

Incidence of Spondyloarthropathy in Patients with Ulcerative Colitis: A Population-based Study

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ABSTRACT. Objective. Spondyloarthritis (SpA) is an important extraintestinal manifestation of inflammatory bowel disease (IBD). We assessed the cumulative incidence and clinical spectrum of SpA in a population-based cohort of patients with ulcerative colitis (UC).

Methods. The medical records of a population-based cohort of residents of Olmsted County, Minnesota, USA, diagnosed with UC from 1970 through 2004 were reviewed. Patients were followed longitudinally until moving from Olmsted County, death, or June 30, 2011. We used the European Spondylarthropathy Study Group, Assessment of Spondyloarthritis International Society (ASAS) criteria, and modified New York criteria to identify patients with SpA.

Results. The cohort included 365 patients with UC, of whom 41.9% were women. The median age at diagnosis of UC was 38.6 years (range 1.2–91.4). Forty patients developed SpA based on the ASAS criteria. The cumulative incidence of a diagnosis of SpA after an established diagnosis of UC was 4.8% at 10 years (95% CI 2.2%–7.3%), 13.7% at 20 years (95% CI 9.0%–18.1%), and 22.1% at 30 years (95% CI 4.3%–29.1%).

Conclusion. The cumulative incidence of all forms of SpA increased to about 22% by 30 years from UC diagnosis. This value is slightly greater than what we previously described in a population-based cohort of Crohn disease diagnosed in Olmsted County over the same time period. SpA and its features are associated with UC, and heightened awareness on the part of clinicians is needed for diagnosing and managing them. (First Release May 15 2013; *J Rheumatol* 2013;40:1153–7; doi:10.3899/jrheum.121029)

Key Indexing Terms:

SPONDYLOARTHRITIS

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EPIDEMIOLOGY

Inflammatory arthritis is one of the most common extra-intestinal manifestations of inflammatory bowel disease (IBD). Musculoskeletal symptoms in general have been described in 6% to 46% of patients with IBD¹, and arthropathies have been estimated to occur in 4% to 23% of all patients with IBD². The arthropathies associated with IBD may be peripheral or axial arthropathies. The prevalence of peripheral arthropathies has been estimated in 5%–20% of patients, while axial arthropathies have been estimated in 3%–25% of patients with IBD^{1,3,4}. While both major subtypes of IBD have an association between active bowel and joint disease, active peripheral arthropathies are

more commonly associated with active ulcerative colitis (UC)¹.

UC has been associated with a lower prevalence of arthropathy compared to Crohn disease^{1,4,5,6}, although others have reported that there is no major difference in the occurrence of spondyloarthritis (SpA) between UC and Crohn disease⁷. Axial arthropathies, which include sacroiliitis and spondylitis, have been estimated to occur in 5%–22% of patients with Crohn disease and 2%–6% of patients with UC. In a retrospective study from 1998, the frequency of pauciarticular peripheral arthritis, which is most strongly correlated with IBD activity, was reported to be 3.6% in patients with UC and 6% in patients with Crohn disease⁸. In contrast, another retrospective study from 2001 noted the frequency of peripheral arthritis to be 6.1% in patients with UC and 1.7% in Crohn disease⁹.

Estimates of the prevalence of SpA in IBD are available from several cohorts, but none have been reported in US populations, and no population-based incidence estimates are available from any established cohort^{1,3,8,9,10,11,12,13}. Our aim was to assess the prevalence and cumulative incidence of SpA in a population-based cohort of patients with UC from Olmsted County, Minnesota, USA. We compared these findings to SpA prevalence and incidence rates in patients with Crohn disease from the same population base.

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MATERIALS AND METHODS

The Rochester Epidemiology Project (REP) is a unique medical records linkage system developed in the 1950s and supported by the US National Institutes of Health. It exploits the fact that virtually all healthcare for residents of Olmsted County is provided by 2 organizations: Mayo Medical Center, consisting of Mayo Clinic and its 2 affiliated hospitals (Rochester Methodist and Saint Marys), and Olmsted Medical Center, consisting of a smaller multispecialty clinic and its affiliated hospital (Olmsted Community Hospital). In any 4-year period, over 95% of county residents are examined at either of the 2 healthcare systems¹⁴. Diagnoses generated from all outpatient visits, emergency room visits, hospitalizations, nursing home visits, surgical procedures, autopsy examinations, and death certificates are recorded in a central diagnostic index. Thus, it is possible to identify virtually all diagnosed cases of a given disease for which patients sought medical attention.

The resources of the REP were used to identify a population-based cohort of patients diagnosed with UC from 1970 through 2004^{15,16,17}. All cases of UC were diagnosed based on finding the following criteria on 2 occasions separated by at least 6 months: (1) diffusely granular or friable colonic mucosa on endoscopy; and (2) continuous mucosal involvement based on endoscopy or barium studies¹⁶.

Approval for this study was obtained from the institutional review boards of Mayo Clinic and Olmsted Medical Center. Data on musculoskeletal symptoms and disease beginning at birth were recorded; the patients were followed longitudinally until moving from Olmsted County, death, or June 30, 2011.

The European Spondylarthropathy Study Group (ESSG) criteria, modified New York criteria, and Assessment of Spondyloarthritis International Society (ASAS) criteria were retrospectively applied in identifying patients with SpA^{18,19,20,21}. Demographic data including sex, date of birth, and date of UC diagnosis were recorded, as described^{15,16,17}, along with date of arthropathy diagnosis by the treating physician, diagnosis of another primary inflammatory arthritis, family history of arthropathy, and characteristics of SpA. These included presence of inflammatory back pain (based on physician diagnosis with medical records indicating presence of protracted back stiffness, which improved with activity), synovitis, psoriasis, nongonococcal urethritis/cervicitis, alternating buttock pain, enthesitis (Achilles tendonitis or plantar fasciitis), sacroiliitis (based on radiographs or magnetic resonance imaging), which was diagnosed both clinically and radiographically, uveitis, limitation in spine motion, lumbar spine pain, limitation of chest expansion, radiographic evidence of ankylosis, HLA-B27 status, oligoarthritis and specific joints involved, or polyarthritis and specific joints involved; this information was recorded based on physician diagnosis in the medical record. The abstracted data included diagnoses of SpA or its clinical features seen in usual practice by treating physicians, most often a primary care physician or rheumatologist. Diagnoses of uveitis and psoriasis were made by an ophthalmologist or dermatologist, respectively.

Diagnosis of specific forms of SpA included those based on treating physician diagnosis. Following a diagnosis of UC, all patients who had either inflammatory back pain or synovitis were included in our study as having SpA based on the ESSG criteria, because all of these patients already carried a diagnosis of IBD^{18,19,20,22}. Patients were also included as having ankylosing spondylitis (AS) if there was evidence of either limitation in spine motion or lumbar spine pain in the setting of radiographic evidence of ankylosis based on the modified New York criteria for this disease²¹. Finally, all patients who had arthritis, enthesitis, or dactylitis were included in our study as having SpA based on the ASAS criteria because all these patients already carried a diagnosis of UC^{19,20}.

In addition to including treating physician diagnoses of SpA, we searched individual medical records for features of this disease even when a formal diagnosis was not made; those with features of SpA that correlated with either the ESSG or the ASAS criteria were included as having this diagnosis.

The cumulative incidence of SpA after diagnosis of UC was estimated using the Kaplan-Meier method. Ninety-five percent CI for the observed

proportions (percentages) were based on the exact binomial distribution. The prevalences of psoriasis, nongonococcal urethritis/cervicitis, alternating buttock pain, enthesitis, sacroiliitis, uveitis, plantar fasciitis, Achilles tendonitis, oligoarthritis, and polyarthritis were also calculated.

RESULTS

Incidence. A total of 366 patients with UC were identified. One patient denied research authorization and therefore our UC cohort consisted of 365 patients, of whom 41.9% were women, and the median age at diagnosis of UC was 38.6 years (range 1.2–91.4 yrs; Table 1). Prior to UC diagnosis, there were 3 patients from the total cohort who had a diagnosis of SpA based on the ESSG criteria, and therefore the pre-UC prevalence of SpA was 0.8% (95% CI 0.2%–2.4%); no patient carried a diagnosis of AS. Based on the ASAS criteria, 14 patients from the total of 365 patients with UC had been diagnosed with SpA prior to a diagnosis of UC; therefore, the prevalence of SpA based on the ASAS criteria prior to UC was 3.8% (95% CI 2.1%–6.4%). The median interval between diagnosis of SpA and diagnosis of UC was 3.5 years (range 0.3–12.7 yrs). These patients were excluded from the analysis of arthritis incidence subsequent to UC diagnosis.

Following the incident date of UC diagnosis, 10 of 362 patients were diagnosed with SpA according to the ESSG criteria. The cumulative incidence of a diagnosis of SpA after an established diagnosis of UC was 1.9% at 10 years (95% CI 0.4%–3.6%), 2.8% at 20 years (95% CI 0.9%–4.8%), and 4.9% at 30 years (95% CI 1.4%–8.2%; Figure 1).

According to the ASAS criteria, 40 of 351 patients were diagnosed with SpA following a diagnosis of UC. The cumulative incidence of a diagnosis of SpA after an established diagnosis of UC was 4.8% (95% CI 2.2%–7.3%) at 10 years, 13.7% (95% CI 9.0%–18.1%) at 20 years, and 22.1% (95% CI 4.3%–29.1%) at 30 years (Figure 2). The median interval between UC diagnosis and SpA diagnosis was 12.3 years (range 1–31.9 yrs).

Of the 13 patients diagnosed with SpA using the ESSG criteria, 8 (61.5%) were female and 5 (38.5%) were male. Of the total 54 patients diagnosed with SpA using the ASAS criteria, 27 (50%) were female and 27 (50%) were male.

Subtypes of SpA. Based on the modified New York criteria, AS was diagnosed in 1 of 365 patients after UC diagnosis.

Table 1. Baseline characteristics of 365 residents of Olmsted County, Minnesota, USA, diagnosed with ulcerative colitis between 1970 and 2004.

Characteristic	N (%)
Sex	
Male	212 (58.1)
Female	153 (41.9)
Age at diagnosis, yrs	
< 18	26 (7.1)
18–39	190 (52.0)
40–59	102 (28.0)
≥ 60	47 (12.9)

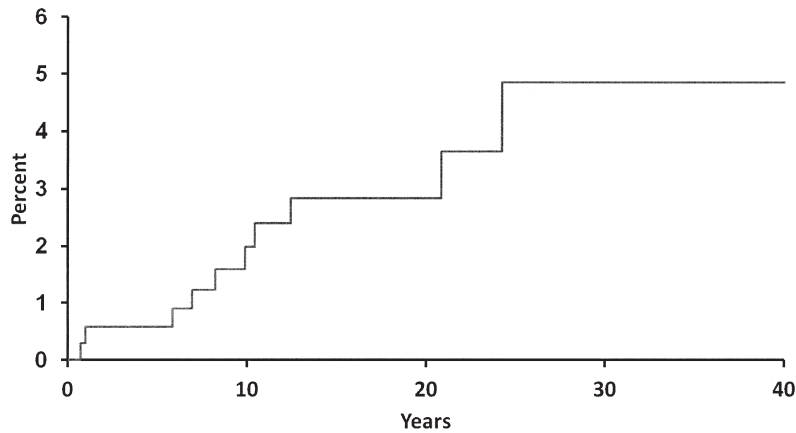


Figure 1. Cumulative incidence (1 minus survival-free) of any spondyloarthropathy (based on European Spondyloarthropathy Study Group criteria) from diagnosis of ulcerative colitis (UC) among 365 patients with UC.

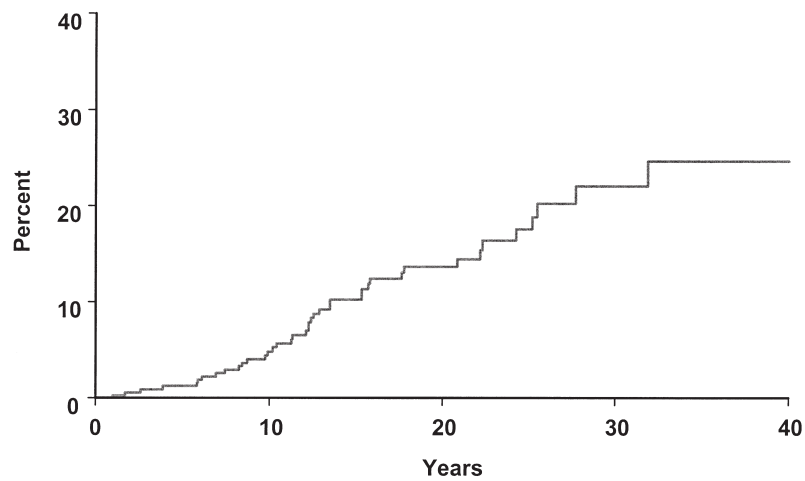


Figure 2. Cumulative incidence (1 minus survival-free) of any spondyloarthritis (based on Assessment of Spondyloarthritis International Society criteria) from diagnosis of ulcerative colitis (UC) among 351 patients with UC.

The 10-year cumulative incidence of AS was 0.3% (95% CI 0–0.9%), while both the 20-year and 30-year cumulative incidences remained the same. No physician diagnoses of reactive, psoriatic, or undifferentiated SpA were found in our cohort.

Clinical characteristics. Clinical features of SpA identified in the cohort of 365 patients are shown in Table 2. In the pre-UC diagnosis period, disease features and frequencies included psoriasis (0.8%), urethritis/cervicitis (0.3%), buttock pain (0.8%), plantar fasciitis (0.5%), uveitis (0.5%), oligoarthritis (0.5%), and polyarthritis (0.3%). In the post-UC diagnosis period, the frequency of SpA disease features in patients with UC were sacroiliitis, 1.7%; oligoarthritis, 3.4%; and polyarthritis, 0.5%. The frequencies of other extraintestinal disease manifestations occurring following the diagnosis of UC were psoriasis, 1.7%; alternating buttock pain, 1.4%; plantar fasciitis, 6.3%; Achilles tendonitis, 1.4%; and uveitis, 2.8%.

DISCUSSION

The major aim of our study was to define the incidence and clinical features of SpA in a population-based cohort of

Table 2. Clinical characteristics of spondyloarthritis in 365 patients with ulcerative colitis (UC) in a population-based cohort from Olmsted County, Minnesota, USA, 1970–2004.

Spondyloarthropathy Feature	Features Present Prior to UC Diagnosis, n (%)	Features Appearing After UC Diagnosis, n (%)
Psoriasis	3 (0.8)	6 (1.7)
Urethritis/cervicitis	1 (0.3)	0 (0)
Buttock pain	3 (0.8)	5 (1.4)
Plantar fasciitis	2 (0.5)	22 (6.3)
Achilles tendonitis	0 (0)	5 (1.4)
Sacroiliitis	0 (0)	6 (1.7)
Uveitis	2 (0.5)	10 (2.8)
Oligoarthritis	2 (0.5)	12 (3.4)
Polyarthritis	1 (0.3)	2 (0.5)

patients with UC. We found that the incidence of SpA increased to about 22% by 30 years from UC diagnosis (Figure 2). The incidence of AS, on the other hand, was much lower, with a cumulative incidence of 0.3% at 30 years from UC diagnosis.

Using the ESSG criteria, the cumulative incidence of SpA in this UC cohort was about half the value detected in a population-based cohort with Crohn disease diagnosed over the same time period. In the Crohn disease cohort, we had found that the cumulative incidence of SpA was about 10% by 30 years after Crohn disease diagnosis²². The cumulative incidence of AS, specifically, was 0.5% at 30 years from Crohn disease diagnosis, and this finding was relatively similar to that of our UC cohort²².

In contrast, based on the ASAS criteria, we found a higher cumulative incidence of SpA in our UC cohort at 30 years compared to that of our Crohn disease cohort²². Specifically, the 30-year cumulative incidence of SpA in UC was 22% compared with the 19% cumulative incidence of SpA found in our Crohn disease cohort. These higher rates may be due in part to the increased sensitivity of the ASAS criteria for diagnosing SpA compared to the ESSG criteria. Also, the frequencies of plantar fasciitis and oligoarthritis were higher in our UC cohort (6.3% and 3.4%, respectively) compared to our Crohn disease cohort (3.9% and 2.9%)²². The ASAS criteria use both of these features to classify SpA, and hence a higher rate of SpA was detected in our UC cohort. This finding is in contrast to the current literature, which suggests a lower rate of SpA in UC compared to Crohn disease^{1,4,5}. Since active joint symptoms are generally reported to be more frequent in active UC compared to active Crohn disease, it is possible that more patients with active UC were presenting for evaluation and were concomitantly diagnosed with arthritis. Also, even though the specificity of the ASAS criteria is higher than that of the ESSG criteria (84.4% vs 65.1%), it may not be specific enough to identify diagnoses of pure SpA^{19,20}.

Similar to what we had found in our Crohn disease cohort, the frequency of features of SpA increased from the pre-UC diagnosis period to the post-UC diagnosis period (Table 2). Plantar fasciitis and psoriasis were equally the most common features prior to UC diagnosis, but plantar fasciitis alone was the most common feature after a diagnosis of UC. The diagnoses of psoriasis, plantar fasciitis, uveitis, oligoarthritis, Achilles tendonitis, and sacroiliitis more than doubled between the pre- and post-UC diagnosis periods. The majority of our cohort had pauci-articular, or Type 1, arthritis (Table 2).

Salvarani, *et al* reported a similar frequency of SpA (based on the ESSG criteria) in UC and Crohn disease, which is in contrast to our findings that the incidence rate of SpA (based on the ESSG criteria) in UC is about half the rate of that in Crohn disease⁹. Also, in contrast to our study, they found a higher frequency of enthesopathy in Crohn disease compared to that in UC. While their study included only 3

years of patient information and primarily data on prevalence of musculoskeletal manifestations, ours is a true incidence study, with more than 30 years of patient followup.

The frequencies of uveitis and arthritis in our UC cohort were lower compared to those of the Swiss Inflammatory Bowel Disease Cohort study, which examined all extra-intestinal manifestations of patients with IBD based on questionnaires completed by treating physicians²³. Uveitis and arthritis were found in 3.8% and 21.3%, respectively, of UC patients in the Swiss study, while we found those frequencies were 3.4% (oligoarthritis), 0.5% (polyarthritis), and 2.8% (uveitis) after UC diagnosis²³. On the other hand, we found a somewhat higher frequency of UC patients with psoriasis (1.7%) compared to the Swiss cohort (0.8%)²³. Some of these differences might be explained by differences in case ascertainment methodology. While we abstracted data on arthritis from individual medical records based on internist, rheumatologist, or gastroenterologist diagnoses, the Swiss cohort relied on data gathered from questionnaires by gastroenterologists only. Similar to our study, psoriasis and uveitis were diagnosed by a dermatologist or ophthalmologist, respectively. Finally, unlike our study, the Swiss study was not a population-based cohort²³.

IBD has been noted to share an immunologic basis with psoriasis, in particular, and an increased frequency of psoriasis than what was observed may have been expected²⁴. The overall incidence of psoriasis in Olmsted County from 1970 to 2000 was relatively low — 62.3 per 100,000 person-years — and this could cause the relatively low frequency of psoriasis associated with UC²⁵.

Our frequencies of polyarthritis, oligoarthritis, sacroiliitis, and AS were lower than those of D’Inca, *et al*². For instance, our frequency of sacroiliitis was 1.7%, while D’Inca, *et al* found a frequency of 2.1%². Their data were obtained through patient questionnaires and rheumatology evaluations, including a total body bone scintigraphy scan. However, our study was based on medical record review of community-based medicine practices, where not all patients are evaluated by rheumatologists and not all undergo extensive testing.

A population-based study from Norway conducted by Palm and colleagues reported the prevalence of AS as 2.6% in UC and overall SpA as 20% in UC¹⁰. In part, their data were obtained by physician and patient questionnaires, while ours were based on individual medical record reviews.

The strength of our study lies in the use of the REP population-based patient database and up to 30 years of followup. Also, data were ascertained based on individual medical records and physician-based diagnoses rather than, for instance, codes in the *International Classification of Diseases*, 9th edition. Because the study was conducted in a usual medical practice, where not all patients were evaluated by a rheumatologist, some diagnoses of SpA features may have been missed. Primary care physicians likely would not

have undertaken rheumatologic classification criteria for SpA, potentially leading to underdiagnosis due in part to difficulty making diagnoses such as inflammatory back pain, which is a required component of the ESSG criteria. However, this was a population-based study of patients not routinely undergoing subspecialty evaluation, so our estimates of SpA incidence and clinical features can be considered the minimum rates in the general population.

AS is the most recognized form of SpA in the general community. Because we could not reliably evaluate reactive or psoriatic SpA in our UC cohort, these diagnoses were not included in our analysis. HLA-B27 determinations were not done routinely in our clinical practice and thus were available for only a few patients in our cohort; this has not been included in our results because of the limited data.

We have for the first time, to our knowledge, defined the cumulative incidence of SpA in a population-based cohort of patients with UC using complete medical record information. This study shows that the cumulative incidence and features of SpA increase from time of UC diagnosis. We have shown that the incidence rate of SpA in UC may be higher than that of Crohn disease. Physicians need to maintain a high level of suspicion for this extraintestinal manifestation. Further studies are necessary to elucidate the reasons for higher rates of SpA and its clinical features in UC compared to Crohn disease.

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