



Clinical Factors that Predict Erosion-Free Status in Rheumatoid Arthritis



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Introduction

The majority of rheumatoid arthritis (RA) patients develop peri-articular erosions even while on treatment. However, there are individuals who remain erosion-free despite years of disease.

Objective

To identify the characteristics of erosion-free RA subjects and significant baseline predictors for remaining erosion-free at 2 years.

Methods

Study population

• Selected from the Brigham Rheumatoid Arthritis Sequential Study (BRASS), a prospective observational cohort of RA patients recruited from the Brigham and Women's Arthritis Center between 2003-2004

Inclusion criteria:

- Age > 18 years
- Diagnosis of RA by rheumatologist
- Bilateral hand radiographs at baseline and 2 year follow-up
- Sharp score assessed for baseline and follow-up radiograph

Outcome

- Erosion-free at baseline (recruitment) **AND** 2 year follow-up
 - Definition of erosion using the erosion score component of the Sharp score:
 - At least one joint with erosion score ≥ 2 **AND**
 - Total erosion score ≥ 3 with ≥ 2 joints affected

Baseline covariates

- Age at RA onset
- Gender
- Disease duration
- C-reactive protein (CRP)
- Disease activity score 28 (DAS28)
- Tender joint count (TJC)
- Swollen joint count (SJC)
- Smoking status
- Methotrexate and/or anti-TNF use
- Multi-dimensional health assessment questionnaire (MDHAQ)

Statistical analysis

- Univariate analysis of baseline characteristics to identify potential predictors
- Primary analysis- logistic regression with backward selection to identify significant predictors of erosion-free disease at 2 year follow-up
- Sensitivity analysis- logistic regression with subjects categorized by baseline disease duration (≤ 2 , 3-5, 5-10 and 11+ years)
- Medication effects assessed by including baseline methotrexate and anti-TNF as indicator variables into the final model

Results

- 540 subjects in cohort with bilateral hand radiographs and Sharp scores
- 133 (24.6%) remained erosion-free at 2 year follow-up (Table 1)

Table 1. Characteristics of subjects who remained erosion-free compared to subjects with erosions in BRASS, n=540

Baseline characteristics	Erosion-free, n=133	Erosions, n=407	P-value
Mean age (SD)	50.5 (13.6)	59.6 (11.6)	<0.0001
Female (%)	77.4	84.7	0.06
Disease duration, yrs (SD)	7.4 (8.2)	16.9 (12.2)	
Ever smoker (%)	46.5	50.4	0.443
MDHAQ	5.1 (5.1)	5.9 (5.1)	0.09
DAS28 (SD)	3.7 (1.6)	4.2 (1.5)	0.002
Swollen joint count (SJC) Mean (SD)	6.1 (7.0)	8.8 (7.2)	0.0003
Tender joint count (TJC) Mean (SD)	7.6 (7.6)	9.5 (8.2)	0.02
Serology			
RF neg, n (%)	67 (50.4)	104 (25.6)	<0.0001
Anti-CCP neg, n (%)	68 (51.1)	100 (25.5)	<0.0001
CRP, median (IQR)	2.6 (4.0)	8.0 (15.5)	0.78
Medications			
Methotrexate	54 (40.6)	203 (49.9)	0.06
Anti-TNF	40 (30.1)	169 (41.5)	0.02

- Among subjects who were erosion-free at baseline and at 2 years:
 - 50% were anti-CCP+ and 49% were RF+
 - 57 (55%) of erosion-free subjects had at least one copy of the HLA-shared epitope (not included in model)
- Significant trend of decreasing % of individuals who remained erosion free with increasing disease duration at the time of recruitment (Table 2)

Table 2. Number and % of subjects who remained erosion-free from baseline to 2-year follow-up by disease duration, n=133

Disease duration at recruitment	N	%
≤ 2 years	45	50
3-5 years	27	42
6-10 years	33	35.5
11+ years	28	10

Table 3. Significant clinical predictors of erosion-free status.

Variables	Full model		Final model*	
	OR	95% CI	OR	95% CI
Age (per 5 years)*	0.77	0.69, 0.85	0.78	0.71, 0.86
Female*	0.40	0.21, 0.76	0.44	0.24, 0.78
Disease duration*	0.93	0.90, 0.96	0.93	0.90, 0.95
RF negative*	1.8	0.97, 3.34	2.2	1.39, 3.47
Anti-CCP negative	1.4	0.73, 2.54	-	-
SJC	0.94	0.88, 1.01	-	-
TJC	1.07	0.99, 1.16	-	-
DAS28	0.90	0.58, 1.42	-	-
MDHAQ	1.98	0.94, 1.04	-	-
Smoking	1.3	0.77, 2.06	-	-

*Significant, p<0.05 // † Non-significant variables removed from the full model using backward selection to determine final model

- Remaining erosion-free from recruitment to 2 year follow-up associated with younger age, male gender, a shorter disease duration, absence of RF (Table 3)
- Sensitivity analysis categorizing subjects by disease duration yielded the same significant factors
- Methotrexate and anti-TNF were not significant factors when included into the full and the final model

Conclusions

- 25% of RA subjects treated per routine practice in this prospective cohort study were erosion-free at baseline and 2 year follow-up
- At baseline, individuals with shorter disease duration were more likely to remain erosion-free
- 50% of subjects who remained erosion-free were anti-CCP+; 55% had at least one copy of the HLA-SE
- Younger age, shorter disease duration, male gender and absence of RF were significant predictors of erosion-free disease
- Further study is needed to identify biomarkers that can improve prediction for development of erosions compared to what is currently available

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