Practical Takeaways

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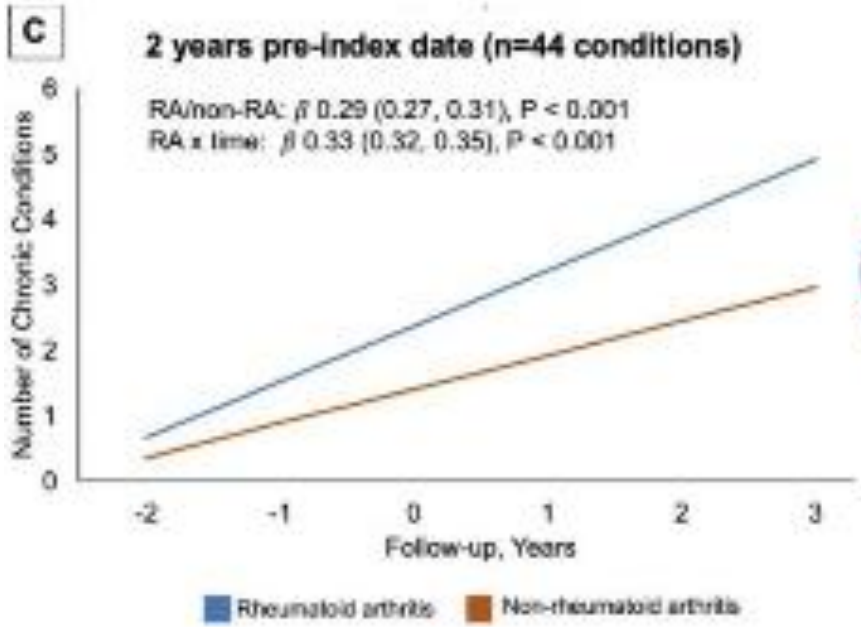
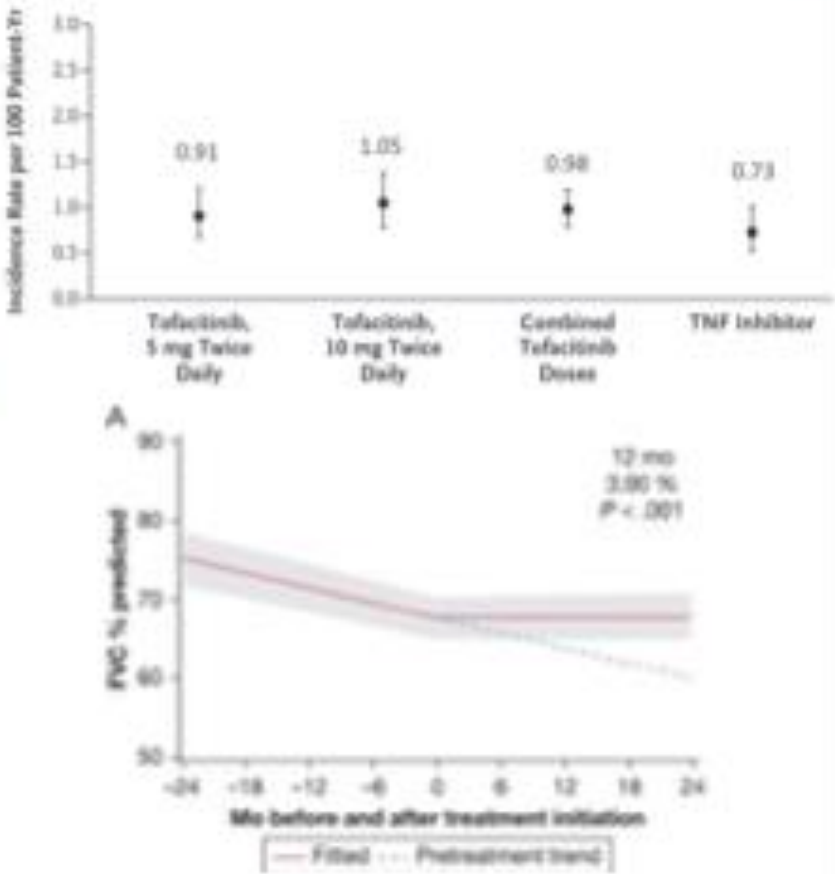
RA is Not a Joint Disease

RA → Chronic Conditions



Multimorbidity Web

DMARDs Have Systemic Impact



England BR et al. *Ann Rheum Dis* 2021;80:286-292. England BR. *Rheum (Oxford)* 2023; 62:SI242-SI251. Ytterberg SR et al. *NEJM* 2022;386:316-326. Matson SM et al. *Chest* 2023;163861-869.

Having More Tender than Swollen Joints is associated with Worse Function and Work Impairment in Patients with Early RA

CANADIAN EARLY ARTHRITIS COHORT (CATCH)

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Introduction

- Early RA patients may present with more tender than swollen joints (tender-swollen joint count difference(s) (TSJD))
- Better understanding of impacts of TSJD on function and work-impairment, and whether associated impacts vary by joint type (large vs small joints) may help identify patients at risk for worse outcomes

Objectives

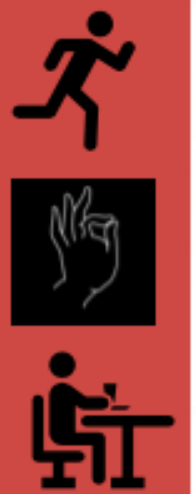
- To estimate the impact of TSJD on function and work-impairment in the first year following RA diagnosis
- To evaluate whether associations may vary by joint type (small vs. large)

Methods

- Used baseline, 3-, 6- and 12-month data from patients with active, rheumatologist-diagnosed, early RA (symptoms<1 year, CDAI>2.8) enrolled in the Canadian Early Arthritis Cohort (CATCH) study
- Separate analyses were performed for 6 large joints (shoulders, elbows, knees) and 22 small joints (wrists, MCPs, PIPs)
- Outcomes:
  - General function (MDHAQ)
  - Upper extremity (UE) function (Neuro-QoL UE index)
  - Work Productivity and Activity Impairment from RA (WPAI-RA)
- Mean (95%CI) changes in T-scores were calculated for a linear increase of 1 in TSJD
- Adjusted associations were estimated using multivariable linear mixed effects models

Conclusions

- **Having more tender than swollen joints is common in patients with early RA**
- **More tender than swollen joints, especially large joints, is associated with worse function and work-impairment**
- **Clinicians should be alerted to the need for earlier and targeted treatment in this higher-risk group**



Patients Experience Worse Function and Work-Impairment with High TSJD*

All 28 joints		Large joints		Small joints	
Mean-change**	95% CI	Mean-change**	95% CI	Mean-change**	95% CI
Physical function (MDHAQ 0-10)					
0.10	(0.08, 0.13)	0.42	(0.33, 0.50)	0.08	(0.05, 0.11)
Upper Extremity Function (Neuro-Qol upper extremity T-score 0-100)					
-0.59	(-0.76, -0.43)	-2.30	(-2.81, -1.79)	-0.49	(-0.67, -0.30)
Work and Activity Impairment (WPAI-RA 0-100%)					
Percent overall work impairment due to RA					
1.95	(0.85, 3.05)	6.67	(3.52, 9.83)	1.79	(0.45, 3.13)
Percent activity impairment due to RA					
1.67	(0.99, 2.36)	7.30	(5.10, 9.40)	1.32	(0.53, 2.10)

*Multivariate mixed effects models adjusted for time, age at baseline, sex, education, current smoker at baseline, RDCI at baseline, osteoarthritis/back pain at baseline as well as time variant treatment at previous visit of oral steroids, methotrexate and advanced therapy

** Mean-changes show change in outcomes averaged over time for linear increase in TSJD of 1 TSJD tender-swollen joint difference; CI confidence interval; MD-HAQ Multi-dimensional Health Assessment Questionnaire; WPAI Work Productivity and Activity Impairment Questionnaire

Results

- Data were from 547 early RA patients (70% female, mean (SD) age 56 (15) years)
- Patient prevalence of TSJD > 0 decreased from 52% to 32% over one year
- TSJD was associated with worsening of general function, upper extremity function and work-impairment (mean-change in scores, Table)
- Large joint-TSJD were associated with greater worsening of all outcomes (Table)

Summary

- Over half of early RA patients have more tender than swollen joints, which persists in a third of patients.
- An increased TSJD score is associated with worse general function, upper extremity function and work-impairment over 1-year of follow-up
- Having more tender than swollen large joints was associated with the worst outcomes
- Elevated TSJD, especially in large joints, may help identify at-risk patients
- There is a need for early identification and intervention of TSJD to prevent its impact on patients

CATCH INVESTIGATORS: Pooneh Akhavan, Claire Barber, Lillian Barra, Louis Bessette, Gilles Boire, Vivian Bykerk, Ines Colmegna, Sabrina Fallavollita, Derek Haaland, Paul Haraoui, Glen Hazlewood, Carol Hitchon, Shahin Jamal, Raman Joshi, Ed Keystone, Bindee Kuriya, Peter Panopalis, Janet Pope, Carter Thorne, Edith Villeneuve, Michel Zummer.

Increased thromboembolic risk during anti-rheumatic treatment: fact or fiction?

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Objectives
To study the activation of the coagulation system of rheumatoid arthritis (RA) patients and assess changes during treatment with tumor necrosis factor blockers (aTNF) and Janus kinase inhibitors (JAKi).

Methods
Biomarkers for the coagulation system, including D-dimer, fibrinogen, pro-thrombin time (PT), activated partial thrombin time (aPTT), prothrombin fragment 1 + 2 (F1+2), thrombin-antithrombin complex (TAT), activated factor IX – antithrombin complex (FIXa:AT) and von Willebrand factor (vWF), were prospectively measured in 83 RA patients treated with aTNF and 38 RA patients with JAKi. Data were collected at baseline, after 1, 3, and 6 months.

Results
Mean age was 57 (±14) years, 76% was female. Mean DAS28-CRP at baseline for aTNF-users was 3.6 (±1.3) and 4.1 (±1.4) for JAKi-users, steadily declining in aTNF users, while decreasing in JAKi users with an intermittent peak at 3 months. Baseline coagulation markers levels were comparable between groups. D-dimer and fibrinogen levels significantly declined in aTNF-users (-0.31mg/L, p = 0.01 and -0.71g/L, p <0.001, respectively), while TAT significantly increased after 6 months follow-up (1.46ug/L, p = 0.03). In JAKi-users, only vWF showed a significant decline during the 6 months follow up (-37.41%, p<0.001).

Conclusion
Overall, the pro-thrombotic tendency in active RA declined during effective treatment with both aTNF as well as JAKi. The transient increase of coagulation activation in JAKi users at three months coincided with increased disease activity. Altogether, our data suggests that an increased VTE risk in the first six months due to either treatment with aTNF or JAKi is unlikely.

Pro-thrombotic tendency in active RA decreased during aTNF and JAKi treatment

Increases in coagulation markers coincided with increased inflammation

Increased VTE risk in the first 6 months due to aTNF/JAKi treatment seems unlikely

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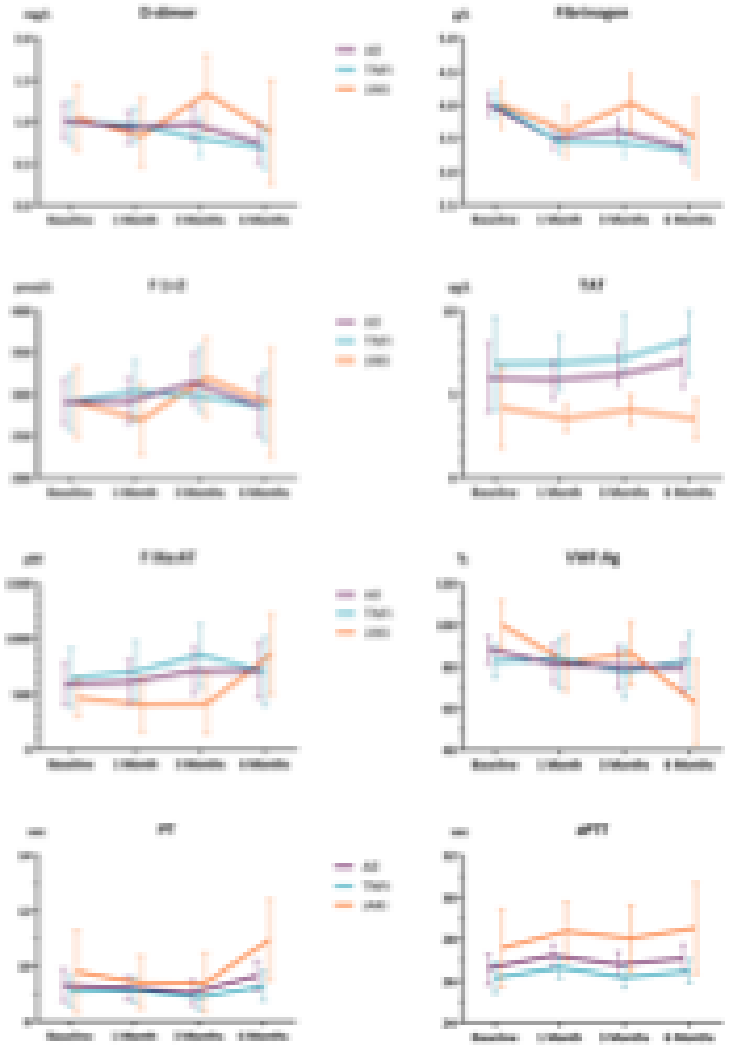

Figure 1: Progression of mean values with 95% confidence interval of coagulation markers. In every graph purple indicates all patients, blue indicates aTNF-users, orange indicates JAKi-users. For every figure, number of patients per timepoint are (aTNF/JAKi): Baseline 83/38, 1 month 54/28, 3 months 47/21, 6 months 39/10.

Risk factors associated with venous thromboembolism in rheumatoid arthritis in clinical practice

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OBJECTIVE

To identify classical or disease-related risk factors of VTE in RA patients in clinical practice.

CONCLUSION

History of VTE is the strongest risk factor of the occurrence of VTE in patients with RA.

Recent hospitalization and surgery are precipitating factors of VTE.

JAKi should be used with caution in patients with risk factors for VTE.

JAK INHIBITORS IN RHEUMATOID ARTHRITIS-INTERSTITIAL LUNG DISEASE. NATIONAL MULTICENTER STUDY OF 73 PATIENTS, 55 OF BARICITINIB

P2174

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BACKGROUND/PURPOSE

Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA). Abatacept and Rituximab are the recommended drugs. JAK inhibitors (JAKi) have demonstrated efficacy in RA. However, in clinical trials patients with active ILD were usually excluded. Moreover, a warning on ILD toxicity is included in SmPC (Summary of Product Characteristics) with tofacitinib (TOFA). Nonetheless, evidence on efficacy of JAKi in RA-ILD is growing. The objective of the study was to assess a) the effectiveness and b) the safety of JAKi in AR-ILD patients.

METHODS

National multicenter study of 73 RA-ILD patients on treatment with JAKi. We analyzed from baseline the following outcomes: a) forced vital capacity (FVC), b) diffusing capacity of the lungs for carbon monoxide (DLCO), c) chest high resolution computed tomography (HRCT), d) dyspnea (modified Medical Research Council scale), e) arthritis activity (DAS28-ESR or clinical records), and f) sparing corticosteroids effect.

RESULTS

We studied 73 patients (50 women/ 23 men; mean age 66 ± 10 years) from clinical practice on treatment with JAKi [Baricitinib (BARI)= 55 (74%), TOFA= 8 (11%), Upadacitinib (UPA)= 8 (11%), Filgotinib (FILGO)= 2 (3%)]. Baseline demographic and clinical characteristics are shown in Table 1. All patients had received disease-modifying antirheumatic drugs (DMARDs) before JAKi [Methotrexate (63; 86%), Leflunomide (46; 63%), Sulfasalazine (19; 26%), Hydroxychloroquine (16; 22%), Abatacept (47; 64%), Tocilizumab (26; 36%) and Rituximab (16; 22%)].

Since most patients were on BARI we focused on this group (n=55). Median [IQR] ILD duration up to BARI initiation was of 29 [15-64] months. Mean baseline values of FVC and DLCO (% predicted) were 88±27 and 69±20, respectively. Patients were followed-up for a mean of 36 ± 23 months. The evolution of FVC and DLCO remained stable during the first 12 months (Figure 1). At the end of the follow-up, available chest HRCT images improved/ stabilized in 76% of patients. Stabilization or improvement of dyspnea was found in 95% of patients. Most patients showed articular remission or low activity. BARI was withdrawn in 22 (42%) patients due to articular inefficacy (n=15), lung inefficacy (n=4), development of hypersensitivity pneumonitis (n=1), and appearance of brain cancer (n=1).

CONCLUSION

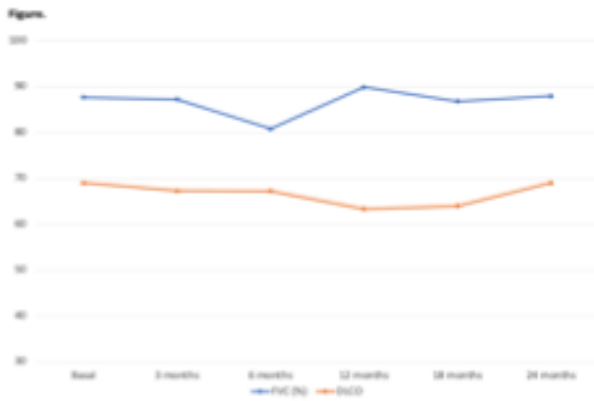
JAKi, especially BARI, may be useful and safe in controlling the course of both pulmonary and joint disease in RA-ILD patients, even in refractory cases.

Table 1. Baseline characteristics of RA-ILD patients treated with JAKi.

	RA-ILD with JAKi (n=73)
Age, years mean±SD	66 ± 10
Women, n (%)	50 (69)
Smoker ever, n (%)	47 (64)
Time since ILD diagnosis, months, median [IQR]	35 [15-64]
RF / ACPA, n (%)	69 (95) / 69 (95)
FVC (% of the predicted), mean±SD	90 ±26
DLCO (% of the predicted), mean±SD	61 ± 16
UIP-like fibrotic pattern on HRCT, n (%)	36 (51)
Joint activity n (%)	40 (56)
Type of JAKi, n (%)	
Baricitinib (BARI)	55 (74)
Tofacitinib (TOFA)	8 (11)
Upadacitinib (UPA)	8 (11)
Filgotinib (FILGO)	2 (3)
Previous immunosuppressive therapy, n (%)	
Conventional / biologic DMARD	73 (100) / 62 (85)
Concomitant immunosuppressive therapy, n (%)	32 (44)
Concomitant antifibrotic therapy, n (%)	6 (8)

ACPA, anti-citrullinated protein antibodies; DLCO, diffusing capacity of the lung for carbon monoxide; DMARD, disease-modifying antirheumatic drug; FVC, forced vital capacity; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; JAKi, JAK inhibitor; RA, rheumatoid arthritis; RF, rheumatoid factor; UIP, usual interstitial pneumonia.

Figure. Evolution of pulmonary function tests (mean % of the predicted FVC and DLCO) in RA-ILD patients with BARI therapy at baseline and 24 months.



Bone marrow edema in MRI is more associated with rapid radiographic progression than clinically relevant radiographic progression

Abstract Number 1300

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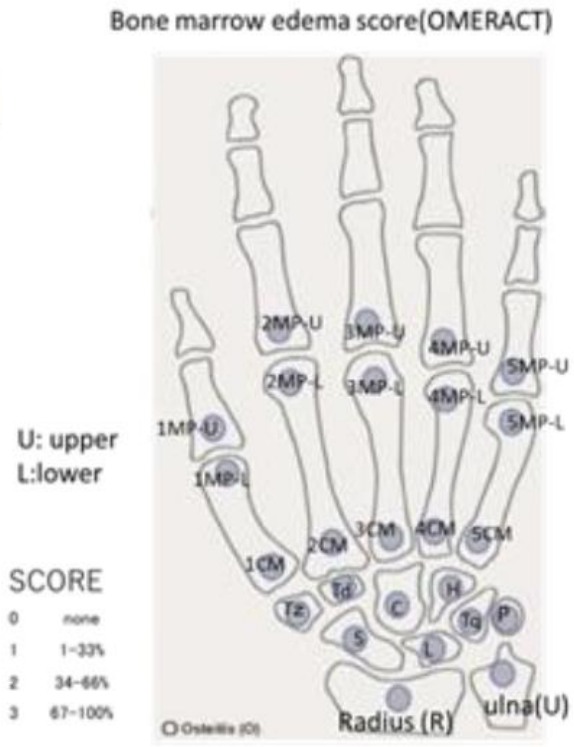
Figure 1



Discussion

This study highlights the importance of BE in the pathogenesis of RRP. Regarding RRP, the following strategies are ongoing:

1) The early induction of biologics in RRP by assessing BE may be effective (RRP rescue study)- ARD 77(supple 2):607,2018.
2) BE may be a predictor for RRP in JAK inhibitor treated RA patients- Eular conference, Abstract AB206, 2023.
3) The application of a BE scoring system in X-ray film derived artificial intelligence (AI) in RRP rescue study- Eular conference, Abstract AB1528,2023.

We anticipate that a new AI system capable of detecting bone marrow edema through hand X-ray films could be a useful tool for diagnosing RRP. The ongoing trial aims to assess the effectiveness of this system in RA patients with MRI-detected BE, both in other areas of Japan and in foreign countries. We would greatly appreciate the cooperation of countries worldwide for this study.

(Conclusion)

BE may be a possible prognostic factor for RRP and more associated with RRP than CRRP.

Hydroxychloroquine: Update to Neuropsychiatric Reactions

- Multiple reports of neuropsychiatric reactions
- Updated Warnings and Precautions
  - Onset: within the first month after the start of treatment with hydroxychloroquine.
  - Population: reported in patients with and without a prior history of psychiatric disorders
  - Time for symptoms to abate: several weeks off drug because of the long half life
- Updated Adverse Reactions
  - Adverse reactions added: depression, hallucinations, anxiety, agitation, confusion, delusions, paranoia, mania and sleep disorders (insomnia, night terrors, nightmares)

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Does Pizza Consumption Favor an Improved Disease Activity in Rheumatoid Arthritis?

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Chun-De Liao, Academic Editor

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Conclusions

To our knowledge, this is the first study investigating whether a higher consumption of pizza (and related food items/groups) could improve the composite, internationally recognized measures of RA disease activity. This study was conducted in Italy—the birthplace of pizza, and second-top consumer country of pizza worldwide—where access to the best pizza ingredients in their freshest state, and certified recipes provide the greatest likelihood of identifying the protective anti-inflammatory and antioxidant effects that pizza is believed to exert. In line with the expected results, participants consuming half a pizza >1 time/week (vs. ≤2 times/month) did report beneficial effects on disease activity, both in the overall analysis, and when the more severe RA forms were considered. These beneficial effects were likely driven by mozzarella cheese and, to a lesser extent, by olive oil, even though we were unable to assess the possible contribution of tomato sauce. These results require confirmation based on properly designed cohort studies that implement an assessment of diet with reproducible and valid tools, and employ internationally recognized measures of RA activity, to find the expected small dietary effects, and to adjust for the large set of confounders typical of RA. As our results are mostly based on patients with optimal disease control, the extent of the beneficial effect observed could be even greater if RA patients with active disease were primarily considered within these studies.

First-Ever Rheumatoid Arthritis Guideline on Integrative Health Recommends Exercise

PUBLISHED 01/12/23 BY BARBARA BRODY

The strongest recommendation: get regular exercise.

Key Takeaways

- New ACR Guideline addresses integrative interventions for rheumatoid arthritis.

- Regular exercise listed as strongest recommendation, type frequency, intensity, and duration not yet formally defined.

- Conditional recommendations favor the Mediterranean diet, physical therapy, and massage.

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Conditional Recommendations

- According to the ACR, there is some support in favor of:

✓A Mediterranean-style diet
✓Aerobic exercise, aquatic exercise, resistance exercise, and mind-body exercise
✓Physical therapy and occupational therapy
✓Acupuncture and massage
✓Splinting, bracing, and/or taping
✓Work-related modifications or rehabilitation

Meanwhile, the authors conditionally recommended *against*:

- Dietary supplements
- Chiropractic therapy
- Electrotherapy

Consistent Exercise

- The only non-pharmacologic treatment for rheumatoid arthritis that ACR strongly recommends is consistent engagement in exercise.

- Conditional recommendations were given for aerobic exercise, water exercise, resistance exercise, and mind-body exercise, such as yoga, tai chi, and qigong.

Rehabilitation

- ✓A comprehensive occupational therapy (OT) and physical therapy (PT) program are conditionally recommended for rheumatoid arthritis management.
- ✓**Noted individualized programs include:**
- ✓hand therapy exercises
- ✓splinting, orthoses, compression, bracing, and/or taping
- ✓joint protection techniques
- ✓activity pacing, energy conservation, activity modification, and/or fatigue management
- ✓assistive devices
- ✓adaptive equipment
- ✓environmental adaptations
- ✓vocational rehabilitation, including work site evaluations and/or modifications

Table I: Non-Pharmacologic Treatment Recommendations for Rheumatoid Arthritis

Exercise	Rehabilitation	Diet	Other
regular exercise (++)	OT (+), PT (+)	Mediterranean (+)	self-management (+)
aerobic exercise (+)	hand therapy (+)	other formal diet (–)	CBT/mind-body (+)
aquatic exercise (+)	splint, orthotics (+)	supplements (–)	acupuncture (+)
resistance exercise (+)	joint protection (+)		massage (+)
mind-body exercise (+)	assistive devices (+)		thermal (+)
	vocational/work (+)		electrotherapy (–)
			chiropractic (–)

++ (double plus sign) Strong recommendation
+ (plus sign) Conditional recommendation
– (negative sign) Conditional recommendation against

Practical Application of Integrative Interventions for Rheumatoid Arthritis

Patient 1

- A 43-year-old female had abrupt onset of polyarthritis involving her fingers, wrists, knees, and feet a few months prior and was soon thereafter referred to a rheumatologist and diagnosed with rheumatoid arthritis. Her past medical history was unremarkable. She smokes, but is active, walking a few times weekly, which she has been unable to do for the past few months.

- Her laboratory tests included a positive anti-CCP antibody and an elevated CRP, and otherwise were unrevealing. She initially responded well to methotrexate and folic acid. After 8 months of this therapy, she reported little pain, and was back to full-time work, but complained of persistent fatigue, difficulty getting back to exercise, and some persistent swelling in her wrists.

How to Apply the New ACR Guidelines

- This is a critical decision-making time for this patient.
- It is likely that her RA, although improved with methotrexate, is still active.
- A careful reevaluation, including acute phase reactants and appropriate joint x-rays may reveal persistent RA, and the rheumatologist likely would add another disease modifying agent to the methotrexate, such as a tumor necrosis factor or a JAK inhibitor.

This is also an important time to review RA non-pharmacologic management.

- Hopefully, this has already been discussed at her earlier appointments but often specialists may wait to see what the treatment response has been to medication before focusing on non-pharmacologic management.
- The wrist swelling may improve with bracing or other devices and the patient should be referred to OT.
- The inability to return to exercise must be addressed and she should be referred to PT, with consideration of an alternative exercise, such as aquatics and/or mind-body therapy, being initiated.

- Although smoking cessation is not considered as specific to RA management, there is strong evidence that it is a risk factor for RA and for poor outcome in RA and it should be addressed.

- The fatigue may be related to persistently active RA but contributing factors, including sleep, stress, and mood, should be discussed and referral considered for cognitive-behavioral therapy.

Patient 2

- A 58-year-old male, a high school mathematics teacher, has a 15-year history of RA. He has been on various disease-modifying medications, as prescribed by his rheumatologist, who told the patient that the RA is currently stable. At his last rheumatology visit, the physical examination revealed no swollen or inflamed joints but some deformities of his fingers and toes.

- The laboratory tests were unremarkable, and no changes were made in his medications. This patient has a 5-year history of hypertension, adult-onset diabetes, and obesity. During the first 10 years of treatment for his RA, he had worked with a physical therapist and had been exercising regularly.

- During the past 5 years, he has not seen the physical therapist and stopped doing regular exercise.
- Currently, he is unable to walk much because of foot and ankle pain, finds it difficult to even stand in the classroom, and is worried that he won't be able to continue working much longer.

How to Apply the New ACR Guidelines

- This patient has long-standing, slightly deforming RA that has been stable with no recent change in medications.
- However, his work ability and overall quality of life, as well as his medical co-morbidities, have become increasingly problematic.

- This patient would benefit from a comprehensive, multidisciplinary, nonpharmacologic reevaluation and treatment.
- Physical and occupational therapy may suggest simple walking/standing modifications, and use of orthotics and bracing.

- The lack of exercise, weight gain, diabetes, and hypertension will require careful and frequent attention by the primary care and rheumatology team.
- Aquatic exercise may be a good way to get him back to regular exercise, and more tolerable than weight-bearing exercise.

- His increasing difficulty with functioning at work should be reviewed by OT, who will assess his workplace and suggest ways to improve his function.
- Vocational counseling should be instituted, including discussion of work-related modification and possible disability.

Practical Takeaways

The use of non-pharmacologic therapy for rheumatoid arthritis should complement to pharmacologic management.

More specifically, care should be implemented along with pharmacotherapy, rather than waiting for medication response.

THANK YOU

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