

Osteoarthritis Year in Review: Clinical

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The background is a dark blue gradient. Two large, overlapping circles are positioned in the upper half of the frame. The circles are a slightly lighter shade of blue than the background, creating a subtle glow effect. The text is centered horizontally between the two circles.

Disclosure: no commercial relationship

Purpose:

highlight clinical research in osteoarthritis

& Epidemiology

& Observational clinical studies

& Pharmacologic treatment

& Non-pharmacologic treatment

Disclaimers!

& Narrative review

& Small sub-sample in this presentation

& Cannot do justice to the work

.....still a valuable exercise

Methods

⌘ Literature search, PubMed

<http://www.ncbi.nlm.nih.gov/pubmed/>

⌘ Search terms

⌘ “osteoarthritis [All Fields] AND treatment [All Fields]”

⌘ “osteoarthritis [All Fields] AND epidemiology [All Fields]”

⌘ Humans, English language, 19+ years

⌘ April 1, 2014 – April 1, 2015

⌘ Literature search, Embase

<http://www.embase.com/>

⌘ Search terms

⌘ “osteoarthritis AND (treatment OR therapy)”

⌘ “osteoarthritis AND epidemiology”

⌘ Limits as above

Methods

& Excluded

- ∅ Surgical outcome studies
- ∅ Case series
- ∅ Studies of surgical technique
- ∅ Tissue sample or culture studies
- ∅ Clinical trial protocols
- ∅ Pilot studies
- ∅ Abstracts
- ∅ Focus on imaging, biomarkers, rehabilitation (other reviews in this session)

& Of 1523, 203 considered relevant

A Venn diagram with two overlapping circles. The left circle is a dark blue, and the right circle is a slightly lighter shade of blue. The background is a dark blue gradient.

Epidemiologic and Observational Clinical Studies

Physical Activity: pain, incident disease

⌘ In mid-age women (Australian Longitudinal Study on Women's Health), physical activity between 47 and 58 yrs of age associated with lower risk of joint pain/stiffness nine years later

Peeters GM, Osteoarthritis Cartilage 2015

⌘ Qualitative study characterizing consequences of symptoms on physical activity

MacKay C, BMJ Open 2014

⌘ Knee pain and vitality associated with activity avoidance

Holla JF, Arthritis Care Res 2015

⌘ Meeting physical activity guidelines not associated with incident radiographic or symptomatic knee OA in mid-age/older adults (Johnston County Osteoarthritis Project)

Barbour KE, Arthritis Care Res 2014

Physical Activity: impact

- ⌘ Being less sedentary associated with better function in knee OA, independent of MVPA minutes (OAI)

Lee J, Arthritis Care Res 2014

- ⌘ More walking associated with lower risk incident function limitation in persons with or at high risk for knee OA (MOST)

White DK, Arthritis Care Res 2014

- ⌘ Greater daily time in light intensity physical activity associated with reduced onset and progression of disability (OAI)

Dunlop DD, BMJ 2014

- ⌘ Graded association between sedentary behavior and increased SBP, independent of MVPA minutes, in persons with or at high risk for knee OA (OAI)

Sohn MW, Osteoarthritis Cartilage 2014

- ⌘ Physical activity level associated with health-related utility in persons with or at high risk for knee OA (OAI)

Sun K, Arthritis Care Res 2014

Early Knee OA

- ⌘ In persons with or at high risk for knee OA (OAI), knee pain most likely to first appear during WB activities involving bending, such as using stairs

Hensor EM, Arthritis Care Res 2015

- ⌘ Questionnaire variables, genetic markers, other-site OA, biochemical markers added only modestly to prediction of knee OA incidence using age, gender, BMI in elderly population (Rotterdam Study-I); doubtful minor x-ray features strongly predicted future knee OA

Kerkhof HJ, Ann Rheum Dis 2014

- ⌘ In persons KL 0 in both knees (OAI), certain MRI lesions associated with incident persistent symptoms and incident cartilage damage

Sharma L, Arthritis Rheumatol 2014

- ⌘ In persons with early symptomatic knee OA (OAI and CHECK), rapid radiological change associated with worsening of pain and function

Wesseling J, Ann Rheum Dis 2015

Pain: associated factors

- ⌘ Metabolic syndrome/knee OA association largely explained by excess weight and not insulin resistance; accumulation of metabolic syndrome components associated with pain severity

Shin D, J Clin Endocrinol Metab 2014

- ⌘ Different quantitative sensory testing measures associated with clinical pain in AA and NHW; reduced pain inhibition important in all

Cruz-Almeida Y, Arthritis Rheumatol 2014

- ⌘ Women (MOST) reported greater knee pain than men regardless of KL, effect sizes small; differences increased in PF OA; central sensitivity plays a role

Glass N, Osteoarthritis Cartilage 2014

- ⌘ Higher BMI associated with greater knee pain even accounting for OA severity in persons with or at high risk for knee OA (OAI)

Weiss E, Rheumatology 2014

Pain: tissue origins

⌘ 3 patterns of synovitis in knee OA: 1) mainly patellar sites, associated with KOOS pain and ICOAP constant pain; 2) mostly near ACL, not associated with pain or disease severity; 3) mainly at loose bodies, associated with disease severity

deLange-Brokaar BJ, Arthritis Rheumatol 2014

⌘ No association between ultrasound features and knee pain severity by KOOS pain or numeric rating scale

Beyers K, Rheumatology 2014

Pain: sensitivity

- ⌘ Pressure-pain threshold associated with single and multijoint symptoms but not asymptomatic knee or hip OA

Goode AP, Arthritis Care Res 2014

- ⌘ Higher neuropathic pain questionnaire score associated with widespread reduction in pressure-pain threshold in OA

Moreton BJ, Arthritis Care Res 2014

- ⌘ Pressure-pain threshold and temporal summation associated with pain severity but not OA presence, severity, or duration in persons with or at high risk for knee OA (MOST)

Neogi T, Ann Rheum Dis, 2015

Pain: characterization, trajectories

- ⌘ Pain flares described most often by quality (sharp), timing (seconds-minutes), antecedents, consequences

Murphy S, Arthritis Care Res 2015

- ⌘ Pain outcome based on development of unpredictable pain; good 2-yr outcome lower with greater catastrophizing and higher with greater self-efficacy

Rayahin, Arthritis Care Res 2014

- ⌘ 5 WOMAC-pain trajectories over 6 yrs in symptomatic knee OA (OAI), none with substantial worsening; greater pain with KL, obesity, depression, comorbidity, female, NW race, lower education, younger age

Collins JE, Osteoarthritis Cartilage, 2014

- ⌘ Mild/non-progressive, progressive, moderate, improving, severe/non-improving pain trajectories in symptomatic OA in Knee Clinical Assessment Study; in OAI, 'progressive' and 'improving' were less evident

Nicholls E, Osteoarthritis Cartilage, 2014

Pain

⌘ Nocturnal knee pain and worse sleep quality associated with knee OA severity

Sasaki E, Arthritis Care Res 2014

⌘ More people with high knee pain/low knee OA (vs. high pain/high OA, low pain/high OA, low pain/low OA) had widespread pain, in persons with or at high risk for knee OA (MOST)

Riddle, Phys Ther 2014

⌘ After naproxen (vs. placebo), fMRI activity reduction in brain regions associated with pain perception; changes in perceived pain intensity associated with changes in activity in regions previously associated with pain intensity

Sanders D, Arthritis Rheumatol, 2014

Confidence/Instability/Falls

- ⌘ Worse knee confidence associated with pain, self-reported knee instability, weakness, varus-valgus motion during gait in medial TF OA

Skou ST, Arthritis Care Res 2014

- ⌘ Knee buckling and sensation of instability without buckling associated with fear of falling, poor balance confidence, activity limitations, and poor function (MOST)

Nguyen US, Osteoarthritis Cartilage 2014

- ⌘ Risk for falls increased with additional symptomatic OA lower limb joints; symptomatic knee or hip OA associated with increased fall risk

Dore AL, Arthritis Care Res, 2014

- ⌘ Fall history + knee OA (vs. neither or only one) associated with worse KOOS-QoL and SF12 physical component scale scores, in persons with or at risk for knee OA (OAI)

Vennu V, Clin Interv Aging, 2014

Hand OA – progression, pain, impact

- ⌘ MRI BMLs, synovitis associated with radiographic JSN progression; synovitis, BMLs, osteophytes, malalignment with development of radiographic erosions

Haugen IK, Ann Rheum Dis 2014

- ⌘ USG inflammatory features, especially when persistent, associated with radiographic progression

Kortekaas MC, Ann Rheum Dis 2014

- ⌘ Diabetes, lower education, female, familial OA, widespread pain, poor mental health, more finger joints with USG-detected synovitis and x-ray OA, associated with hand pain

Magnusson K, Arthritis Care Res, 2015

- ⌘ Symptomatic (but not radiographic) hand OA associated with increased risk coronary heart disease events (Framingham Heart Study)

Haugen I, Ann Rheum Dis, 2015

Hand OA – erosive

⌘ Similar frequency of joint involvement and patterning in erosive OA and severe non-erosive OA – erosive OA may be more severe form of hand OA; erosive OA (vs. non-erosive) associated with metabolic syndrome, especially dyslipidemia

Marshall M, Ann Rheum Dis 2015

⌘ 1st CMC erosive disease in 2.2% in population-based cohort, North Staffordshire; 0.5% with combined 1st CMC and IP erosive disease; 1st CMC erosive disease associated with greater pain but similar function (than non-erosive OA)

Kwok WY, Osteoarthritis Cartilage 2014

Foot OA

⌘ Hallux valgus associated with female, AA race, older age, pes planus, knee/hip OA, and inversely with higher BMI

Golightly YM, Arthritis Care Res 2014

⌘ 1st MTP OA severity associated with dorsal hallux and 1st MTP pain, hallux valgus, 1st IP hyperextension, dorsal hallux and 1st MTP keratotic lesions, and decreased 1st MTP dorsiflexion, ankle/subtalar eversion and ankle dorsiflexion range

Menz HB, Osteoarthritis Cartilage 2015

⌘ Population prevalence of symptomatic radiographic OA 16.7%, 1st MTP 7.8%, 1st CM 3.9%, 2nd CM 6.8%, NCJ 5.2%, TNJ 5.8%; greater in females, with age, lower SES; 75% reported disabling symptoms (Clinical Assessment Study of the Foot)

Roddy E, Ann Rheum Dis, 2015

⌘ In symptomatic knee OA, 25% with foot pain (more often bilateral), associated with worse function

Paterson KL, Arthritis Care Res, 2015



Symptom Outcomes of Pharmacologic Treatments

⌘ Methotrexate reduced pain and improved function in symptomatic knee OA, 28 weeks

Abou-Raya A, Ann Rheum Dis 2014

⌘ Adalimumab not superior to placebo to alleviate pain in hand OA not responsive to analgesics and NSAIDs

Chevalier X, Ann Rheum Dis 2014

⌘ Strontium ranelate over 3 yrs associated with symptom and function improvement

Bruyère, Rheumatology, 2014

⌘ Bisphosphonate users with symptomatic OA in OAI had lower NRS pain scores vs. non-users (until year 4), but did not differ in WOMAC pain or function

Laslett LL, Ann Rheum Dis, 2014

Anti-nerve Growth Factor Monoclonal Antibodies

⊗ Individuals receiving partial symptom relief with NSAIDs may receive greater benefit with tanezumab monotherapy; adverse event frequency higher with tanezumab than with NSAIDs, highest with combination

Schnitzer TJ, Ann Rheum Dis 2014

⊗ Adding tanezumab to diclofenac SR improved pain, function, global assessment, but higher adverse events in combination group suggests this approach unfavorable

Balanescu AR, Ann Rheum Dis 2014

⊗ Fasinumab, DB, placebo-controlled, parallel group, exploratory study: generally well tolerated, all 3 doses better than placebo for walking knee pain and WOMAC

Tiseo PJ, Pain, 2014

Glucosamine and Chondroitin Sulfate

⌘ Meta-analysis of placebo-controlled trials: most heterogeneity explained by brand; trials using one product had better outcome but large inconsistency, and low risk of bias trials showed small effect size

Eriksen P, Arthritis Care Res 2014

⌘ RCT, DB, non-inferiority trial vs. celecoxib: CS + GH had comparable efficacy to celecoxib for symptoms, function, joint swelling/effusion at 6 months

Hochberg MC, Ann Rheum Dis 2015

NSAIDs

- ⌘ Long-term NSAID use in OAI associated with modest clinical (but not significant) change in stiffness, function, structure

Lapane KL, Arthritis Rheumatol 2014

- ⌘ Fixed-dose tramadol-diclofenac resulted in greater pain reduction and was well tolerated vs. tramadol-paracetamol for acute OA flare


Chandanwale AS, J Pain Res 2014

- ⌘ No association of traditional NSAIDs with nonfatal AMI when background CV risk was low-intermediate; moderate association in those at high risk or with NSAID use >365 days (nested case-control, primary care database)

de Abajo FJ, Pharmacoepidemiol Drug Saf 2014

- ⌘ Celecoxib as effective and safe as naproxen for knee OA in Hispanic sample

Essex MN, Int J Gen Med, 2014



Structural Outcomes of Pharmacologic Treatments

⌘ Strontium ranelate 2 g/d, beneficial effect on cartilage volume and BML, some regions, SEKOIA phase III clinical trial subset

Pelletier JP, Ann Rheum Dis 2015

⌘ Recombinant human fibroblast growth factor 18, negative for primary medial TF cartilage thickness outcome, but secondary end points showed dose-dependent reductions

Lohmander LS, Arthritis Rheumatol 2014

⌘ GH/CS associated with less cartilage volume loss in observational study (OAI), albeit not in multivariable analyses

Martel-Pelletier J, Ann Rheum Dis 2015

⌘ GH/CS not associated with symptom relief or modification of disease progression in OAI

Yang S, Arthritis Rheumatol 2014

⌘ No evidence structure benefit by MRI at 6 months or urinary CTX-II excretion from GH

Kwoh CK, Arthritis Rheumatol 2014



Symptom Outcomes of Non-pharmacologic Treatments

Exercise/PT in Knee OA

- ⌘ Intensive diet and exercise program (vs. diabetes support/education) prevented incident knee pain at year 1, in overweight adults with diabetes

White DK, Arthritis Care Res 2015

- ⌘ Neuromuscular and quad strengthening similarly improved pain and function but did not change KAM in moderate-severe medial knee OA with varus alignment

Bennell KL, Arthritis Rheumatol 2014

- ⌘ Neuromuscular more effective for non-obese and with varus thrust; quad strengthening more effective for obese and without thrust

Bennell KL, Arthritis Care Res 2015

- ⌘ Pressure-pain sensitivity, temporal summation, pain reduced with exercise

Henriksen M, Arthritis Care Res 2014

- ⌘ Boosters with a PT did not influence pain, function, or home exercise adherence

Bennell KL, Arthritis Care Res, 2014

Exercise/PT in Hip or Hand OA

⌘ Exercise therapy + education (vs. education) associated with later THR

Svege I, Ann Rheum Dis 2015

⌘ Hip PT did not result in pain or function improvement vs. sham treatment for painful hip OA

Bennell KL, JAMA 2014

⌘ Joint protection (vs. no protection) effective using OARSI/OMERACT responder criteria by 6 months; hand exercise (vs. no exercise) not effective

Dziedzic K, Ann Rheum Dis 2015

⌘ RCT home based exercise hand OA, well tolerated, improved function, grip strength, pain, fatigue

Hennig T, Ann Rheum Dis, 2014

⌘ RCT group and home exercise for hand OA, well tolerated but small short-term improvement only on self-reported measures

Østerås N, Osteoarthritis Cartilage, 2014

Behavioral Therapy

- ⌘ Weight reduction in obese patients with a 1-year maintenance improved knee OA symptoms, irrespective of maintenance program

Christensen R, Arthritis Care Res 2014

- ⌘ DB, RCT with active placebo, cognitive behavior therapy for insomnia in knee OA reduced sleep maintenance insomnia and clinical pain

Smith MT, Arthritis Rheumatol 2015

- ⌘ Secondary analysis of RCT data, short term sleep improvement predicted long term improvements for sleep, pain, fatigue, not attributable to psychological benefits

Vitiello MV, Pain 2014

- ⌘ Web-based therapeutic exercise resource center feasible and efficacious in improving pain, function, self-efficacy in knee OA

Brooks MA, BMC Musculoskelet Disord 2014

- ⌘ Telephone reinforcement and negotiated maintenance contracts positively affected physical activity behavior in OA

Desai PM, Am J Health Behav 2014

Other Non-pharmacologic Therapies

⊗ RCT, sham-controlled, no additional benefit of TENS over education + exercise for knee OA


Palmer S, Arthritis Care Res 2014

⊗ RCT, double-blind, sham-controlled, therapeutic ultrasound provided no additional benefit over exercise training

Cakir S, Am J Phys Med Rehabil 2014

⊗ Neither laser nor needle acupuncture conferred benefit over sham for pain or function in patients older than 50 with moderate or severe chronic knee pain

Hinman RS, JAMA 2014



Structural Outcomes of Non-pharmacologic Treatments

& RCT, PF brace reduced PF (but not TF) BML volume and pain at 6 weeks

Callaghan MJ, Ann Rheum Dis 2015



Reviews, Treatment

⌘ Cochrane: evidence does not support topical rubefacients containing salicylates for chronic conditions

Derry S, Cochrane Database Syst Rev, 2014

⌘ Comparative effectiveness of pharm interventions for knee OA, systematic review and network meta-analysis

Bannuru RR, Ann Intern Med 2015

⌘ Systematic review and meta-regression analysis of RCTs, single-type exercise programs were more efficacious than programs including different exercise types

Juhl C, Arthritis Rheumatol 2014

⌘ Meta-analysis of RCTs, valgus bracing, small to moderate improvement in pain

Moyer RF, Arthritis Care Res 2014

⌘ Cochrane: inconclusive evidence, bracing for symptoms, function, QoL in medial compartment knee OA; moderate evidence shows lack of effect, LWO vs. neutral insole, for symptoms and function

Duivenvoorden T, Cochrane Database Syst Rev 2015

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Thank-you