INTRODUCTION:

- Pre-Rheumatoid Arthritis (RA) is a period of elevations of antibodies to citrullinated protein antibodies (ACPAs) before clinically-apparent inflammatory arthritis (IA).
- Gaps in understanding Pre-RA include:
  - How symptoms evolve in transition to IA
  - Progression to IA in ACPA+ asymptomatic individuals
  - How ACPA+ individuals who are prospectively followed to IA compare to those with new RA found through standard rheumatology referrals.

METHODS:

Participants, no IA at baseline:
- ACPA (+) (CCP3, Inova) with no history or examination evidence of IA
- Recruited from clinics, health fairs, and screening of relatives of patients with RA
- Followed prospectively for IA development

Participants, EarlyRA:
- CCP3+ patients with a baseline study visit <30 days since RA diagnosis

Data Collection:
- Questionnaires capturing pain, stiffness and swelling in 68 joints
- Physical examination
- Disease activity (DAS28CRP)
- Autoantibody levels

Statistical Analysis:
- Independent samples t-test
- Chi Square

RESULTS:

- 19/84 (22%) of CCP3+ participants developed IA ('converters') at a median of 509 days of follow up. 79% of them met 2010 ACR/EULAR criteria at time of IA identification.
- At baseline, converters reported longer duration of morning stiffness and had higher levels of CCP3 and RFlgM compared to non-converters.
- Converters had 2 trajectories of symptoms prior to IA: 1) waxing and waning or 2) period of minimal symptoms followed by steady worsening of symptoms.
- Converters with no joint symptoms at baseline (n=5) trended towards a longer duration to developing IA compared to those with baseline symptoms (median 686 days vs 363 days, p<0.09).
- At the time of diagnosis of IA, converters had lower levels of symptoms, DAS28CRP and CCP3 than patients with EarlyRA identified through standard clinic referrals

CONCLUSIONS:

- For ACPA-positive individuals without IA at baseline, self-reported morning stiffness and high levels of CCP3 and RFlgM are associated with developing inflammatory arthritis.
- These findings contribute to understanding the natural history of RA and building prediction models for future disease as well as to correlate biomarker changes with symptoms.
- Lower disease activity in 'converters' to IA compared to EarlyRA could indicate that prospective follow-up of ACPA+ individuals can identify IA at a time point where disease activity and CCP3 levels are less than in standard referral patterns, perhaps indicating a stage of disease more responsive to therapy.

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