Databases of patients with early rheumatoid arthritis in the USA

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ABSTRACT

Several databases of patients with early rheumatoid arthritis (RA) have been established in the USA.

The University of Tennessee at Memphis Cohort was organized in 1967-1971 to enroll 50 young adults (16-44 years) with symptom onset of ≤ 6 months who met the 1958 American Rheumatism Association (ARA) criteria for at least probable RA. Two important observations from this database were that many patients seen within the first 6 months of meeting the criteria for probable RA have a self-limited rather than progressive disease, and that progressive disease is predicted by a high number of baseline swollen and tender joints.

The National Institutes of Health (NIH) cohort of patients with peripheral synovitis for ≥ 6 weeks but < 12 months in at least one peripheral joint was established in 1994. At the one-year follow-up, 45% of the patients met the RA criteria, 9% had reactive arthritis, 6% had psoriatic arthritis, 5% had other rheumatic diseases, and 35% had undifferentiated arthritis. The number of active joints, rather than meeting the criteria for RA, was the primary determinant of function and performance after one year.

The Western Consortium of Practicing Rheumatologists (CPR) was established in 1993 to enroll patients with an RA duration <1 year, positive rheumatoid factor, ≥ 6 swollen and ≥ 9 tender joints, and no previous treatment with disease modifying anti-rheumatic drugs (DMARDs). Data from this cohort indicated the validity of self-report joint counts. American College of Rheumatology 20% improvement (ACR20) responses were seen in 50% of patients at 6 months and in 57% of patients at 24 months, while antinuclear antibodies (ANA) were seen in 69% of patients prior to the availability of biologic agents.

The North American Cohort of Patients with Early RA (SONORA), which included patients with symptoms for > 3 but <12 months, indicated that methotrexate (MTX) was the most frequently prescribed DMARD, being taken by more than half the patients.

The Consortium for the Longitudinal Evaluation of African-Americans with RA (CLEAR) registry and DNA repository has enrolled 123 African-American patients with early RA of less than 2 years' duration to analyze genetic and non-genetic factors associated with disease severity.

The Early RA Treatment Evaluation Registry (ERATER) of patients with early RA (<3 years) was established in 2001. In this registry, MTX was the first DMARD used in 83% of patients, and most patients would not meet the criteria for inclusion in recent clinical trials of biological agents.

Further observation of recent cohorts of patients with early RA over the next decade should be informative regarding whether aggressive intervention strategies and new DMARDs and biologic agents lead to improved long-term outcomes.

The University of Tennessee (UT) Early Rheumatoid Arthritis (RA) Cohort (The UT Memphis Cohort)

In 1967-1971, 50 young adults (16-44 years) with early arthritis who had a diagnosis of RA by a physician within 6 months of symptom onset, were enrolled in the University of Tennessee (UT) Memphis Cohort (1, 2). All patients met the 1958 American Rheumatism Association (ARA) criteria (3) for at least probable RA. These data are presented in detail in a report on early arthritis and early RA in this supplement (4).

Five years after study entry, 18 patients (36%) had no swollen joints and no erosions (Category I), 22 (44%) had swollen joints but no erosions (Category II), and 10 patients (20%) had erosions (Category III) (5,6). These results were interpreted initially to pertain to all patients with RA, with a suggestion

that only a small minority of patients had a progressive course, and many had a self-limited or single course (5). Such interpretations may account in part for the advocacy of a "pyramid" approach to therapy for patients with RA, which involved the observation of patients taking non-steroidal anti-inflammatory drugs (NSAIDs) for several years prior to the introduction of DMARDs (7,8).

Interpreting the study data in the light of our contemporary understanding of the course of RA, it must be recognized that recruitment of the 50 patients required 5 years in a busy clinic, that the reports included only 5 years of follow-up and did not include data on quantitative radiographic scores, detailed functional disability, and work disability, which were not commonly measured at that time.

Therefore, in retrospect, this early RA database probably included fewer than 1% of the patients seen in this clinic over the recruitment period, and likely underestimated the outcome of most patients with RA. Spontaneous remission is rare in most individuals who have persistent evidence of RA for > 6 months, and certainly > 1 year. Most patients with RA seen in clinical settings are likely to have a persistent and progressive disease.

The National Institutes of Health (NIH) early synovitis cohort

A cohort of 238 patients with peripheral synovitis of less than 12 months' duration has been established at the National Institutes of Health (NIH) in Bethesda, Maryland beginning in 1994 (9,10). Inclusion criteria were persistent synovitis for at least 6 weeks but less than 12 months in at least one peripheral joint. Patients with traumatic, septic or crystal-induced arthritis were excluded, as were those with well defined, diffuse connective tissue diseases such as systemic lupus erythematosus or scleroderma.

At the one-year follow-up visit, 45% of the patients met the ACR criteria for RA, 9% were found to have reactive arthritis, 6% psoriatic arthritis, 5% other rheumatic diseases, and 35% undifferentiated arthritis (11). It was observed that the number of active joints, rather than the criteria for RA, was the primary determinant of function and performance in early RA (12). Polyarticular arthritis, independent of rheumatoid factor, is associated with poor functional outcome in recent onset inflammatory arthritis (12,13).

Serum samples for RA-associated antibodies were collected at the baseline. Among the results was the finding that rheumatoid factor had a sensitivity of 66% and specificity of 87% for RA. Anti-Sa, antifilaggrin antibody, and anti-cyclic citrullinated peptide all had specificities of more than 90%, but sensitivities of less than 50%,and had little additional diagnostic value for RA over rheumatoid factor alone (11). In a subset of the cohort patients, active synovial matrix metalloproteinase-2 was found to be associated with radiographic erosions (14).

Further observations concerning the NIH early synovitis cohort are described elsewhere (15, 16), and in this supplement (13, 17-19).

The Western Consortium of Practicing Rheumatologists (CPR) Early RA Cohort

The Western Consortium of Practicing Rheumatologists (CPR) is a regional consortium of 25 rheumatology practices in the Western United States and Mexico, organized in 1993 to enroll patients with early RA into a long term observational study. Inclusion criteria were symptoms for less than one year, no previous treatment with DMARDs, positive rheumatoid factor, 6 or more swollen and 9 or more tender joints (20).

Self-reported joint counts were elicited

Table I. Comparison of joint counts in 50 patients from the Western Consortium of Practicing Rheumatologists (CPR) by self-report from patients using either a pictorial format with a joint mannequin or a listing of the rapid assessment of disease activity in rheumatology (RADAR) versus a joint count performed by a physician. Data include mean values of patient and physician joint counts: mean ± SD and Spearman correlations between patient and physician joint counts before and after visit to MD.

	Mannequin Joint Count, Pictorial Format			
	Tender joint count		Swollen joint count	
	Mean ± SD	Correlation with MD	Mean ± SD	Correlation with MD
Patient, before MD visit	11.0 ± 10.6	r = 0.61, p = 0.001	6.8 ± 7.7	r = 0.58, p = 0.001
Patient, after MD	11.3 ± 12.6	r = 0.69, p = 0.0001	8.3 ± 10.9	r = 0.61, p = 0.001
MD joint count	10.1 ± 9.2		8.9 ± 9.6	
ICC	r = 0.65, p < 0.0001		r = 0.64, p < 0.0001	

	RADAR Joint Groups Count, Text Format			
	Tender joint count		Swollen joint count	
	Mean ± SD	Correlation with MD	Mean ± SD	Correlation with MD
Patient, before MD visit	8.5 ± 5.3	r = 0.37, p = 0.03	5.2 ± 3.5	r = 0.58, p = 0.001
Patient, after MD	8.0 ± 5.6	r = 0.45, p = 0.01	5.7 ± 3.6	r = 0.55, p = 0.001
MD joint count	7.2 ± 5.9		5.4 ± 4.4	
ICC	r = 0.56, p < 0.0001		r = 0.61, p < 0.0001	

ICC: intraclass correlation coefficient.
Source: (20)

Table II. Use of disease modifying anti-rheumatic drugs in 251 patients with early rheumatoid arthritis of less than one year's duration from the Western Consortium of Practicing Rheumatologists (CPR) between 1993 and 1996 at baseline, and 6 months, 12 months, and 24 months after baseline.

Drug	Baseline	6 months	1 year	2 years
Methotrexate	35.7%	53.6%	55.3%	57.4%
Hydroxychloroquine	16.7%	30.0%	30.2%	31.2%
Injectable gold	3.6%	2.7%	2.0%	0%
Sulfasalazine	7.1%	9.1%	13.1%	12.1%
Prednisone	40.1%	43.2%	44.2%	45.4%

Source: (22)

in two formats – pictorial (the schematic drawing of a mannequin) and text [the RADAR questionnaire (21)] – in 60 patients. Twenty-seven patients were randomized to complete the mannequin tender and swollen joint counts one day before and one day after their examination by a physician (20), while 33 were randomized to the RADAR text format to assess the tender and swollen joint counts. Spearman correlations comparing the physician and patient assessments were significant: 0.58 – 0.69 for the mannequin and 0.37 – 0.58 for the RADAR. Intra-class correlations were 0.65 and 0.64 for the mannequin tender and swollen joint counts, and 0.56 and 0.61 for the RADAR tender and swollen joint counts, indicating agreement among the 3 joint count ratings for each patient (Table I). Patient test-retest reliability using the RADAR was 0.58 for tenderness and 0.90 for swelling, and was greater than 0.90 for the mannequin swollen and tender joint counts. Low patient educational level was associated with greater differences between the physician and patients on the RADAR swollen joint count, but not the mannequin swollen joint counts. These data indicate that patient self-reports of joint findings can be used effectively in clinical assessments (20).

Analysis of therapies in 251 patients showed that after 2 years, 57% of patients were taking MTX, 31% hydroxychloroquine (HCQ), 1% sulfasalazine (SSZ), and 45.4% prednisone (22) (Table II). An ACR20 improvement (23) was seen in 50% of patients at 6 months, 53% at 12 months, and 57% at 24 months. Response rates differed by less than 3% whether the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), or plasma viscosity assays were used as the acute phase reactant to assess the ACR20 responses, indicating that any one of these 3 measures could be used as the acute phase reactant in the assessment (22). The study documented ACR20 response rates of more than 50% using standard DMARD therapy in early RA, rates comparable to those seen with biological agents in randomized clinical trials. The presence of autoantibodies in early

Table III. Characteristics of 276 patients with early rheumatoid arthritis from the Western Consortium of Practicing Rheumatologists (CPR), according to the anti-nuclear antibodies (ANA) status at the baseline. Data are expressed as the mean ± SD (number of subjects), or percentages.

Variable	ANA< 8 IU/ml (n = 85)		ANA 8 IU/ml (n = 72)		ANA> 8 IU/ml (n = 119)	
Baseline demographics						
Age, years	50.50 ± 14.05	(85)	50.57 ± 13.96	(72)	49.20 ± 12.68	(118)
Sex, % female	77.65%	(85)	80.56%	(72)	76.47%	(119)
Duration of RA, mo.	8.37 ± 8.84	(85)	7.56 ± 4.96	(72)	6.72 ± 6.07	(115)
Initial DMARD						
Methotrexate %	45.9%		52.8%		44.5%	
Hydroxychloroquine %	24.7%		13.9%		22.7%	
Methotrexate ± Hydroxychloroquine %	3.5%		5.6%		10.3%	
Sulfasalazine %	7.1%		16.7%		10.1%	
Step-down bridge %	7.1%		2.8%		4.3%	
Gold %	3.5%		4.2%		4.3%	
None or other %	8.3%		4.2%		4.2%	
RA course during an average of 3.5 years follow-up						
ACR 20% responders %	50.00%	(41/82)	53.73%	(36/67)	53.27%	(57/107)
ACR 50% responders %	31.71%	(26/82)	31.34%	(21/67)	41.12%	(44/107)
Sharp Score progression rate/year	0.68 ± 3.13	(54)	1.12 ± 2.44	(47)	0.86 ± 1.93	(74)
First-year change in HAQ	-0.50 ± 0.59	(52)	-0.50 ± 0.79	(51)	-0.41 ± 0.54	(85)
New extraarticular manifestations %	6.02%	(83)	8.96%	(67)	7.21%	(111)
New nodules %	8.43%	(83)	20.90%	(67)	11.61%	(112)

Source: (24)

Table IV. Correlations between single radiograph scores at various durations of rheumatoid arthritis (RA) and calculated individual progression rates in patients from the Western Consortium of Practicing Rheumatologists (CPR)

RA duration** at time of radiograph (mos.)	No. of single radiographs (pts.)	Correlation between single radiograph scores and progression rate		
		Total score	Erosion score	Joint space narrowing score
0-6 months	106 (104)	0.072	0.072	-0.015
7-18 months	277 (165)	0.255*	0.347*	0.225*
19-30 months	130 (121)	0.483*	0.599*	0.364*
31-42 months	88 (83)	0.589*	0.647*	0.415*
43-72 months	109 (72)	0.745*	0.810*	0.571*

*p < 0.001 Spearman correlation coefficient; **months since onset of persistent symptoms of RA. Source: (25)

RA was examined in 276 patients enrolled between January 1, 1993 and April 15, 2000 prior to the availability of biologic agents (Table III) (24). Among the 276 patients, 119 (43%) were positive for antinuclear antibodies (ANA), while 72 (26%) were borderline positive and 85 (31%) were negative for ANA. During an average of 3.5 years follow-up, ANA results changed from negative to positive in 12.5% and from positive to negative in 12.3% of patients. Anti-double-stranded DNA was detected in 5.5% of patients, of whom 4 changed from negative to positive and one from positive to negative. These observations suggest that the autoantibodies were present in many patients with RA prior to the availability of new biological agents, and may not necessarily be attributable to treatment with these agents (24).

Analyses of the predictive value of radiographs (Table IV) (25) indicated that radiographs taken within 6 months of the first symptoms were not correlated with the rates of radiographic progression (r=-0.01–0.07), and even those between 7 and 18 months were only weakly correlated with progression (r= 0.23 – 0.35) on a Sharp radiographic scoring scale. As expected, correlations between single scores and rates of progression increased with time and were highest after 72 months (r=0.57–0.81). This report also confirmed that 55.3% of patients took MTX, 54.2% had ACR20 responses and 30.7% had ACR50 responses over 2 years (25).

North American Cohort of Patients with Early RA (SONORA)

SONORA is a prospective 5-year study designed to examine the clinical course, treatment patterns, and outcomes of patients with early RA (26). It is planned that this study will examine the course of RA longitudinally over time, and analyze prognostic factors affecting outcomes, including the role of genetic predictors. SONORA will provide data concerning outcomes including work disability and health care costs. Enrollment of most patients took place prior to the availability of biologic agents and this cohort will provide valuable control data to compare to more recent patients who have been treated with biologics, as well as to analyze patients who are treated with biologic agents later in their disease course.

Patients diagnosed as having new onset RA by a board-certified rheumatologist, with symptoms for more than 3 but less than 12 months, were recruited from 98 rheumatology practices in the US and Canada. Clinical and laboratory data are collected by the enrolling rheumatologist at baseline, and 1, 2, and 5 years. Patients complete validated questionnaires, including the short form 36 (SF-36) and health assessment questionnaire (HAQ), every 4 months.

Baseline data concerning DMARDs in 726 SONORA patients were presented at the American College of Rheumatology (ACR) 2002 meeting (26). Of these 65% had taken DMARDs. The most frequently prescribed DMARDs were MTX (41%) and HCQ (24%). Only 7% had taken SSZ, 3% leflunomide, 2% minocycline, 1% gold and 1.7% a biologic agent. Eleven percent of patients took two DMARDs, while 2% took three. Of the 553 patients who entered the study within 3 months of their diagnosis 39% had not yet received a DMARD, while 22% of patients with more than 3 months of disease had not yet had DMARDs prescribed. Overall, the patients who had not taken DMARDs had more active disease than the patients who had taken DMARDs, as measured by patients' global assessments of pain (5.5 vs 4.6) and disease activity (5.0 vs 4.6) (26).

The results indicate that MTX and HCQ are the most frequently used DMARDs in early RA. Despite the fact that recent ACR guidelines recommend initiation of DMARD therapy within the first 3 months (27), 20% of patients with more than 3 months of disease had not received DMARD therapy. These observations suggest the need for further analysis concerning why patients are not receiving these drugs at an early stage of RA.

Follow-up data concerning the SONORA patients were presented at the annual European Congress of Rheumatology 2003. At the one-year follow-up, 88% of the 343 SONORA patients had received a DMARD (28). The overall improvement in disease activity over the first year was 64% in the tender joint count, 56% in the swollen joint count, 25% in the HAQ score, 0% in CRP, 14% in pain, 50% in morning stiffness, and 33% in the physician's and 25% in the patient's assessment of global disease activity (28). It was also observed that after the first year of the study, physicians consistently reported greater improvements than patients in multiple measures of disease activity (29).

In 343 SONORA patients, the smoking status of males at baseline did not appear to affect ACR20 responses at one year, while ACR20 responses were less likely in females who were smokers at study entry compared with female non-smokers (p=0.03) or female former smokers (p=0.05) (30).

Consortium for the Longitudinal Evaluation of African-Americans with RA (CLEAR)

The CLEAR registry and DNA repository has the goal of identifying 500 African-American patients with early RA of less than 2 years' disease duration, in order to analyze genetic and non-genetic factors associated with disease severity. Since 2000, 123 subjects have been enrolled in the CLEAR registry at 4 academic institutions in the southern United States. The CLEAR registry is described in greater detail in another chapter of this supplement (31).

Demographic, medical, and socioeconomic data are collected at baseline. Disease activity, functional capacity, and quality of life will be monitored over 5 years. Blood samples will be obtained for the isolation of DNA. Bone densitometry will be obtained at baseline, and radiographs of the hands, wrists and feet at baseline and at 3 and 5 years of disease duration.

Early RA Treatment Evaluation Registry (ERATER)

Between February 2001 and June 2003, 560 patients with early RA for less than 3 years were enrolled in an early rheumatoid arthritis treatment evaluation registry (ERATER) study, initially established in Nashville, Tennessee (32), which includes 360 patients in Nashville, as well as 73 in Massachusetts, 63 in New York and 64 at other sites (Table V). The patients were evaluated according to a standard protocol to evaluate rheumatoid arthritis (SPERA) (33) which includes four one-page questionnaires, 3 to be completed by a physician or assessor and one by the patient:

1. Clinical features – Classification criteria, co-morbidities, extra-articular manifestations, surgeries, laboratory results, and work status.
2. All medications used for RA.
3. A 42-joint count which includes 10 proximal interphalangeal (PIP) joints of the hand, 10 metacarpophalangeal (MCP) joints of the hand, 2 wrists, 2 elbows, 2 shoulders, 2 hips, 2 knees, 2 ankles and 10 metatarsophalangeal (MTP) joints (hips and shoulders are not scored for swelling). All joints are scored for tenderness, swelling (except the hips and shoulders), limited motion, and surgery, with a space to indicate that a joint is normal.
4. A patient self-report Multi-Dimensional Health Assessment Questionnaire (MDHAQ) including the modified Health Assessment Questionnaire (MHAQ) for functional capacity, visual analog scales to assess pain, global health, and fatigue, minutes of morning stiffness, and a symptom list (34). The MDHAQ is completed at each visit to the rheumatologist as well as twice a year by mail.

Table V. Demographic measures in 560 patients enrolled in the Early Rheumatoid Arthritis Treatment Evaluation Registry (ERATER) between 2001 and June 2003.

Site	Nashville, Tennessee	Burlington, Massachusetts	Brooklyn, New York	Other	Total
No. of pts. enrolled	360	73	63	64	560
% Female	73%	58%	73%	72%	72%
% White	90%	96%	22%	71%	81%
% Black	8%	1%	38%	21%	12%
% Hispanic	1%	0%	27%	7%	4%

Patients from participating sites differ in demographic characteristics as well as their initial DMARD therapies. The Tennessee cohort is 90% white, 8% black, and 1% Hispanic, while the New York cohort is 22% white, 38% black, and 27% Hispanic (Table V). Results concerning 426 patients (not including the Massachusetts and New York patients) are presented in another chapter of this Supplement (35).

MTX was the first DMARD used by 84% of the patients in Tennessee, compared to 37% in Massachusetts and 38% in New York, while HCQ was the first DMARD for 40% in Massachusetts,24% in New York, and only 8% in Tennessee (Table VI).

Data concerning the first 232 ERATER patients, all seen in Tennessee, were analyzed to determine which DMARDs are used in early RA in routine clinical care (Table VII) (32). MTX was the first DMARD used in 192 patients (82.8%), including 3 in combinations. During the first year of drug treatment, 89.2% of the patients had taken MTX, 15.9% HCQ, 3.9% SSZ, 22.0% leflunomide, 9.5% etanercept, 4.3% infliximab, and 87.0% prednisone. Thus, MTX appeared to be the "anchor drug" taken by almost 90% of patients during the first year, while 30% took

Table VI. Comparison of first DMARD by site (% of patients) in 560 patients enrolled in the Early Rheumatoid Arthritis Treatment Evaluation Registry (ERATER) between 2001 and June 2003.

DMARD	Nashville, Tennessee	Burlington, Massachusetts	Brooklyn, New York	Other
Any DMARD	98.9%	93.2%	96.8%	95.3%
Methotrexate	84.2%	37.0%	38.1%	62.5%
Hydroxychloroquine	7.5%	39.7%	23.8%	9.4%
Sulfasalazine	0.8%	8.2%	12.7%	0
Leflunomide	1.7%	2.7%	3.2%	15.6%
Hydroxychloroquine + sulfasalazine/leflunomide	0.3%	2.7%	3.2%	1.6%
Infliximab	0.3%	0	0	0
Etanercept	0	1.4%	3.2%	0
Azathioprine	0	0	0	1.6%
Prednisone*	2.5%	0	3.2%	1.6%

*Prednisone was recorded as the first DMARD only if other DMARDs were not started.

Table VII. Percentage of patients taking DMARDs in the first 232 patients with recent onset rheumatoid arthritis enrolled in the Early Rheumatoid Arthritis Treatment Evaluation Registry (ERATER).

DMARD	No. (%) of pts. taking as the 1st DMARD	No. (%) of pts. taking DMARD at study entry	No. (%) of pts. who had ever taken this drug only or in combination
MTX only	189 (81.5%)	130 (56.0%)	207 (89.2%)
HCQ only	15 (6.5%)	4 (1.7%)	37 (15.9%)
SSZ only	2 (0.9%)	1 (0.4%)	9 (3.9%)
LEF only	6 (2.6%)	14 (6.0%)	51 (22.0%)
ETAN only	0	2 (0.9%)	22 (9.5%)
INFLIX only	0	1 (0.4%)	10 (4.3%)
MTX + HCQ and/or SSZ	2 (0.9%)	16 (6.9%)	
MTX + LEF	0	20 (8.6%)	
MTX + ETAN	1 (0.4%)	8 (3.4%)	
MTX + ETAN + HCQ	0	3 (1.3%)	
MTX + INFLIX	0	8 (3.4%)	
LEF + ETAN	0	3 (1.3%)	
Other DMARDs	0	1 (0.4%)	
No DMARDs	17 (7.3%)	21 (9.1%)	

DMARD: disease-modifying anti rheumatic drug; MTX: methotrexate; HCQ: hydroxychloroquine; SSZ: sulfasalazine; LEF: leflunomide; ETAN: etanercept; INFLIX: infliximab.
Source: (32)

leflunomide, etanercept, or infliximab, usually in combination with MTX (32, 36).

Data concerning the 232 first patients in the ERATER database were analyzed to identify the proportion of patients who met the criteria for inclusion in the early rheumatoid arthritis (ERA) clinical trial of etanercept versus MTX (37, 38). In the ERATER cohort at the baseline, only 16% of all patients met the ERA inclusion criteria (Table VIII) (39). In another report, it was observed that only 34% of the ERATER patients met 3 of 4 of the most common criteria for inclusion in RA clinical trials, i.e. ≥ 6 swollen joints, ≥ 6 tender joints, ESR ≥ 28, and/or morning stiffness ≥ 45 minutes (40). Similar inclusion criteria have been used in RA clinical trials for more than 20 years, despite possible improvement in the severity of RA. It was suggested that data in recent RA clinical trials may not be generalizable, and that re-examination of the inclusion criteria would be of value (40).

Table VIII. Analysis of patients who met the criteria for inclusion in the early rheumatoid arthritis (ERA) clinical trial, according to therapies taken, in the first 232 patients enrolled in the Early Rheumatoid Arthritis Treatment Evaluation Registry (ERATER).

	No. of pts.	≥ 12 tender and ≥ 10 swollen joints	Positive rheumatoid factor or radiographic erosions	Morning stiffness ≥ 45 min. or ESR ≥ 8 mm/hr
No prior MTX, 1st visit	19	10 (53%)	8 (42%)	8 (42%)
No prior MTX, not 1st visit	17	3 (18%)	3 (18%)	3 (18%)
No prior MTX, any visit	36	13 (36%)	11 (31%)	11 (31%)
Prior MTX	135	25 (19%)	20 (15%)	17 (13%)
Prior LEF, ETAN, INFLIX (+ MTX)	61	10 (16%)	10 (16%)	9 (15%)
Prior MTX, LEF, ETAN or INFLIX	196	35 (18%)	30 (15%)	26 (13%)
All patients	232	48 (21%)	41 (18%)	37 (16%)

MTX:methotrexate; HCQ: hydroxychloroquine; SSZ:sulfasalazine; LEF:leflunomide; ETAN:etanercept; INFLIX: infliximab.
Source: (39)

Preliminary analyses of work disability in the ERATER study were performed in 127 patients who were less than 65 years of age and were working either full time (n = 118) or part time (n = 9) at the onset of symptoms (41). At study entry (mean and median disease duration 22 months from the first symptoms), 13 patients (10%) had stopped working due to RA, 5 of whom were receiving disability payments. The finding that only 10% of patients with early RA stopped working during the first two years of RA differs from several studies in Europe, which found that 20-30% of patients with early RA became permanently work disabled during the first 2-3 years of RA (42). These findings may suggest possible reduced work disability in this cohort, but further longitudinal data are required over time.

Conclusion

Early RA databases in the USA will provide an opportunity to study the long-term outcomes of early RA over several years, including radiographic outcomes, functional and work capacity, and mortality, in an era when several new therapies have become available for RA within the last few years. Certain unique data will be elicited by early RA databases in the USA which will not be available from any other sources over the next decade. First, the latest (and expensive) biologic agents are available at this time for early RA patients in the USA, whereas different social and health care systems restrict the use of these new DMARDs largely only to patients with advanced RA in many European countries. Secondly, disparities in the patient population with regard to social, economic, educational, cultural, and racial background, as well as differences in treatment strategies between clinics in the USA are wide, thus facilitating research on various approaches applied in various

types of patients. Longitudinal observational studies will be required to evaluate the influence of aggressive treatment on the actual long-term outcomes of RA, such as work disability, joint replacement surgery and premature mortality, as well as the effects of long-term usage (effectiveness and possible rare or serious adverse events) of the new DMARDs and biologic agents.

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