Early Management of Newly Diagnosed Rheumatoid Arthritis by Canadian Rheumatologists: A National, Multicenter, Retrospective Cohort

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ABSTRACT. ***Objective.*** To describe early rheumatologic management for newly diagnosed rheumatoid arthritis (RA) in Canada.

Methods. A retrospective cohort of 339 randomly selected patients with RA diagnosed from 2001-2003 from 18 rheumatology practices was audited between 2005-2007.

Results. The most frequent initial disease-modifying antirheumatic drugs (DMARD) included hydroxychloroquine (55.5%) and methotrexate (40.1%). Initial therapy with multiple DMARD (15.6%) or single DMARD and corticosteroid combinations (30.7%) was infrequent. Formal assessment measures were noted infrequently, including the Health Assessment Questionnaire (34.6%) and Disease Activity Score for 28 joints (8.9%).

Conclusion. Initial pharmacotherapy is consistent with guidelines from the period. The infrequent reporting of multiple DMARD combinations and formal assessment measures has implications for current clinical management and warrants contemporary reassessment. (First Release Sep 1 2011; J Rheumatol 2011;38:2342–5; doi:10.3899/jrheum.110249)

Key Indexing Terms:
RHEUMATOID ARTHRITIS DISEASE-MODIFYING ANTIRHEUMATIC DRUGS
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Rheumatoid arthritis (RA) disease management aims to control disease activity and prevent functional and radiographic decline[1,2,3,4]. This is optimally achieved with early intervention with multiple disease-modifying antirheumatic drugs (DMARD) in combination therapy[5,6,7]. Since 1999, evidence has been mounting to support intensive clinical management strategies using formal measures of disease activity to improve patient outcomes[8]. The status of clinical management for Canadian patients with RA relative to these benchmarks is unknown. In this context, our study investigated the initial pharmacotherapy and clinical management for patients with RA newly diagnosed between 2001 and 2003 by rheumatologists across Canada.

MATERIALS AND METHODS

Study design. Our study is a retrospective cohort of patients with RA newly

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diagnosed by a Canadian rheumatologist between June 2001 and May 2003.

Patients. Eligible patients were 18 years of age or older at RA diagnosis and were free of comorbidities that precluded standard pharmacologic treatment for RA. A confirmed RA diagnosis was a clinical diagnosis recorded in the rheumatologist's chart without one in the differential. Patients with juvenile rheumatoid arthritis, or whose diagnosis subsequently changed from RA, were excluded.

Eighteen study investigators were recruited from a convenience sample of 50 practicing rheumatologists, targeted on the basis of Canadian geographical and population density representation. Each rheumatologist's billing system was prescreened for patients with at least 1 RA billing code and 1 first consultation visit billing between 2001 and 2003, inclusively. Prescreened charts were randomly screened by the first letter of the patients' surnames until either 20 eligible charts were identified per rheumatologist, or all charts were screened. Research ethics approval was obtained for all participating rheumatologists.

The charts were audited at a single timepoint between 2005 and 2007, resulting in 4.0 ± 1.5 years of followup. Charts were reviewed for the onset and termination of antirheumatic therapy and evidence of assessments described in guidelines for the period[2]. Assessments were identified by category: clinical (pain, joint examination, function), laboratory tests, and radiography. Specific assessments ever recorded in the chart were also noted. Patients were classified as having high (versus low) baseline disease activity based on the fulfillment of common eligibility criteria for RA randomized controlled trials[9]. In our study, rheumatoid factor positivity, a marker of poor prognosis[10], replaced duration of morning stiffness greater than 45 minutes as a criterion for low disease activity..

Statistical analysis. The Cochran-Mantel-Haenszel test was used to compare proportions of incident pharmacotherapies and investigator characteristics across applicable classifications using SAS 9.1.3 (SAS Inc., Cary, NC, USA).

Table 1. Baseline characteristics of patients with newly diagnosed rheumatoid arthritis (RA) under rheumatologic care in Canada. Baseline refers to the period under rheumatologic care preceding a confirmed diagnosis of RA.

Variable	n = 339
Age at symptom onset, mean yrs (SD)	50.5 (14.2)
Male, n (%)	83 (24.5)
Swollen joint count*, mean (SD)	10.6 (7.2)
Tender joint count*, mean (SD)	14.1 (9.4)
Erythrocyte sedimentation rate, mm/h, mean (SD)	37.0 (24.7)
C-reactive protein, mg/l, mean (SD)	30.3 (36.4)
Rheumatoid factor positivity, n (%)	237 (69.9)
Duration of symptoms at rheumatology presentation, weeks, median (interquartile range)†	30 (15–62)
Arthritic comorbidity, n (%)	137 (40.4)
Osteoarthritis	91 (26.8)
Fibromyalgia	36 (10.6)
Osteoporosis	47 (13.9)
Other	3 (0.9)
Radiographic evidence of erosions, n (%)	55 (16.2)
Previously seen by another rheumatologist, n (%)	142 (41.9)
Use of NSAID prior to diagnosis, n (%)	288 (85.0)

* Maximum value recorded in the clinical chart up to the date of diagnosis. † Among 191 of 197 patients with complete data, who did not previously consult another rheumatologist. Six patients had missing data for either date of symptom onset or initial consultation with study investigator. NSAID: nonsteroidal antiinflammatory drug.

RESULTS

A total of 339 patient charts were randomly selected from 2444 clinical charts screened at 18 rheumatology practices representing 9 provinces and territories (Table 1). The investigators were compared to all Canadian rheumatologists on the basis of gender, decade of graduation, hospital privileges, academic status, and provincial representation using data available in the *Canadian Medical Directory*[11]. Distributions were similar between study investigators and all listed Canadian rheumatologists.

The majority (90.8%) of patients began DMARD therapy within 3 months after clinical diagnosis of RA (Table 2). Overall, the most frequent initial DMARD used were hydroxychloroquine (HCQ; 55.5%), methotrexate (MTX; 40.1%), and sulfasalazine (11.2%). MTX use was more frequent in cases of high (50.5%) versus low disease activity (35.8%; p = 0.014). Initial DMARD treatment included corticosteroids such as oral prednisone (34.8%) and/or intraarticular methylprednisolone (15.9%). Multiple DMARD was the initial therapy for 15.6% of patients. An additional 30.7% were started on a combination regimen of single DMARD and corticosteroid.

Over time, initial single DMARD therapy decreased (p = 0.02), the single DMARD plus corticosteroid combination increased (p = 0.0053), and the multiple DMARD combination remained unchanged (p = 0.43). Initiation of multiple DMARD combination therapy tended to be more frequent in patients treated prior to (21.1%) versus after confirmed diagnosis (13.1%; p = 0.053) but was not associated with disease activity (p = 0.34). Initial use of HCQ decreased with time (p = 0.04) and MTX use tended to increase (p = 0.08).

The use of formal measurements of pain, functioning, and disease activity was infrequently reported at all points over followup (Table 3). Patient qualitative self-report was the most frequent measure of pain reported (71.5%). Quantitative measures of pain, e.g., visual analog scales, were reported in 43.6% of charts. Homunculi were frequently included in rheumatologic charts (75.2%). Written summaries of joint counts (54.6%) and physician global impression (31.6%) were less frequent. The Disease Activity Score was recorded in 8.9% of charts. The Health Assessment Questionnaire and its modification were ever reported in 34.6% and 16.0% of charts, respectively. Radiographs of the hands were most commonly reported (75.9%), followed by the feet (58.0%) and wrists (56.0%). Generally, formal assessment measures were infrequently reported over followup.

DISCUSSION

The majority of patients with RA diagnosed between 2001 and 2003 in Canada were treated with DMARD within 3 months after diagnosis, as targeted in the 2002 American

Table 2. Incident DMARD treatment by low and high baseline disease activity. Patients with at least 6 swollen and 6 tender joints, an erythrocyte sedimentation rate of at least 28 mm/h, and rheumatoid factor positivity, inclusively, were classified as having high disease activity. All others were classified as having low disease activity.

Incident DMARD Regimen, %	All Patients, n = 339	Low Disease Activity, n = 240	High Disease Activity, n = 99
Single DMARD			
Hydroxychloroquine	27.4	29.6	22.2
Methotrexate	16.8	16.3	18.2
Sulfasalazine	4.7	5.0	4.0
Other*	2.1	2.5	1.0
Single DMARD-corticosteroid† combination			
Hydroxychloroquine	14.7	15.0	14.1
Methotrexate	12.1	10.0	17.2
Sulfasalazine	2.4	3.3	0
Other*	1.5	0.8	3.0
Multiple DMARD combination ± corticosteroids†			
Hydroxychloroquine + methotrexate	8.0	6.7	11.1
Other 2-DMARD combination*	3.8	4.2	3.0
≥ 3-DMARD combination*	3.8	3.3	5.0
No DMARD	2.7	3.3	1.0

* Overall for any incident DMARD regimen, other DMARD used included etanercept (3.0%), leflunomide (2.1%), gold compounds (0.9%), infliximab (0.9%), adalimumab (0.3%), and investigational new drugs, or other treatments not specifically collected in the case review form. Azathioprine, cyclophosphamide, cyclosporine, or penacillamine were not used at DMARD initiation. † Corticosteroids (overall percentage use) included prednisone (34.8%), methylprednisolone (15.9%), triamcinolone (2.4%), and prednisolone (0.6%). Two patients not initiating DMARD therapy were treated with prednisone. DMARD: disease-modifying antirheumatic drug.

Table 3. Clinical management measurements reported on referral*, at baseline**, and over followup†.

Assessment (%)	Referral	Referral or Baseline	Followup
Laboratory tests	81.0	98.8	90.0
Rheumatoid factor	69.8	91.7	33.7
Erythrocyte sedimentation rate	65.3	89.7	78.4
Complete blood count	60.2	86.7	88.2
Antinuclear antibodies	50.3	72.0	15.4
Creatinine	35.9	71.1	66.6
Liver function tests	34.1	69.6	74.6
C-reactive protein	24.2	55.5	41.4
Other	< 50.0	< 50.0	< 50.0
Pain	50.2	92.9	87.0
Joint examination	40.7	91.7	84.4
Function	28.9	83.8	82.6
Radiography	49.8	83.8	56.9

* All documentation included in the referral letter from the referring physician (most commonly a general practitioner). ** Period under rheumatologic care preceding a confirmed diagnosis of rheumatoid arthritis. † The period following baseline until the date of chart review. Twenty-two of 339 patients were lost to followup after diagnostic confirmation.

College of Rheumatology guidelines[2]. The frequent use of HCQ and increased use of MTX in patients presenting high disease activity is consistent with rheumatologist survey data from this period[12,13].

The incident use of multiple DMARD combination therapy was infrequent despite evidence to support this strategy since the late 1990s[5,6,7]. Nonetheless, its use in this cohort was greater than the 9% in a more recent UK cohort[14]. Formal measurements of disease activity, function, and disease progression were also infrequently recorded in this cohort. This limits the implementation of intensive clinical management strategies in routine care[8]. Yet the effect of recent guidelines[3,4] on current care remains undetermined. Pending contemporary confirmation of these findings, strategies may need to be developed to overcome the treatment decision-making[2] obstacles limiting the use of formal assessment measures to guide in clinical practice.

Our research provides an overview of early clinical management of newly diagnosed RA in Canada from 2001 to 2003. Beyond known limitations with chart reviews[15], the date of this cohort may limit the inferences drawn from it. The temporal findings along with advances in laboratory tests (e.g., anticitrullinated protein antibodies) and diagnostic imaging (e.g., ultrasonography, magnetic resonance imaging) set the expectation to find differences in current care. These findings and more recent guidelines highlight the need for periodic quality assurance of RA clinical management.

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