The Spondyloarthritis Research Consortium of Canada Registry for Spondyloarthritis

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ABSTRACT. The Spondyloarthritis Research Consortium of Cananda (SPARCC) is a transdiscliplinary research network of investigators interested in spondyloarthritis. The group has been supported by a new research initiative by The Arthritis Society. SPARCC aims to address the genetic basis of susceptibility of the disease and develop and validate clinical and imaging outcomes to assess disease activity and structural damage over time, the response to therapy, and the clinical burden of illness in terms of quality of life and disability. The first step was to develop a database that would allow ascertainment of phenotype for genetic studies, as well as accurate and detailed longitudinal information for disease expression and outcome studies. This article describes the SPARCC database and outlines difficulties and possible solutions for maintaining such a database. (J Rheumatol First Release April 15 2011; doi:10.3899/jrheum.101102)

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Spondyloarthritis (SpA) encompasses a group of disorders of which the hallmark is chronic inflammation in the sacroiliac joints and the spine, accompanied frequently by peripheral arthritis. The prevalence of SpA approaches that of rheumatoid arthritis (RA), and like RA, SpA can lead to disability and significant economic burden. SpA has been comparatively underrepresented in terms of research investment in Canada, and indeed in other parts of the world. The SpondyloArthritis Research Consortium of Canada (SPARCC) was established in 2003 to address this deficiency. The founding members of SPARCC initially concentrated on validating clinical and imaging measurement tools used to assess peripheral joints and axial disease in SpA, and on development of treatment recommendations for the use of anti-tumor necrosis factor (anti-TNF) therapies[1,2,3,4,5]. Then, through a pilot project grant from the Canadian Arthritis Network, the investigators started to work on some key issues related to SpA. Members of SPARCC recognized that the pathogenesis of SpA was not known, necessitating innovative new approaches to resolving the genetic, molecular, and environmental factors that may interact to initiate and perpetuate joint inflammation. It was evident that traditional approaches to early detection and staging had been inadequate, necessitating clinical research into the development of more sensitive and specific measures of disease severity and progression, as prognostic factors were largely unknown. Moreover, significant challenges remain in defining the burden of illness of SpA.

To address these issues a collaborative transdisciplinary initiative was forged to link SPARCC investigators across the country into an effective research network to apply state-of-the-art methodologies of basic and clinical research to address the important gaps in existing knowledge in SpA. This initiative received the support of the first National Research Initiative grant from The Arthritis Society. The 2 themes in this initiative were (1) The biologic basis of SpA: aimed at addressing the genetic basis of susceptibility of the disease and of the expressed gene profile, the serological assessment of disease activity, severity and prognosis by cytokine and biomarker measurements; and (2) Clinical outcomes in SpA: aimed at developing and validating clinical and imaging outcomes to assess disease activity and structural damage over time, the response to therapy, and the clinical burden of illness in terms of quality of life and disability.

Development of the SPARCC database

The first step to address these issues has been to develop a common database to facilitate ascertainment of phenotypes. The database was developed on a Web-based Oracle platform allowing the collection of both physician- and patient-derived information, as well as laboratory and imaging information. Thus a complete history, including both disease-related and comorbid conditions, family history of SpA-related diseases, extraarticular features, and detailed medication information are recorded at each visit. A complete examination including a general physical examination and detailed musculoskeletal, skin, and nail examinations is recorded. Patient information is recorded in the database at 12-month intervals.

A homunculus allows the recording of individual joints with tenderness, swelling, or both, with the total numbers of actively inflamed joints being calculated immediately on the Web. Similarly, clinically damaged joints are marked depending on the presence of deformity, limitation of range of movement not due to effusion, flail or fused joints, and previous surgery. Enthesitis sites are scored according to the SPARCC enthesitis score[5]. Dactylitis is scored according to the Leeds Dactylitis Index[6]. Spinal assessment is performed according to the INSPIRE and Edmonton AS mobility index methods (EDASMI)[7,8,9]. Cervical rotation, occiput and tragus to wall distance, chest expansion at the xiphisternum, lateral spinal bending using Domjan and INSPIRE measures, Schober test, intermalleolar distance, and internal hip rotation are measured. If psoriasis is present, its type is recorded and its extent is measured by the body surface area and the Psoriasis Area Severity Index (PASI) score. Nail changes, if present, are recorded according to the modified Nail Psoriasis Area Severity Index (NAPSI)[10].

Patients complete several questionnaires directly on the Web in conjunction with their clinic visit. These include the Health Assessment Questionnaire (HAQ)[11], the Medical Outcome Study Short-Form 36 (SF-36)[12], Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[13], Bath Ankylosing Spondylitis Functional Index (BASFI)[14], Ankylosing Spondylitis Quality of Life questionnaire (ASQoL)[15], Dermatology Life Quality Index (DLQI)[16], the Fatigue Severity Scale (FSS)[17], the FACIT-fatigue[18], and a utility measure, the EQ5D[19].

The SPARCC database

Recruitment was initiated at the 3 sites of the principal investigators in the SPARCC grant submission that contributed patients, but the number of active sites has increased. Now there are a total of 9 centers actively contributing patients into the SPARCC database. Table 1 illustrates the distribution of patients entered into the SPARCC database since its inception in 2006. As designed, the database includes patients with a variety of SpA conditions, including ankylosing spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis (ReA), and undifferentiated spondyloarthritis (USpA).

There are 2028 patients registered, of whom the majority (1078, 54.6%) have AS, 803 (39.6%) have PsA, 24 (1.2%) have ReA, and 93 (4.6%) have USpA. There are 6053 visits recorded for these 2028 patients.

The patients entered into the SPARCC dataset are very carefully phenotyped according to clinical features. We aim at standardization of physical assessments through a process of group training of nurse coordinators attending annual meetings of the SPARCC consortium. The diagnosis of AS is based on the New York criteria[20]. The Anklyosing Spondylitis Assessment Group (ASAS) axial spondyloarthritis (axSpA) definition is used if the sacroiliac joint radiographs are not diagnostic[21]. For ReA we use a documented antecedent gastrointestinal or genitourinary infection, but this can be clinically defined and does not necessitate identification of the pathogen. USpA is based on ASAS criteria[22]. For PsA we use the CASPAR criteria[23]. This information is crucial for genetic studies, but is also needed

Table 1. Distribution of patients entered onto the SPARCC database by site and disease.

Site	Disease				
	AS	PsA	ReA	USpA	Total
Toronto	437	608	21	88	1156
St. John's	65	120	0	0	185
Edmonton	498	0	0	0	498
Montreal	34	54	1	5	94
Winnipeg	39	0	0	0	39
Saskatoon	12	6	2	0	20
London	16	13	0	0	29
Newmarket	7	0	0	0	7
Total	1108	803	24	93	2028

AS: ankylosing spondylitis; PsA: psoriatic arthritis; ReA: reactive arthritis; USpA: undifferentiated spondyloarthritis.

to identify predictors of disease expression and disease progression. This dataset is thus important to achieve the objectives set out by SPARCC.

Clinical and laboratory characteristics of 2028 patients registered in the SPARCC database. Table 2 contains the demographic characteristics of the SPARCC patients according to their diagnoses. Most patients are Caucasian, married, and have at least college education. There is a male predominance, which is more apparent among patients with AS than the other SpA groups. Patients with PsA are older at diagnosis than the rest of the SpA groups. Family history of psoriasis is more common among patients with PsA, whereas family history of AS and inflammatory bowel disease is more common among patients with AS.

The clinical features observed in the SPARCC patients at first visit are shown in Table 3. Patients with PsA have a higher body mass index than the remaining patients, and are more likely to have arthritis and more severe arthritis, as demonstrated by higher counts of actively inflamed and damaged joints. By definition patients with PsA are more likely to have psoriasis and nail lesions and higher PASI scores. On the other hand, patients with AS are more likely to have uveitis and enthesitis and have more restricted spinal movement, as demonstrated by their reduced cervical rotation, greater occiput-to-wall distance, and lower scores on the Schober test.

Patient-reported outcomes are presented in Table 4. There does not appear to be a great difference in the scores for patients in the different SpA categories in terms of the various patient-reported outcomes. Of note, although the BASDAI scores are somewhat higher among patients with AS, the percentage with a score of 4 or greater is similar among all SpA groups.

With regard to comorbid conditions, patients with PsA are more likely to have cardiac disease and diabetes than the remaining SpA groups (Table 4).

The majority of the patients with AS are HLA-B*27-positive (Table 4), otherwise there are no important differences in the acute-phase reactants and hemoglobin among the SpA groups.

Addressing the objectives of SPARCC

Since 2006, concurrent with the development of the database, several studies were undertaken by SPARCC to address its objectives.

Theme 1: The biologic basis of SpA. SPARCC investigators have studied several candidate genes in the susceptibility of AS and PsA. Interleukin 1 gene cluster was found to be associated with the susceptibility to AS[24]. A metaanalysis confirmed this association[25]. Interleukin 23 receptor gene was also found to be associated with AS, as well as PsA[26,27]. A specific haplotype of ARTS-1, a non-MHC gene encoding an aminopeptidase, was strongly associated with AS in all 3 Canadian cohorts tested[28]. This was noted despite differences in the genetic structure of these populations[29]. STAT4 and MSX-2 variants were also found to be associated with susceptibility to AS[30,31]. IRF5 was found to be associated with PsA[32]. Biomarkers for disease have been investigated in AS and PsA[24,33]. Soluble biomarkers for response to anti-TNF agents were demonstrated in PsA[35].

Theme 2: Clinical and imaging outcomes in SpA. Validation of the clinical assessment tools used in SpA was carried out. The SPARCC study confirmed the reliability of the assessment of peripheral joints, dactylitis, and enthesitis[1]. In addition, SPARCC was a major participant in the INSPIRE study that confirmed the reliability of both peripheral and axial measures in AS[8,9]. The SPARCC enthesitis index was developed[5]. Imaging methods were developed and validated[3,4]. In addition, SPARCC investigators analyzed what matters to patients with SpA in terms of participation[36]. SPARCC also developed treatment guidelines for patients with SpA through a process that actively engaged patients and other stakeholders in a progressive national multidisciplinary stakeholder project, and both the process and the recommendations have been adopted by the Canadian Rheumatology Association[37].

Table 2. Demographic features by disease type in 2028 patients with SpA in the SPARCC database assessed at the first clinic visits after January 1, 2006; database as of February 2, 2010.

Characteristic	AS	PsA	ReA	USpA
No. patients	1108	803	24	93
Age at diagnosis, yrs, mean ± SD	30.9 ± 11.6	37.9 ± 13.1	31.6 ± 8.1	30.2 ± 14.8
Female, n (%)	288 (26.1)	353 (44.0)	11 (50.0)	35 (38.5)
Caucasian, n (%)	913 (87.5)	643 (94.1)	22 (100)	78 (86.7)
Married, n (%)	631 (60.2)	555 (69.4)	13 (61.9)	47 (52.8)
≥ College education, n (%)	607 (60.0)	542 (68.6)	17 (94.4)	62 (69.7)
Family history of psoriasis, n (%)	124 (12.0)	217 (27.1)	0 (0)	4 (4.4)
Family history of PsA, n (%)	9 (1.6)	69 (8.6)	0 (0)	1 (1.1)
Family history of AS, n (%)	214 (20.8)	8 (1.0)	1 (5.0)	13 (14.4)
Family history of IBD, n (%)	39 (6.7)	20 (2.5)	1 (5.0)	5 (5.6)

AS: ankylosing spondylitis; PsA: psoriatic arthritis; ReA: reactive arthritis; USpA: undifferentiated spondyloarthritis.

Table 3. Disease characteristics at first visit after january 1, 2006; database as of February 2, 2010.

Characteristic	AS	PsA	ReA	USpA
No. patients	1108	803	24	93
Mean body mass index, mean ± SD (kg/m^2)	28.5 ± 15.2	31.2 ± 21.1	26.6 ± 5.8	26.2 ± 5.7
Patients with uveitis, n (%)	324 (32.6)	13 (1.6)	5 (20.8)	16 (17.2)
Patients with psoriasis, n (%)	117 (12.4)	429 (68.1)	0 (0)	4 (4.4)
PASI score, mean ± SD	0.2 ± 0.5	4.1 ± 6.0	0.4 ± 0.8	0 ± 0
Nail disease, n (%)	19 (5.5)	441 (61.9)	0 (0.0)	2 (6.9)
Patients with tender joints, n (%)	201 (34.7)	427 (56.5)	10 (41.7)	26 (28.6)
No. tender joints, mean ± SD	1.7 ± 4.1	4.5 ± 8.1	2.8 ± 4.7	1.6 ± 3.5
Patients with swollen joints, n (%)	107 (10.4)	303 (40.1)	4 (16.7)	10 (11.0)
No. swollen joints, mean ± SD	0.3 ± 1.4	1.7 ± 4.2	1.2 ± 3.3	0.2 ± 0.6
Damaged joint count, mean ± SD	0.6 ± 1.5	9.7 ± 13.3	0.4 ± 1.0	0.4 ± 1.3
Patients with enthesitis, n (%)	350 (33.3)	171 (23.0)	5 (20.8)	12 (13.6)
No. enthesitis sites, mean ± SD	3.1 ± 2.6	3.7 ± 3.7	2.6 ± 1.3	1.7 ± 1.2
Patients with dactylitis, n (%)	19 (1.9)	97 (13.2)	1 (4.3)	2 (2.2)
Patients with tenosynovitis, n (%)	21 (3.8)	89 (11.9)	2 (8.3)	3 (3.4)
Occiput to wall distance, cm, mean ± SD	4.7 ± 6.6	1.7 ± 4.3	0.5 ± 1.7	0.9 ± 2.8
Chest expansion, cm, mean ± SD	4.4 ± 2.2	6.2 ± 5.4	5.5 ± 2.0	5.9 ± 2.4
Cervical rotation, °, mean ± SD	57.9 ± 26.2	70.6 ± 17.5	73.3 ± 16.6	62.7 ± 24.0
Schober test, cm, mean ± SD	3.4 ± 1.8	4.5 ± 1.5	5.0 ± 1.6	4.6 ± 1.7
Domjan, cm, mean ± SD	13.3 ± 6.6	16.0 ± 4.7	19.6 ± 4.7	16.8 ± 4.7
Internal hip rotation, cm, mean ± SD	35.2 ± 14.4	36.8 ± 13.2	41.8 ± 15.5	39.8 ± 12.3
Intermalleolar distance, cm, mean ± SD	94.6 ± 31.3	102.0 ± 24.8	94.3 ± 38.2	103.1 ± 24.1
BASMI, mean ± SD	3.1 ± 2.5	1.6 ± 1.6	1.3 ± 1.9	2.2 ± 1.8

AS: ankylosing spondylitis; PsA psoriatic arthritis; ReA: reactive arthritis; USpA: undifferentiated spondyloarthritis. BASMI: Bath AS Metrology Index.

Table 4. Patient-reported outcomes, comorbidities, and laboratory features in patients with spondyloarthritis (SpA) in the SPARCC registry.

Characteristic	AS	PsA	ReA	USpA
No. patients	1108	803	24	93
Patient-reported outcomes				
BASDAI, mean ± SD	4.7 ± 2.5	4.1 ± 2.5	4.5 ± 2.5	4.2 ± 2.5
BASDAI ≥ 4, n (%)	607 (59.0)	143 (51.1)	11 (55.0)	44 (52.4)
BASFI, mean ± SD	3.9 ± 2.8	3.2 ± 2.7	3.1 ± 2.8	2.5 ± 2.6
ASQol, mean ± SD	7.8 ± 5.9	6.7 ± 5.7	7.4 ± 5.8	5.7 ± 6.0
Patient global assessment, mean ± SD	4.8 ± 2.9	3.8 ± 2.8	5.0 ± 2.9	4.3 ± 3.0
HAQ, mean ± SD	0.7 ± 0.6	0.7 ± 0.7	0.9 ± 0.9	0.5 ± 0.6
SF-36 physical component, mean ± SD	36.7 ± 11.8	37.4 ± 13.9	36.0 ± 11.7	40.7 ± 12.1
SF-36 mental component, mean ± SD	45.0 ± 12.4	44.7 ± 14.1	43.2 ± 11.6	45.8 ± 11.1
EQ5D, mean ± SD	0.6 ± 0.3	0.7 ± 0.2	0.6 ± 0.3	0.8 ± 0.2
Fatigue severity scale, mean ± SD	5.0 ± 2.7	4.7 ± 2.9	4.8 ± 3.6	4.5 ± 3.0
Presence of comorbidities, n (%)				
Cardiac disease	124 (20.7)	310 (38.8)	3 (12.5)	19 (20.4)
Diabetes	15 (2.5)	86 (10.8)	1 (4.2)	5 (5.4)
Cancer	13 (2.2)	25 (3.3)	0 (0)	2 (2.2)
Trauma	40 (7.1)	80 (10.6)	0 (0)	3 (3.6)
Infection	51 (19.8)	121 (38.8)	9 (69.2)	13 (20.3)
Laboratory features				
Presence of HLA-B*27, n (%)	715 (79.0)	87 (16.1)	15 (68.2)	53 (63.1)
ESR, mm/h, mean ± SD	16.4 ± 17.6	15.3 ± 16.6	16.8 ± 24.2	11.1 ± 11.5
CRP, mg/d, mean ± SD	11.9 ± 17.6	9.6 ± 15.0	16.2 ± 33.2	7.1 ± 8.8
Hemoglobin g/dl, mean ± SD	141.8 ± 15.3	139.7 ± 16.2	137.5 ± 20.8	139.4 ± 13.8

AS: ankylosing spondylitis; PsA psoriatic arthritis; ReA: reactive arthritis; USpA: undifferentiated spondyloarthritis; BASDAI: Bath AS Disease Activity Index; BASFI: Bath AS Functional Index; HAQ: Health Assessment Questionnaire; SF-36: Medical Outcomes Study Short-form 36; EQ5D: EuroQol utility measure; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; ASQoL: Ankylosing Spondylitis Quality of Life questionnaire.

Challenges facing SPARCC

Recruitment from multiple sites across a large network has proved to be a challenge in developing multicenter registries in many diseases. The development and implementation of the Web-based data entry system has facilitated recruitment from the various sites. Second, the financial support from The Arthritis Society proved to be crucial, since this provided a financial incentive for individuals working in community practice to be able to participate in this program. Support was provided for patient recruitment, database entry, and for shipping blood samples and uploading radiographs to the database. Currently, 7 additional sites have been added, with 5 already contributing patient data.

SPARCC is now entering the second phase of its research strategy, the first phase being focused on developing the network. Its initial funding through the National Research Initiative from The Arthritis Society reaches its 5-year mandate at the end of this year. The SPARCC database is now operating and SPARCC is recruiting patients from across the country; and the network investigators are now poised to make maximum use of the national database to address the research questions defined in the original research plan. The report to The Arthritis Society for a second cycle of support has been submitted. It is expected that this unique resource will provide new answers to fundamental questions in SpA and ultimately improve outcomes in patients with these chronic disabling diseases.

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