Aging in place: Management of OA

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Disclosures

• I will mention a few brand names and some non-FDA approved drugs and drugs under study
• My funding sources include NIH/NIAMS, CDC, Rheumatology Research Foundation
• Editorial Board of *Osteoarthritis & Cartilage* and a member of the ACR and OARSI
• Consultant to GSK
• I attended Overland HS in Aurora and got my BA from The Colorado College
Overview

- Osteoarthritis as a common chronic condition
- OA and aging, mobility, and independence
- The Johnston County OA Project overview
- OA management guidelines summary
- The OA Action Alliance: a resource for patients and providers
- Future directions in OA management
OA is a common chronic condition
Prevalence of OA

- Arthritis is the most common cause of disability (1) in the US
  - MSK disorders are 2nd globally
- OA is the most common form of arthritis
- Over 50 million in the U.S. were affected as of 2012 (2), projected >75 million by 2040
- Numbers continue to increase due to aging and obesity trends

Joint replacement for OA

• Most joint replacements are done for OA.
• Rates of joint replacement are on the rise and will soon outpace capacity.

http://hcupnet.ahrq.gov/HCUPnet.jsp
OA is a key factor in aging, mobility, and independence
Aging and OA (Aging ≠ OA)

- **Age-related factors**
  - “Inflammaging”
  - Reduced muscle mass
  - Increased fat mass
  - Low grade inflammation
  - Altered mechanical properties of cartilage, meniscus, and ligaments
  - Altered function and composition of bone

- **Normal aging**
  - Intact but thin cartilage
  - Cartilage cross-linking by AGEs
  - Increased chondrocyte density overall
  - Reduced matrix activity
  - Decreased bone mass and density

- **OA**
  - Fibrillation of cartilage surface and focal loss of GAGs
  - Clusters of chondrocytes near tissue damage
  - Increased matrix activity
  - Synovial inflammation
  - Subchondral bone thickening

Burden of chronic disease on HRQL

- 5849 UK participants, mean age 74, ½ male, 1/3 with one and ¼ with 2 or more morbid conditions
- The greatest and clinically significant negative impacts on HRQL were seen for:
  - osteoarthritis (-0.08)
  - neurologic disease (-0.17)
  - depression (-0.27)
- Smaller declines were seen from htn, CHF, cancer, RA, diabetes, and CAD

OA and mobility: The Ontario Hip and Knee Cohort

• >18,000 respondents, median age 68, 60% female, median BMI 26
  – 10% had hip, 15% had knee, 16% had hand OA
  – ¼ reported walking limitation
• Over 13-year follow-up, 32% had 1+ CV event
  – Dose-response relationship between # joints and CV risk
  – Fully attenuated by adjustment for walking limitation

63% of people with knee/hip OA had walking limitations compared with 17% of those without OA
OA and mobility: The Ontario Hip and Knee Cohort

- Among those with hip or knee sx OA and self-reported physician diagnosed diabetes (n=359)
  - Mean age 71, 2/3 women, median of moderate to severe walking disability at baseline
- Over 6 years follow-up, ½ were hospitalized for a diabetes complication
- Time to complications was shorter for those who were older, had pre-existing CV disease, and greater difficulty walking including use of walking aids

Multimorbidity, OA, and participation restriction

- Adults from UK, median age 65, 2/3 female, with lower extremity OA (n=1053)
- 17% had incident participation restriction at 3 years
  - Limitations in social activity, volunteering, working, etc.
- **2-3x higher odds of PR** with multimorbidity
- Locomotor disability and depression had the greatest mediation effect and are potentially modifiable

Mobility outside the home


- 1802 UK adults, mean age 66, 56% female
- 13% had restricted mobility (RM) at 3-year follow-up
- Associated with health and environmental factors
- Associations between health conditions and RM were greater in the presence of environmental factors

<table>
<thead>
<tr>
<th>Frequency of the onset of restricted mobility outside the home at 3-year follow-up</th>
<th>Crude</th>
<th>Associations adjusted for confounders*</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>OR (95% CI)</td>
<td>Adjusted OR (95% CI)</td>
</tr>
<tr>
<td>Walking disability and hills and steep slopes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No walking disability, no hills and steep slopes</td>
<td>6.8</td>
<td>1</td>
</tr>
<tr>
<td>Walking disability, no hills and steep slopes</td>
<td>29.3</td>
<td>5.71 (4.00 to 8.13)</td>
</tr>
<tr>
<td>No walking disability, hills and steep slopes</td>
<td>29.2</td>
<td>5.69 (3.69 to 8.78)</td>
</tr>
<tr>
<td>Walking disability, and hills and steep slopes</td>
<td>47.9</td>
<td>12.67 (8.05 to 19.94)</td>
</tr>
</tbody>
</table>
Environmental barriers to participation

- Data from MOST (n=322): associations between environmental barriers (Home and Community Environment Q) and participation restriction (Late Life Disability Index) in those with/at risk for knee OA
  - Mean age 70, 93% white, 69% female
- 18% had developed participation restriction @ 30mo, increasing to 27% at 60mo
- Those with high community mobility barriers* had 2x risk of participation restriction at 5 years
  *Uneven sidewalks, lack of parks, benches, curb ramps

Long term value of improved mobility

- Combined data (clinical trial and 2012 MEPS) to model the effects of improved QoL and mobility on health economic outcomes
- Compared status quo to improvement of ~550 steps/day
- Over 18-year simulation, improved mobility resulted in:
  - 7.4 million fewer patient years of ADL limitations
  - 6% fewer patients each year with ADL limitations
  - Medical savings of $44 billion (over half to Medicare)
  - 2.8% reduction in nursing home utilization
  - 1.2 million employed patient-years, $78 billion in earnings
  - A total “value to society” of ~$482 billion

Summary

• Aging and OA are related but not synonymous
• OA along with other comorbidities reduces QoL
• Reduced mobility due to OA contributes to morbidity and mortality, including participation restriction
• Restricted mobility and participation restriction are associated with environmental factors
  – Poor walking conditions, unsafe, lack of seating
• Modification of these factors could improve individual and societal outcomes
The Johnston County OA Project
The Johnston County OA Project

Dr. Joanne Jordan, PI 1990-2017

Drs. Amanda Nelson and Yvonne Golightly, Co-PIs 2017-
The Johnston County OA Project

- prospective, population-based cohort study
- non-institutionalized adults 45+ years
- African American and white, men and women
- Began in 1990 and has involved more than 4000 individuals over ~25 years
- follow-up approximately every 5 years
The Johnston County OA Project

- Recruited from 6 townships
- Over-sampled African Americans
The Johnston County OA Project

• All participants provide/undergo:
  – self-report data via questionnaires
    • general health, comorbidities, function, pain, psychosocial, etc.
  – physical examination
  – radiography (hips, knees; later hands, spine, feet)
  – blood and urine samples
  – performance-based functional assessment
The Johnston County OA Project

• In general, participants:
  – range from 45 to over 90 years of age
  – have a mean BMI around 30 kg/m²
  – are 1/3 women
  – are 1/3 African American
The Johnston County OA Project

- A sampling of findings…
The Johnston County OA Project

- Population-based OA prevalence

<table>
<thead>
<tr>
<th></th>
<th>KNEE</th>
<th>Symptoms</th>
<th>Radiographic</th>
<th>Symptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>African American</td>
<td>47.1%</td>
<td>32.4%</td>
<td>19.0%</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>42.4%</td>
<td>26.8%</td>
<td>15.9%</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>HIP</th>
<th>Symptoms</th>
<th>Radiographic</th>
<th>Symptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>African American</td>
<td>37.1%</td>
<td>32.1%</td>
<td>12.0%</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>36.0%</td>
<td>26.6%</td>
<td>9.2%</td>
<td></td>
</tr>
</tbody>
</table>

The Johnston County OA Project

Annual Incidence Rates (IR) per 1000 person-years, age and sex-standardized

- Population-based OA incidence

<table>
<thead>
<tr>
<th>KNEE</th>
<th>Symptoms</th>
<th>Radiographic OA</th>
<th>Symptomatic OA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>58</td>
<td>36</td>
<td>24</td>
</tr>
<tr>
<td>African American</td>
<td>68</td>
<td>37</td>
<td>28</td>
</tr>
<tr>
<td>White</td>
<td>55</td>
<td>35</td>
<td>23</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HIP</th>
<th>Symptoms</th>
<th>Radiographic OA</th>
<th>Symptomatic OA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>38</td>
<td>24</td>
<td>17</td>
</tr>
<tr>
<td>African American</td>
<td>28</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>White</td>
<td>39</td>
<td>24</td>
<td>15</td>
</tr>
</tbody>
</table>

Lifetime risk of symptomatic OA

- Estimated risk by 85 years of age:
  - 40% for **hand** OA (higher for women and whites)\(^1\)
  - 25% for **hip** OA (no differences)\(^2\)
  - 45% for **knee** OA (higher for obesity, injury)\(^3\)

JoCo OA: OA outcomes and function

- Knee pain is more significantly associated with difficulty performing HAQ activities compared with radiographic OA\textsuperscript{1}
- A composite score of symptoms (pain/aching/stiffness in multiple sites) was strongly related to gait speed and HAQ while radiographic measures were not\textsuperscript{2}

Fall risk and OA

- Baseline to 6 year follow up, mean age 62, mean BMI 31, 1/3 African American and 1/3 men
- The odds of self-reported falls increased with an increasing number of symptomatic OA joints
- Higher odds of falls for whites, women, older participants, and those with prior falls

Table 2. Associations between number of lower-extremity joints with symptomatic OA, covariates, and future falls*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptomatic OA joints†</td>
<td>1.00</td>
</tr>
<tr>
<td>1 symptomatic OA joint</td>
<td>1.53 (1.10–2.14)</td>
</tr>
<tr>
<td>2 symptomatic OA joints</td>
<td>1.74 (1.19–2.53)</td>
</tr>
<tr>
<td>3–4 symptomatic OA joints</td>
<td>1.85 (0.96–3.55)</td>
</tr>
<tr>
<td>White</td>
<td>1.39 (1.05–1.84)</td>
</tr>
<tr>
<td>Female</td>
<td>1.36 (1.04–1.77)</td>
</tr>
<tr>
<td>Age, per year</td>
<td>1.02 (1.01–1.04)</td>
</tr>
<tr>
<td>BMI, per kg/m²</td>
<td>1.01 (0.99–1.03)</td>
</tr>
<tr>
<td>Falls at baseline</td>
<td>2.37 (1.80–3.12)</td>
</tr>
<tr>
<td>Lung problems</td>
<td>1.50 (1.12–2.01)</td>
</tr>
<tr>
<td>Neurologic problems</td>
<td>1.63 (1.07–2.49)</td>
</tr>
<tr>
<td>Narcotic use</td>
<td>1.88 (0.99–3.57)</td>
</tr>
</tbody>
</table>

* OA = osteoarthritis; OR = odds ratio; 95% CI = 95% confidence interval; BMI = body mass index.
† Symptomatic OA is defined as radiographic evidence of OA and pain, aching, or stiffness in the same joint.

## Mortality and Knee OA

<table>
<thead>
<tr>
<th></th>
<th>No Knee rOA or Pain</th>
<th>Knee Pain Only</th>
<th>Knee rOA Only</th>
<th>Both Knee rOA and Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Deaths/Cohort</strong></td>
<td>511/1271</td>
<td>264/561</td>
<td>497/1173</td>
<td>550/1177</td>
</tr>
<tr>
<td><strong>All-Cause Deaths</strong>§</td>
<td>ref.</td>
<td>0.95 (0.83-1.09)</td>
<td>1.19 (1.04-1.35)</td>
<td>1.17 (1.03-1.34)</td>
</tr>
<tr>
<td><strong>Deaths/Cohort</strong></td>
<td>189/1271</td>
<td>88/561</td>
<td>178/1173</td>
<td>222/550</td>
</tr>
<tr>
<td><strong>CVD Deaths</strong>*</td>
<td>ref.</td>
<td>0.96 (0.76-1.23)</td>
<td>1.11 (0.89-1.38)</td>
<td>1.21 (0.97-1.51)</td>
</tr>
</tbody>
</table>

§ Adjusted for birth cohort, age, sex, race, education, enrollment cohort, hip rOA, knee injury, cancer, non-steroidal anti-inflammatory drugs, hypertension, smoking, liver disease, alcohol use, depressive symptoms, physical activity, obesity, diabetes, cardiovascular disease

* Adjusted for birth cohort, age, sex, race, education, enrollment cohort, hip rOA, knee injury, cancer, non-steroidal anti-inflammatory drugs, hypertension, smoking, liver disease, alcohol use, depressive symptoms, physical activity, obesity, diabetes
# Mortality and Hip OA

<table>
<thead>
<tr>
<th></th>
<th>No Hip rOA or Pain</th>
<th>Hip Pain Only</th>
<th>Hip rOA Only</th>
<th>Both Hip rOA and Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths/Cohort</td>
<td>560/1321</td>
<td>382/787</td>
<td>509/1156</td>
<td>311/655</td>
</tr>
<tr>
<td>All-Cause Deaths§</td>
<td>ref.</td>
<td>1.04 (0.91-1.17)</td>
<td><strong>1.33 (1.17-1.51)</strong></td>
<td>1.01 (0.87-1.18)</td>
</tr>
<tr>
<td>Deaths/Cohort</td>
<td>205/1321</td>
<td>142/787</td>
<td>199/1156</td>
<td>115/655</td>
</tr>
<tr>
<td>CVD Deaths*</td>
<td>ref.</td>
<td>1.01 (0.82-1.24)</td>
<td>1.22 (0.99-1.50)</td>
<td>1.01 (0.80-1.28)</td>
</tr>
</tbody>
</table>

§ Adjusted for birth cohort, age, sex, race, education, enrollment cohort, knee rOA, hip injury, cancer, non-steroidal anti-inflammatory drug use, high blood pressure, smoking, liver disease, alcohol use, depressive symptoms, physical activity, body mass index, diabetes, cardiovascular disease

*Adjusted for birth cohort, age, sex, race, education, enrollment cohort, knee rOA, hip injury, cancer, non-steroidal anti-inflammatory drug use, high blood pressure, smoking, liver disease, alcohol use, depressive symptoms, physical activity, body mass index, diabetes
OA Management Guidelines

A systematic review of recommendations and guidelines for the management of osteoarthritis: The Chronic Osteoarthritis Management Initiative of the U.S. Bone and Joint Initiative

Amanda E. Nelson, MD, MSCR\textsuperscript{a,b,*}, Kelli D. Allen, PhD\textsuperscript{c}, Yvonne M. Golightly, PT, PhD\textsuperscript{a,d,e}, Adam P. Goode, DPT, PhD\textsuperscript{f}, Joanne M. Jordan, MD, MPH\textsuperscript{a,b,d,g}

\textsuperscript{*}Thurston Arthritis Research Center, University of North Carolina, Chapel Hill, NC
\textsuperscript{b}Department of Medicine, University of North Carolina, Chapel Hill, NC
\textsuperscript{c}Department of Medicine, Duke University Medical Center & Health Services Research & Development, VA Medical Center, Durham, NC
\textsuperscript{d}Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC
\textsuperscript{e}Injury Prevention Research Center, University of North Carolina, Chapel Hill, NC
\textsuperscript{f}Department of Community and Family Medicine, Duke University Medical Center, Durham, NC
\textsuperscript{g}Department of Orthopaedics, University of North Carolina, Chapel Hill, NC

Guidelines Review

- MEDLINE 2003-2013: 188 articles, 16 included in final synthesis
- Quality of guidelines assessed using AGREEII
- Generated summary statements regarding recommendations (following slides)
- Found high levels of agreement across guidelines, indicating that suboptimal uptake is more likely due to lack of dissemination and utilization in practice
Non-pharmacologic 1

• **Education and self-management**
  – Provide or refer pts to self-management programs, provide education, regular contact to promote self-care, joint protection strategies, and individualized treatment plans to OA pts

• **Exercise and weight loss**
  – Encourage pts to engage in low-impact aerobic exercise and if overweight to lose weight. Consider ROM/flexibility and/or endurance/strengthening exercises, combination exercise with manual therapy, and PT/OT referral.
Evidence: Exercise and Weight Loss

• The IDEA trial
  – Compared a restrictive diet to an exercise intervention and the combination
  – Combination group vs. Exercise alone at 18 months:
    • 50% reduction in pain
    • 40% had little or no pain
    • Better WOMAC function scores
    • Reduced knee joint loads
    • Reduced plasma IL-6 levels
    • Improved walking speeds

Messier et al, JAMA 2013;310(12):1263-73
http://walkwithadoc.org/our-locations/chapel-hill-north-carolina/

We were the first arthritis-based group to have a chapter.
Non-pharmacologic 2

• Assistive devices, bracing, taping
  – Walking aids (cane, crutch) and other assistive devices for ADLs recommended as needed (PT/OT)
  – Inconclusive evidence for bracing, heel wedges, thumb splints

• Alternative and complementary modalities
  – Thermal modalities are recommended. Therapeutic ultrasound is not, and insufficient evidence for acupuncture, Tai Chi, or TENS

• Surgical
  – Joint replacement is recommended when appropriate. Arthroscopy with debridement is not recommended*.

Pharmacologic

• First line
  – Acetaminophen up to 3 grams/day
  – Topical NSAIDs (especially in 75+ or with comorbidities)

• Second line
  – Oral NSAIDs (with appropriate risk stratification, GI prophylaxis)
  – COX-2 inhibitor with or without gastroprotection
  – Intra-articular corticosteroids (knee and hip)

• Other (refractory disease)
  – Tramadol (recommended)
  – +/- Opioid analgesics (consider, along with AE’s)
  – +/- Duloxetine (less evidence)

• Controversies
  – Glucosamine/chondroitin
  – Intra-articular hyaluronan
<table>
<thead>
<tr>
<th>Core recommendations (always recommended):</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Self-management programs</td>
</tr>
<tr>
<td>✓ Education</td>
</tr>
<tr>
<td>✓ Individualized treatment plans</td>
</tr>
<tr>
<td>✓ Weight loss or maintenance</td>
</tr>
<tr>
<td>✓ Exercise (land or water-based)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommended for most situations (if appropriate for clinical situation, comorbidities, etc.):</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Intra-articular corticosteroid injection</td>
</tr>
<tr>
<td>✓ Topical non-steroidal anti-inflammatory medications (NSAIDs)</td>
</tr>
<tr>
<td>✓ Acetaminophen</td>
</tr>
<tr>
<td>✓ Oral NSAIDs or COX-2 inhibitors</td>
</tr>
<tr>
<td>✓ Walking aids and assistive devices</td>
</tr>
<tr>
<td>✓ Thermal modalities</td>
</tr>
<tr>
<td>✓ Physical or Occupational therapy referral</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Consider in some situations (e.g. specific patient populations or presentations):</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Duloxetine</td>
</tr>
<tr>
<td>✓ Capsaicin</td>
</tr>
<tr>
<td>✓ Mind and body therapies (e.g. yoga, Tai Chi, acupuncture)</td>
</tr>
<tr>
<td>✓ Splinting and bracing</td>
</tr>
<tr>
<td>✓ Transcutaneous electrical nerve stimulation (TENS)</td>
</tr>
<tr>
<td>✓ Surgical intervention (specifically joint replacement)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Not recommended:</th>
</tr>
</thead>
<tbody>
<tr>
<td>✗ Therapeutic ultrasound</td>
</tr>
<tr>
<td>✗ Needle lavage</td>
</tr>
<tr>
<td>✗ Arthroscopy with debridement</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Controversial across guidelines, insufficient data, or not addressed:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Intra-articular hyaluronic acid injection</td>
</tr>
<tr>
<td>• Other intra-articular treatments (e.g. platelet rich plasma, stem cells)</td>
</tr>
<tr>
<td>• Glucosamine/chondroitin</td>
</tr>
<tr>
<td>• Other surgical interventions (e.g. osteotomy, partial joint replacement)</td>
</tr>
<tr>
<td>• Herbal or botanical treatments</td>
</tr>
</tbody>
</table>
OARSI Guidelines for the Non-surgical Management of Knee OA

Core Treatments
Appropriate for all individuals
- Land-based exercise
- Weight management
- Strength training
- Water-based exercise
- Self-mgmt and education

Recommended treatments*
Appropriate for the following OA types:

Knee-only OA without co-morbidities
- Biomechanical interventions
- Intra-articular Corticosteroids
- Topical NSAIDs
- Walking Cane
- Oral COX-2 Inhibitors
  (selective NSAIDs)
- Capsaicin
- Oral Non-selective NSAIDs
- Duloxetine
- Acetaminophen (Paracetamol)

Knee-only OA with co-morbidities
- Biomechanical interventions
- Walking Cane
- Intra-articular Corticosteroids
- Topical NSAIDs

Multi-joint OA without co-morbidities
- Oral COX-2 Inhibitors
  (selective NSAIDs)
- Intra-articular Corticosteroids
- Oral Non-selective NSAIDs
- Duloxetine
- Biomechanical interventions
- Acetaminophen (Paracetamol)

Multi-joint OA with co-morbidities
- Balneotherapy
- Biomechanical interventions
- Intra-articular Corticosteroids
- Oral COX-2 Inhibitors
  (selective NSAIDs)
- Duloxetine

*OARSI also recommends referral for consideration of open orthopedic surgery if more conservative treatment modalities are found ineffective.

Fig. 1. Appropriate treatments summary.
OA algorithms

- Used prior systematic review to inform example algorithms

Meneses, OAC 2016;24:1487-99
Arthritis Foundation: Living with Arthritis

March 5, 2018: 6 tips for adapting your house when you have arthritis

1. Identify the issues
   - Consider an OT Certified Aging-in-Place Specialist or Certified in Environmental Modification

2. Conserve energy
   - Keep items at counter-height, downsize items, sit to wash dishes

3. Avoid falls
   - Transfer aids, seats for bathroom

4. Stair and hallway safety
   - Slip grips on stairs, cane, guard rail, lighting, remove rugs

5. Kitchen habits
   - Keep cookware/appliances on counter, replace heavy pans, ergonomic utensils

6. Change locations
   - Move bedroom downstairs, mini-fridge for medications, relocate laundry facilities
The OA Action Alliance
OA Action Alliance

• The OA Action Alliance is a national coalition of over 90 member organizations.

• Advancing the recommendations outlined in the National Public Health Agenda for Osteoarthritis (2010), or the OA Agenda.
• **Policy & Advocacy** – educating federal and state level legislators about OA, OAAA, importance of evidence-based programs

• **Community + Healthcare + Individuals** – WWE mini-grant program; developing value propositions for health systems and large employers; WWE health messaging to encourage participation

• **OA Prevention**
  - *Weight Management* – childhood obesity, physical activity, joint health
  - *Injury Prevention* – training strategies to minimize risk for lower limb injury and maintain joint health
OAAA: Connecting

OAAction.unc.edu

OAAction

#OAActionAllianc

Osteoarthritis Action Alliance

Osteoarthritis Action Alliance

CONTACT US

OAAction@unc.edu

#StandUp2OA
OAAA: Community Programming

• Physical activity can decrease pain and improve physical function by about 40% and may reduce healthcare costs.
  – **BUT** 1 in 3 adults with arthritis are inactive

• Adults with arthritis also can reduce their symptoms by participating in disease management education programs.
  – **BUT** only 1 in 10 have taken part in these programs

Walk With Ease

• Walking program
• 2 formats: Group/Instructor-led OR self-directed
• 1 hour; 3x/week; 6 weeks
• Includes:
  – Pre-walk discussion covering a specified topic related to exercise and arthritis
  – 10- to 40-minute walk (includes warm-up and cool-down)
• Trained group exercise leaders

www.arthritis.org/living-with-arthritis/tools-resources/walk-with-ease/
Future directions in OA management
Future directions in management

- Anti-NGF
- Sprifermin/FGF-18
- TissueGene
- Joint distraction
- MSC/PRP

Anti-NGF

• Higher levels of NGF = more pain via nociceptor sensitization
• Tanezumab: Anti-nerve growth factor
• Highly significant improvements at 16 weeks in 2010 clinical trial

Meta-analysis of anti-NGF in OA

- 10 RCTs with over 7000 participants
- Similar effect size for pain and function, smaller for PGA
- More AE for tx
- ?RPOA

Sprifermin/FGF-18

- Fibroblast growth factor 18 (FGF-18) is a signal for chondrocyte proliferation, osteoblast differentiation, and matrix production.
- Sprifermin is a recombinant, truncated, non-glycosylated form given intra-articularly.
- The first-in-human study (1) showed no safety concerns and possible benefit to cartilage\(^1\).
- Subsequent abstracts on phase II work suggest prevention of cartilage loss (by MRI, next slide) at 2 and 3 years with no difference in symptoms\(^2,3\).

Sprifermin 2 year cartilage thickness

Figure 2. Primary endpoint: change from baseline in cartilage thickness in the TFJ over 2 years (qMRI)

Analysis population: modified ITT (all subjects with BL and ≥1 post-treatment qMRI in the double-blind treatment period); error bars = 95% CI.

Total qMRI cartilage thickness = total volume divided by total surface area (i.e. average cartilage thickness)

At baseline, qMRI total cartilage thickness was similar in all treatment arms and averaged ~ 1.8 mm.

CI, confidence interval; q6mo, every 6 months; q12 mo, every 12 months; qMRI, quantitative magnetic resonance imaging; TFJ, total femorotibial joint

Hochberg ACR 2017;69 (suppl10), 1L.
TissueGene

- Currently phase III
- IA injection of genetically engineered chondrocytes transduced with TGF-beta 1 (TGF-B stimulates PG synthesis, chondrocyte proliferation)
- Modest benefits in pain and IKDC
- No clear safety signals

Cherian, Osteoarthritis Cartilage 2015;23;2109-18.
Joint Distraction

• External fixation to distract the joint
• Knee oint distraction for ~6 weeks demonstrated increased joint space width at 1-2 year follow-up\textsuperscript{1,2}
  – Improved collagen synthesis: breakdown, reduced pain
  – Pain still better at 5 years, reduced progression
• May reduce secondary inflammatory and resultant cartilage degeneration and bone remodeling
• Most troubling AE is pin tract infection

MSCs and PRP

- MSCs: Mesenchymal stem cells
- PRP: Platelet-rich plasma
- Given IA, both have theoretical benefits (and risks!) on cartilage and joint tissues
- Suffer from lack of standardization and sound RCTs
- Neither recommended by any guidelines, high quality studies are needed
- Many active studies are listed on clinicaltrials.gov

Ongoing trials

• As of 8/6/18, there were 733 studies active or recruiting on ClinicalTrials.gov
• These included behavioral, biomechanical, topical, IA, and drug interventions as well as device trials
• A few examples:
  – Senolytic in phase I
  – Longer duration IA corticosteroids
  – Drugs to enhance chondrogenesis (IA), phase I-II
  – Novel analgesic pathways (neurotrophin)
  – RFA for geniculate nerves
  – Geniculate artery embolization
Take Home Points

• Osteoarthritis is common, increasing in prevalence, and debilitating
• OA in relation to other common chronic diseases significantly affects QoL and mobility
• The JoCo OA Project has provided unique insights
• OA management is primarily through lifestyle and behavioral interventions
  – Resources are available including WWAD, AF, OAAA
• There are several promising treatments under study
Acknowledgments

Thank you!