LATE ONSET RHEUMATOID ARTHRITIS

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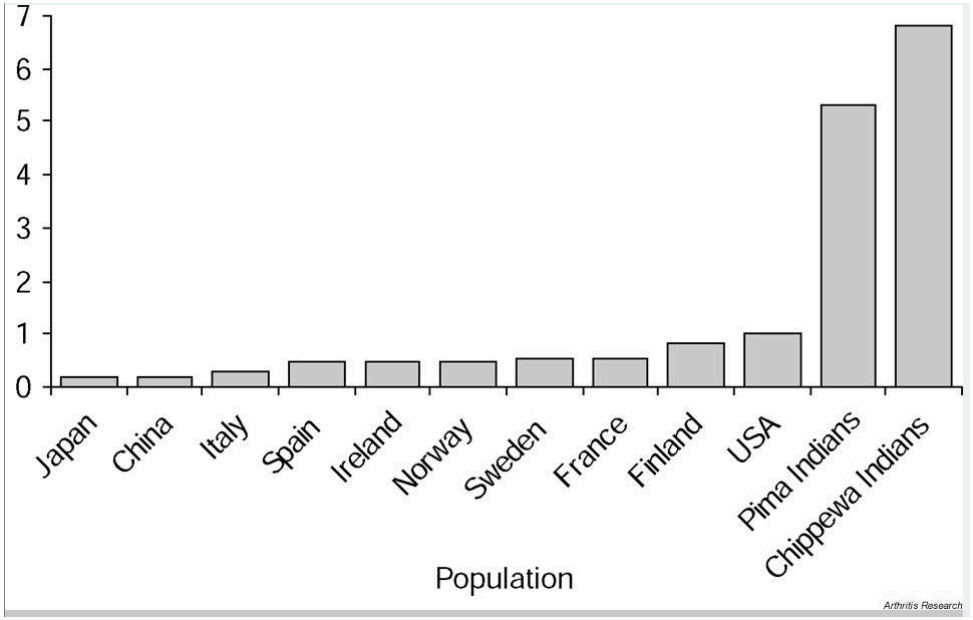
WHAT IS IT?

- Rheumatoid Arthritis is a chronic systemic disease that occurs when an individual's immune system attacks the synovium (lining of the membranes that surround the joints) resulting in inflammation. [1]
- RA causes painful swelling and stiffness, which can result in bone erosion and joint deformity. [1]
- The symptoms and progression vary in severity across individuals.[1]
- The leading hypothesis for the cause of RA is that RA is the result of an environmental exposure or "trigger" in genetically susceptible individuals.[1]

WHO IS AFFECTED?

- RA affects ~0.3 – 1% of the world population[2]
- RA is more common in women and in developed countries[2]
- Native American-Indian populations have the highest recorded occurrence of RA[3]



RA IN THE ELDERLY

- RA can occur at any age but onset is most common between ages 40 - 60[1]
- RA can be classified into two subtypes:
  - Young-onset Rheumatoid Arthritis (YORA)
  - Late-onset Rheumatoid Arthritis (LORA)
    - ≥ 60 years old at onset [4, 5, 6, 7,] or
    - ≥ 65 years old at onset [8, 9, 10, 11,]
- RA studies have focused on RA progression & age at disease onset has been implicated as a predictor for disease activity and disability [4, 12]

TREATMENT

GOAL: To achieve remission by preventing joint damage and disability

Treatment options include[1]:

- **Nonsteroidal anti-inflammatory drugs (NSAIDs)** relieve pain and reduce inflammation.
- **Steroids** (corticosteroid medications) reduce inflammation and pain and slow joint damage.
- **Disease-modifying antirheumatic drugs (DMARDs)** slow the progression of RA and save the joints and other tissues from permanent damage.
- **Biologic DMARDs** (aka biologic response modifiers) target parts of the immune system that trigger inflammation that causes joint and tissue damage.

DIFFERENCES IN TREATMENT

- Studies have found that LORA patients receive corticosteroids more frequently than DMARDs compared to YORA patients [11, 12] despite identical disease duration and comparable disease severity and activity [6]
  - Tutuncu et al. found that 31% of patients with LORA were on multiple DMARD treatment and 25% on biological DMARD treatment compared to those with YORA (40.5% and 33.1%, respectively; $p<0.0001$).
- While the role of DMARDs and bDMARDs has been well established in middle-aged RA patients[14] observational studies on the long-term safety of bDMARDs in elderly RA patients have been inconclusive [12]

WHY WOULD TREATMENT EFFECT BE DIFFERENT IN THE ELDERLY?

- Increased risk of infection due to increasing comorbidities [4, 14]
  - diabetes mellitus
  - cardiovascular disease
  - liver disease
  - Chronic lung disease
  - Frailty

DISEASE COMPOUNDED BY AGE FACTORS MAY HAVE WORSE PROGNOSIS

Table 1 Comparison of main demographic and clinical features. Results are shown as mean ± SD except when noted. *DMARDs* disease-modifying antirheumatic drugs

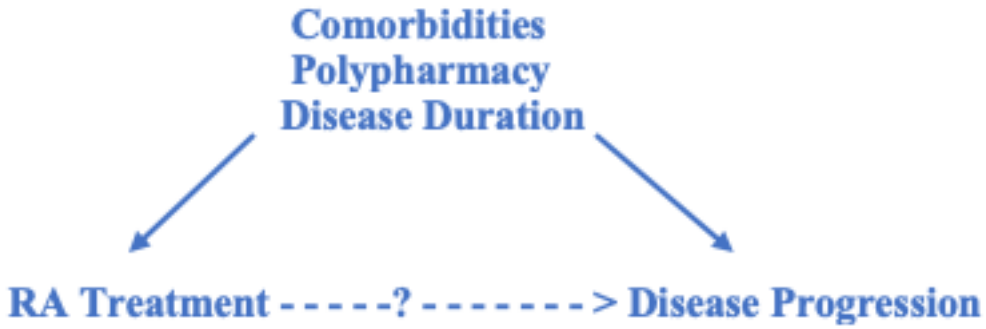
Feature	EORA	LORA	*p*
Age at disease onset	35.5 ± 7.2	73.1 ± 5.7	NS
Disease duration (months)	53.6 ± 18.5	54.1 ± 19.4	NS
Female (%)	68	66	NS
Anemia (%)	27	34	NS
IgM-RF (%)	55	60	NS
ANA (%)	48	31	NS
Extra-articular disease (%)	3	6	NS
Number of DMARDs used	2.5 ± 1.4	1.9 ± 1.3	0.050
Number of combined DMARD treatments	0.8 ± 1.1	0.3 ± 0.6	0.010
Number of hospitalizations	0.3 ± 0.6	0.8 ± 0.8	0.003
Number of surgical interventions	0.06 ± 0.2	0.1 ± 0.3	NS

Table 3 Comparison of main outcome parameters. Results are shown as median (interquartile range) except when noted. *ACR-FC* ACR functional classification, *M-HAQ* modified Health Assessment Questionnaire

Feature	EORA	LORA	*p*
ACR-FC (mean ± SD)	1.9 ± 0.9	2.2 ± 0.9	NS
M-HAQ	0.13 (0–0.6)	0.4 (0.13–1.2)	0.007
Number of damaged joints	0 (0–2)	1 (0–5)	0.02
Erosive disease (%)	52	71	NS
Joint erosion score	1.3 (0.7–6)	4 (1.7–16.3)	0.02
Joint narrowing score	8 (2–19.3)	17 (10.3–38.3)	0.001
Total Sharp Index score	11.7(2.3–22.3)	22(13–53.7)	0.001

- Note: EORA (N=31) LORA (N=35)

METHODS CHALLENGE: UNMEASURED CONFOUNDING



- Comorbidities are not consistently available in studies [4]
- Limited information on medications in cross-sectional studies[4,15] - could provide information on polypharmacy[15]
- Disease duration - it has been noted that longer disease duration is associated with reduced response to treatment in patients.[7]

A TREATMENT DEFICIT

- Greater functional impairment can occur in older patients bc they have a smaller functional reserve than then younger patients. [11]
- "Rheumatologists are less likely to treat LORA patients with DMARDs within 3 months from disease onset compared with YORA"[12]
  - Studies have shown that patients with longer disease durations do not respond to treatment to the same extent as patients with early disease [12]

Public Health Implication

- Treatment difference may have important implications for the prognosis and development of comorbidities in the long term

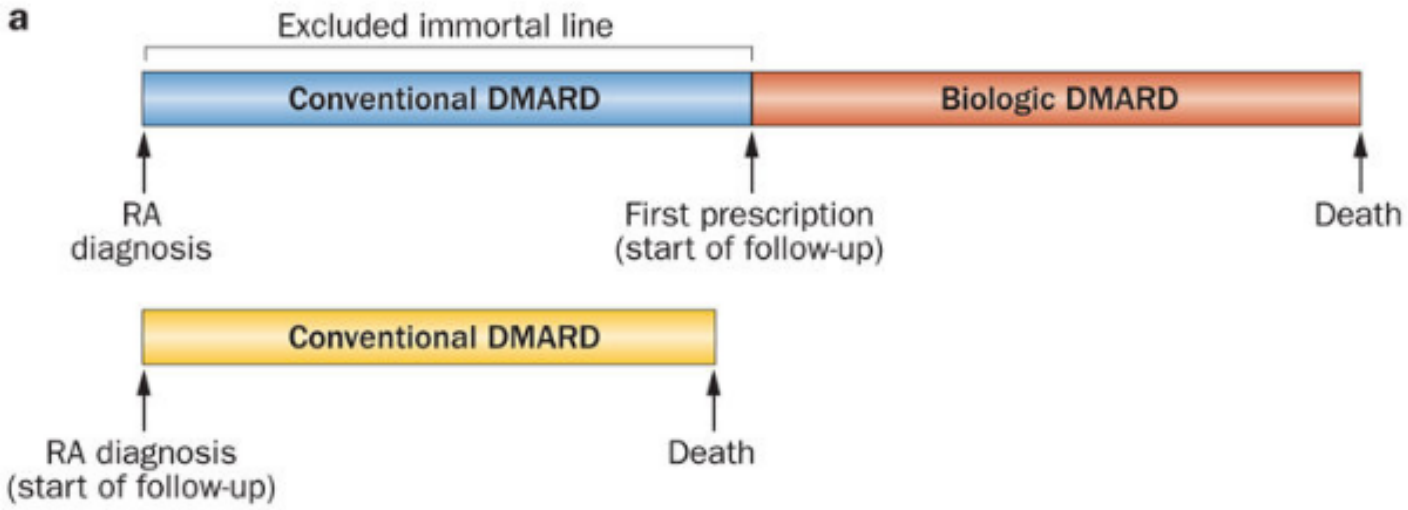
DISCUSSION QUESTIONS

- Given the lack of available research of bDMARDs use in the elderly, should LORA patients receive the same treatment as YORA patients at the onset of disease?
- What threshold for potential comorbidity or other undesirable side effects of treatment should be used to determine whether or not patients with LORA receive the same treatment as YORA patients?

NOW CONSIDER THIS:

- One showed that "toxicity due to methotrexate and biological agents was very low in all patients studied, regardless of age. However, patients with LORA were treated significantly less often with biological agents compared with YORA patients."

ANOTHER CHALLENGE: SELECTION BIAS



- Immortal time bias
- Loss to follow-up due to adverse drug effects

THANK YOU