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Study of Prognostic Value of Rheumatoid Factor and Anti Cyclic Citrullinated Peptide Antibodies in Patients with Rheumatoid Arthritis

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Abstract: ***Aims and Objectives: To correlate Rheumatoid factor(RF) and Anti-CCP antibody in RA and to evaluate prognostic value of RF and Anti-CCP antibody in RA. Methods: Retrospective study of total 40 patients admitted to our hospital between april 2013 to may 2014. All patients were diagnosed as rheumatoid arthritis as per diagnostic criteria of American College of Rheumatology. All patients had symptom duration of at least year. Anti-CCP and IgM-RF were evaluated in all patients. Disease activity score 28 was calculated in all patients. Radiological Damage was assessed by Larsen Score. Results: Anti-CCP and RF were significantly correlated with each other and both were seen as significant independent predictors of radiological outcomes. Combination of these two had the highest risk for erosive joint damage. Conclusion: RF and Anti-CCP antibodies are significantly correlated with each other and both are having a high predictive value for erosive joint disease. Combined use of RF and Anti-CCP has high predictive value for erosive joint disease than RF or Anti-CCP alone and may facilitate to make a decision about the individual treatment in Rheumatoid arthritis***

Keywords: Anti-CCP, RF, RA, peptide, Antibodies

1. Introduction

Rheumatoid arthritis is a chronic autoimmune inflammatory disease with articular and extra-articular manifestation that affects 0.5 to 1% of total population. Diagnosis of RA depends on clinical symptoms, lab investigation and imaging. Joint damage accounts for a considerable part of the disability caused by RA. Most effective way to manage RA patients is early diagnosis and timely treatment with disease modifying anti rheumatic drug, which prevent the exacerbation of disease and improves outcome. Availability of better prognostic marker would make it possible to select predictably severe cases for aggressive therapy at early stage.

Antibodies against cyclic citrullinated peptide (anti-CCP) are a new and highly specific marker for RA. Anti-CCP antibodies are now considered as an important serological marker for the diagnosis of RA and as a possible prognostic marker the development of erosive disease.

2. Objective

- To correlate RF with Anti-CCP antibody
- To determine predictive value of anti-CCP and RF for radiological damage in patients with RA.

3. Methods

Retrospective study of 40 patients who were diagnosed as rheumatoid arthritis as per diagnostic criteria of American college of rheumatology. All patients had symptom duration of minimum 1 year. Clinical evaluation of disease was based on number of swollen joints, number of tender joints, and morning stiffiness duration. Disease activity was assessed by 28 joint disease activity score (DAS28).

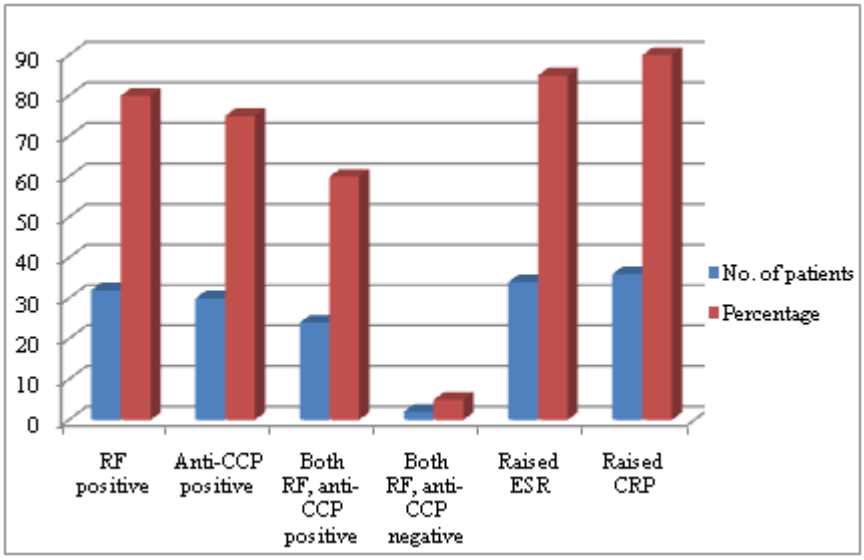
Radiographic measurement: Standardized Radiographs of hands were performed to calculate the Larsen score. In each case, 22 joints were scored: all metacarpalphalangeal joints (=10), all proximal interphalangeal joints (=8), both first interphalangeal joints (=2) and wrists (=2) in the hands. Each joint was scored from 0 to 5. The Larsen score is the total sum of the grading in all 22 joints, ranging from 0 to 110. Joint damage was defined if Larsen score was 10 or higher, otherwise it was not present.

RF and antibodies to cyclic citrullinated peptide were analysed. Anti-CCP was considered positive if titre was greater 5 RU/ml. IgM-RF was determined positive if result of >20 IU/ml. ESR (erythrocyte sedimentation rate) and CRP (C-reactive protein) was measured in the all patients.

4. Result

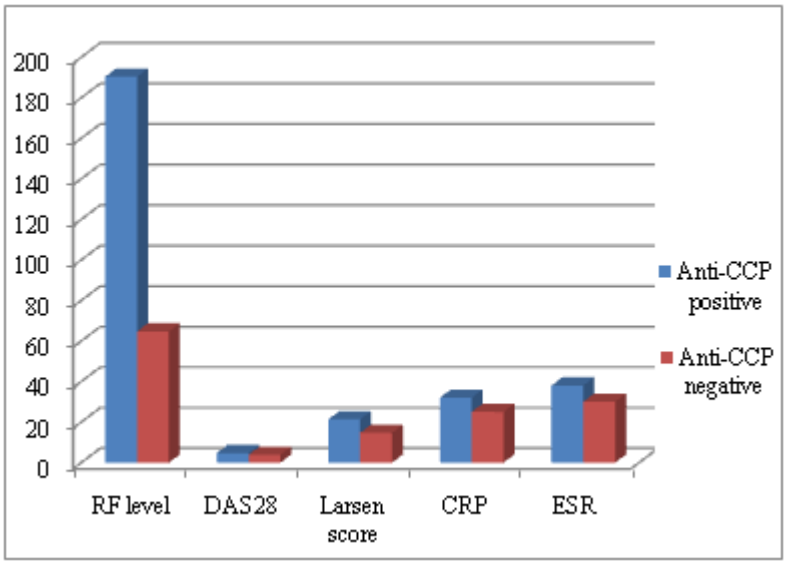
Mean age of patients was 47.5 years and mean duration of disease was 8.9 years. 32 (80%) of all 40 patients were RF positive while 8 (20%) were negative. 30 (75%) of all patients were positive for anti-CCP while 10 (25%) were negative. 24 patients (60%) were positive for both RF and anti-CCP whereas 2 patients (5%) was negative for both. In addition 6 (75%) of 8 RF negative patients were anti-CCP positive whereas 8 (80%) of 10 anti-CCP negative patients were RF positive.

	No. of patients	*Percentage*
RF positive	32	80
Anti-CCP positive	30	75
Both RF, anti-CCP positive	24	60
Both RF, anti-CCP negative	2	05
Raised ESR	34	85
Raised CRP	36	90



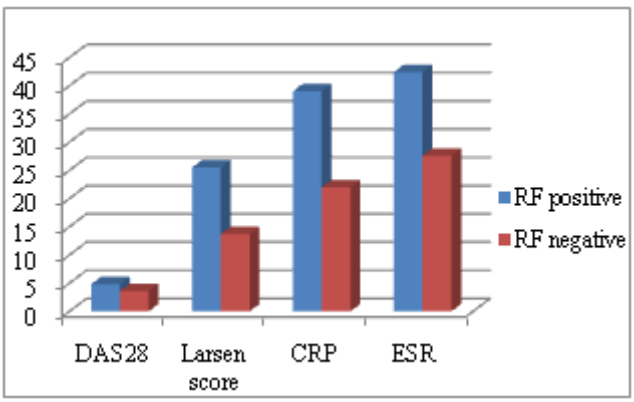
The level of RF was significantly high in anti-CCP positive patients than in anti-CCP negative patients ($p<0.01$) means significant correlation between RF and anti-CCP. Larsen score, DAS28 were higher in anti-CCP positive patients than in anti-CCP negative patients. There were early destructive changes in joints in anti-CCP positive patients than in anti-CCP negative patients indicates prognostic value of anti-CCP antibody.

Mean value of	*Anti-CCP*	
	Positive	*Negative*
RF level	190.4	64.7
DAS28	4.64	3.86
Larsen score	21.3	14.7
CRP	32	25
ESR	38	30



On the other hand, Larsen score and DAS28 were significantly higher in RF positive patients than RF negative patients. ($p<0.05$, $p<0.001$, $p<0.05$, respectively).

Mean value of	*RF positive*	*RF negative*
DAS28	4.8	3.6
Larsen score	25.5	13.7
CRP	39	22
ESR	42.4	27.6



5. Discussion

The critical strategy to prevent joint damage in RA is to initiate DMARD early in course of the disease. The ability to predict severe disease outcome is as important as a correct diagnosis. Anti-CCP antibody and RF are shown as important serological marker for RA diagnosis and as a possible prognostic marker for development of early erosive disease. A recent study showed that in patients with synovitis of three months duration, a combination of anti-CCP and RF has high specificities (97%) and PPV (83%) for development of persistent RA. Furthermore Anti-CCP have been incorporated in to newly proposed diagnostic criteria for RA and proved to be strongly associated with erosive arthritis.

In this study, anti-CCP and RF positivities and the duration of the disease were independent predictors of erosive development, and combination of these antibodies had the highest for erosive damage.

Most studies agree that a positive RF is an important predictor for joint damage over the years of disease. Jansen et al concluded that radiographic progression at one year was predicted by positive RF. Similar to previous studies, our results suggested the prognostic value of RF.

It appears that anti-CCP antibodies have prognostic relevance similar to RF. Vencovsky et al found that anti-CCP positivity was better than RF at predicting progression of Larsen score over 2 years. Also, in prospective study of 242 patients with early RA followed up for three years, the anti-CCP antibody results correlated with RF, but were better than RF as predictor of more aggressive disease.

Finally this study showed that the presence of anti-CCP and RF antibodies was associated with high probability of erosive disease. The combined use of RF and anti-CCP had greater specificity and PPV for erosive damage than anti-CCP or RF alone.

6. Conclusion

- RA is more common in female.
- There is significant correlation between RF and anti-CCP antibody
- Anti-CCP antibody and RF both in combination were associated with higher propabilities of erosive disease.

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