Clinical Outcomes of a Cohort of Early Rheumatoid Arthritis (ERA) Patients: A Newfoundland and Labrador Experience

Kassem Abouchehade, Majed Khraishi, Fraser Clift, Karen White, Gerry Mugford, and Michelle Young. Nexus Clinical Research and the Arthritis Center, St. John's, NL

Abstract:

Objectives: to demonstrate the effectiveness of the early diagnosis and management of ERA utilizing experienced health professionals in rheumatology.

Methods: Data were collected from patients (n=102) who were admitted to the ERA clinic between 2003 and 2006. They were evaluated by an expert nurse and a GP with special training in rheumatology. The assessments were validated by the rheumatologist. The following criteria were predetermined to assess the possibility of ERA when reviewing patients' referrals:

- Joint pain localized in the hands and feet
- Swelling of the hand and feet joints
- Prolonged AM stiffness
- Presence of rheumatoid factor (RF) positivity and elevation of ESR
- Diagnosis of rheumatoid arthritis (RA) by the referring physician

The patients who were diagnosed with RA according to the ACR 1987 criteria and had two or more visits were included. We collected the Health Assessment Questionnaire (HAQ), the swollen joint counts (SJC), duration of symptoms from onset until first visit, ESR and CRP. We collected their treatment and response. Data were collected prospectively and reviewed retrospectively and analyzed for statistical comparisons using Students' *t*-test (*paired* and *unpaired*) and *ANOVA* where applicable.

Results: Thirty-eight patients were identified with ERA and had multiple assessments. The mean 4.5 ±2.9, range 1-12. Females to Males ratio = 4.4. The mean age 53.3 ±15.7 years. Mean waiting period was 88.2 ±66.5 days. The mean duration of patients' symptoms was 12.2 ±11.1 months. Of ERA patients, 82% have positive RF and 71% elevated CRP. ESR was 41.1 ±29.6 mm/hr. Initial SJC was 8.9 ±6.5 at initial presentation. The initial mean HAQ was 0.88 ±0.57. Treatment resulted in significant reduction in ESR and SJC (ESR$_f$ = 22.0 ±17.7 mm/hr; SJC$_f$ = 3.8 ±4.7). Fifteen ERA patients achieved an SJC of zero. Their HAQ$_f$ was 0.45 ±0.49.

Conclusions: The utilization of well-trained health professionals (a nurse and a GP in this case) may be an effective tool in early diagnosis and management of ERA. We also demonstrated that a significant proportion of ERA patients could achieve remission if treated effectively in an early stage.

Introduction:

RA is an autoimmune disorder characterized by a persistent inflammatory synovitis that usually involves peripheral joints causing damage and bone erosions. Proper management and timely therapeutic intervention following the onset of RA symptoms have become a necessity that ensures optimal outcomes and overall improvement of quality of life in RA patients. It was suggested that disease duration plays a significant role in the prediction and the successful response to DMARD therapy (2). Severe and chronic manifestations of RA are associated with increase risk in developing cardiovascular diseases leading to mortality (3, 4). Currently, it is estimated that there are about 300,000 Canadian adults including 5,000 from Newfoundland and Labrador (NL) suffer from RA. Early diagnosis of patients is made difficult due to lack of sufficient rheumatologists across Canada. Waiting periods (up to 12 months) for patients to be seen by a rheumatologist in NL has been very devastating for RA patients. Therefore, the need of innovative approaches and development of early RA clinic in our province was essential to overcome these challenges and improve early detection and appropriate treatments for RA patients in the NL population.

Methodology:

Data were collected from patients (n=102) who were admitted to the ERA clinic between 2003 and 2006. Data from 88 patients was eligible to be included for the current study. Fifty-eight percent (58%) of the eligible patients were seen 2003-2004 and 42% were seen 2005-2006. They were evaluated by an expert nurse with 10 years experience (Ms Karen White) and a GP with special training in rheumatology. The referrals were mainly from GPs from Eastern and Central Newfoundland. The assessments were validated by the rheumatologist. The following criteria were predetermined to assess the possibility of ERA when reviewing patients' referrals:

- Joint pain localized in the hands and feet
- Swelling of the hand and feet joints
- Prolonged AM stiffness
- Presence of rheumatoid factor (RF) positivity and elevation of ESR
- Diagnosis of RA by the referring physician

The patients who were diagnosed with RA according to the ACR 1987 criteria (1) and had two or more visits were included. Two cohorts of patients satisfied the aforementioned criteria and were used for data analysis. One cohort of 38 patients were diagnosed with ERA and the other consisted of patients (n=50) who were determined to have no early RA (Non-ERA) but with at least one of the following diagnoses: inflammatory arthritis, osteoarthritis, psoriatic arthritis, spondylitis and/or sero(-ve) arthropathy, and fibromyalgia. We collected the Health Assessment Questionnaire (HAQ), the swollen joint counts (SJC), Lag-time or duration of symptoms from onset until first visit and DMARD treatment, ESR and CRP. We collected their treatment and response. Data were collected prospectively and reviewed retrospectively and analyzed for statistical comparisons using *Students' t*-test (*paired and unpaired*) and *ANOVA* where applicable.

Results:

Thirty-eight patients were identified with ERA and had multiple assessments (Table 1). Males to females ratio = 4.4. The age mean 53.3 ±15.7 years. Mean waiting period was 88.2 ±66.5 days. The mean duration of patients' symptoms was 12.2 ±11.1 months. Of ERA patients, 82% have positive RF and 71% elevated CRP. ESR was 41.1 ±29.6 mm/hr. Initial SJC was 8.9 ±6.5 at initial presentation. The initial mean HAQ was 0.88 ±0.57. Treatment resulted in significant reduction in ESR and SJC (ESR$_f$ = 22.0 ±17.7 mm/hr; SJC$_f$ = 3.8 ±4.7). Fifteen ERA patients (40%) achieved an SJC of zero (45% of ERA patients achieved SJC=0-1). Their HAQ$_f$ was 0.45 ±0.49. Early intervention resulted in significant reduction in ESR and SJC during patients' final assessments ESR$_f$ = 22.0 ±17.7 mm/hr; SJC$_f$ = 3.8 ±4.7.

X-rays of hands and feet were done at one point for most of the patients. They were done in different; locations and read by different radiologists. The majority were read as normal. No other radiologic studies were done.

The early RA patients were treated traditionally by a combination of Methotrexate (SQ or orally) and hydroxychloroquin.

Figure 1 shows the distribution of Lag-Time (from symptom onset to DMARD treatment) in ERA patients. The Median Lag-Time (at 50% Cumulative Frequency, *red line*) was 6 months. Figure 2 shows the distribution and association of lag-times with the corresponding patients' HAQ values initially and later in the course of treatment. Patients who were treated within a short period of their symptoms onset showed dramatic improvement in their functional status (Figure 2) following treatment. HAQ Patients who did not fulfill the criteria as Early RA (Non-ERA) but with at least one of the following diagnoses: inflammatory arthritis, osteoarthritis, psoriatic arthritis, spondylitis and/or sero(-ve) arthropathy, and fibromyalgia (Table 3). Table 2 describes data from both, ERA and Non-ERA patients as they were presented to our Early RA Clinic. The rest of the patients either have established RA or early RA but had only one visit.
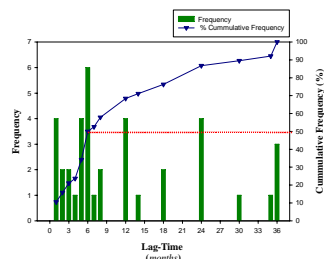

Figure 1. Distribution of Lag-Time (from symptom onset to DMARD treatment) in ERA patients. The Median Lag-Time (at 50% Cumulative Frequency, red line) was 6 months. Adapting the criteria set at our early RA clinic, approx. 70% of ERA patients were treated within one year of onset of their symptoms.

Table 1. Characteristics of patients with ERA and their outcomes following RA treatment

	Mean (SD)	Median	Min-Max	n
Age *(years)*	53.3 (16)	53	20-88	38
WP *(days)*	88.2 (67)	61.5	2-280	38
Total Visits	4.5 (2.9)	4	1-12	38
ESR$_i$ *(mm/hr)*	41.1 (30)	30	6-103	38
ESR$_f$ *(mm/hr)*	22.0 (18)*	18	4-75	38
HAQ$_i$	0.88 (0.6)	0.88	0-2	38
HAQ$_f$	0.45 (0.49)*	0.38	0-2	38
SJC$_i$	8.8 (6.6)	9	0-34	38
SJC$_f$	3.8 (4.7)*	2	0-15	38
Lag-Time *(months)*	12.2 (11)	6	1-36	38
Duration of Therapy *(days)*	453.3 (334)	483	35-1135	38

* P<0.001 *final (f)* compared to its *initial (i)* assessment value

Abbreviations: **WP**= waiting period from referral to initial diagnosis; **CRP**= C-reactive protein; Lag-Time, period estimated from symptom onset to DMARD treatment; **ESR**= Erythrocyte Sedimentation Rate level during initial (*i*) and last or final (*f*) assessment period; **HAQ**= Health assessment questionnaire reported during initial (*i*) and last or final (*f*) assessment period; **SJC**= swollen joint count determined during initial (*i*) and last or final (*f*) assessment period; n= number of patients;

Table 2. Comparison of characteristics of patients with ERA and non-ERA admitted between 2003 and 2006

	Early RA			Non-ERA		
	Mean (SD)	**Min-Max**	**Median**	**Mean (SD)**	**Min-Max**	**Median**
Age *(years)*	53.3 (16)	20-88	53	53	20-88	53
Lag-Time *(months)*	12.2 (11.1)	1-36	6	6.5	1-36	6.5
ESR$_i$ *(mm/hr)*	41.1 (30)	6-103	30	30	6-103	30
HAQ$_i$	0.88 (0.57)	0-2	0.88	0.88	0-2	0.88
SJC$_i$	8.8 (6.6)	0-34	9	9	0-34	9

Table 3. Diagnoses of the Non-ERA patients and their distribution profiles

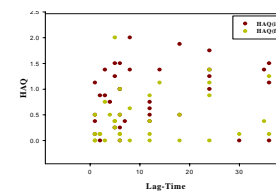| Non-ERA prognosis	n	Female:Male	Age Group (years)		
			Mean (SD)	**(Min-Max)**	**Median**
Inflamm. Arthritis and/or Polyarthritis	25	19:6	48.7 (13.8)	(20-88)	53
OA	11	9:2	62.3 (10.6)	(45-79)	62
Sero(-ve)arthropathy and/or Spondylitis	7	5:2	50.4 (7.7)	(41-61)	50
PsA	7	4:3	49.4 (8.4)	(32-57)	53
Fibromyalgia	3	3:0	43.7 (11.1)	(31-52)	48

Figure 2. Correlation between Lag-Time and ERA patients' health status at the beginning of their assessment and during their last follow-up visit. Patients who were diagnosed and treated within a short duration upon onset of their RA symptoms showed dramatic remission in their daily function.

Conclusions:

Our study demonstrates that the utilization of well trained health associated professionals, a nurse and a GP in this case, may be an effective tool in screening and management of patients with ERA in regions with few rheumatologists. We also demonstrated that a significant proportion of the ERA patients can achieve clinical remission (achieving no swollen or tender joint counts) if treated early and effectively. We believe that our criteria for identifying possible RA patients was very stringent as manifested by the presence of a high percentage of those screened with inflammatory arthritis and definite RA. A closer look at the group of undifferentiated inflammatory arthritis may give clues on their characteristics and referral patterns.

References:

1. Arnett, F.C., Edworthy, S.M., Bloch, D.A., *et al*. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum*, 1988; 31:315-24.
2. Anderson, J.J., Wells, G., Verhoeven, A.C., and Felson, D.T. Factors predicting response to treatment in rheumatoid arthritis. *Arthritis Rheum*, 2000; 43(1):22-29.
3. Gonzalez-Gay, M.A., Gonzalez-Juanatey, C., and Martin, J. Rheumatoid arthritis: a disease associated with accelerated atherogenesis. *Semin. Arthritis Rheum*. 2005, 35(1):8-17.
4. Sattar, N., and McInnes, I.B. Vascular comorbity in rheumatoid arthritis: potential mechanisms and solutions. *Curr. Opin. Rheumatol.*, 2005, 17(3): 286-92.