthritis, juvenile spondyloarthritis or undifferentiated spondyloarthritis.

This article reported on the very first data after one year of activity, encompassing epidemiological data and clinical profile of respective forms of SpA. In the whole group of patients in our registry, 69.8% of patients were allocated to axial SpA (in this group 82.2% fulfilled modi-

fied New York criteria of AS [4], and 17.8% had non-radiographic axial SpA according to ASAS criteria [1, 2]), while 30.2% of patients were allocated to peripheral SpA (30% in this group fulfilled CASPAR criteria of psoriatic arthritis). These proportions are consistent with our expectations, because the majority of patients with spondyloarthritis had axial symptoms resulting from inflammation in sacroiliac joints and spine. Relatively small number of patients had dominant peripheral symptoms (arthritis, enthesitis and/or dactylitis), which conforms in line with data from other registries and scientific databases. As mentioned, most patients with axial SpA had advanced structural damage in the sacroiliac joint allowing to diagnose ankylosing spondylitis according to modified New York criteria. In the current analysis the mean duration of symptoms typical for SpA was 7.9 years for axial disease and 5.6 years for peripheral disease. Therefore, we can assume that our database has included so far relatively early cases of SpA, allowing research according to our assumption. Actually, a number of patients from PolSPI registry have been participating in a project financed by the National Science Centre of Poland, exploring the role of peripheral blood mononuclear cells in bone remodelling in patients with axial and peripheral spondyloarthritis. Among the differences between axial and peripheral SpA, the higher BASDAI score in patients with peripheral SpA is surprising. The BASDAI score was evolved and validated to assess the activity of ankylosing spondylitis, although as well as questions concerning the severity of axial symptoms, it includes questions about the symptoms resulting from involvement of peripheral joints (question 3) and soft tissues as enthesopathy (question 4). Da Costa et al. [9] reported higher BASDAI score in patients with concomitantly active axial and peripheral symptoms (overlapping form of SpA), comparing to purely axial or peripheral disease. Taking into account higher DAS28 score in perSpA, we suppose that the reason for the higher BASDAI score in this group results just from more evident peripheral involvement, with pain and swelling of joints, and enthesopathy. This could also explain the lack of difference in ASDAS score, which is supposed to be more objective than BASDAI, even though we would have expected higher ASDAS score in axial group, because it was also dedicated to ankylosing spondylitis patients. In all, above results necessitate gathering of more data for analysis. By contrast, according to our expectations in patients with axSpA we discovered more advanced structural damage in sacroiliac joints, higher mSASSS score, and lower T-scores in femoral neck.

These results confirm a suitable clinical allocation of patients based on ASAS classification criteria in our registry, and suggest different course of these two forms of SpA disease. The aim of PolSPI registry in subsequent years is to increase our knowledge of the different pathophysiology and natural course of axial and peripheral SpA on their early stages, with particular consideration of bone remodelling pathways [10–12]. Moreover, the PolSPI registry will allow an explanation of the relationship between disease activity and structural damage. On the grounds of current cross-sectional data, it is difficult to arbitrarily deduce if a given 45-year-old patient with advanced structural damage, had rather late-onset but "fast progressing" disease, with risk factors of early damage i.e. elevated serum CRP or baseline syndesmophytes, or rather had an early-onset, but "slow progressing" disease with over 20-year duration. As mentioned above, in order to provide a precise explanation of this problem, we limited study population to patients ≤ 45 years old at the moment of enrolment. The data from one-year observation must be considered with regard to its limitation. First, this is not a consecutive patient-based but rather random patient-based research, and as such the data might not be considered as epidemiologic. Second, at present the number of patients is certainly not sufficient for in-depth analysis but we assume, that having at our disposal a significantly larger cohort of patients, we will be able to answer several questions in SpA research, including that about interaction between inflammation and bone remodelling as well as response to different treatment modalities.

## Conclusions

As expected, patients with axial spondyloarthritis at early stage of the disease had more advanced structural damage of sacroiliac joints and spinen in comparison to those with perSpA. Patients with axSpA were more likely to have an HLA-B27 (92.6% vs. 50% perSpA) and more often had uveitis. Similarly, a lower bone mineral density in the femoral neck was noted in axSpA group.

Inflammatory bowel disease was observed only in the axSpA group, and, as expected enthesopathy, dactylitis and skin psoriasis dominated in the peripheral spondyloarthritis group. Interestingly, a higher rate of BASDAI was demonstrated in the perSpA but there was no statistically significant differences between the groups in the activity of inflammatory indicators such CRP and ESR. For upcoming years the PolSPI registry will prospectively follow-up patients with SpA, recording response to treatment and carrying out research on interaction of inflammation and bone remodelling.

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