Chronic Debilitating Conditions on Women: Sex and Gender Impact on Osteoarthritis

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Osteoarthritis Prevalence

CDC data

Burden of Musculoskeletal Conditions in the US, 2015
Knee OA Prevalence

- Meta-analysis with ~3.7 million people
- Rates increase with age
- US about 130 per 10,000 person-years
- Ratios of prevalence, incidence females to males 1.69/1.39

Cui et al. *E Clin Med* 2020
Sex/Gender-Specific Knee OA Risk Factors

• Acquired
  injury
  patterns of overuse

• Inherent
  anatomy
  gait pattern
  impact of estrogen
  muscle strength

• Inflammatory response (to injuries, obesity, OA)
Joint Injury

• Higher risk in women (especially ACL)
• Significantly higher risk of OA in younger people after knee injury—even with reconstruction
• Earlier among women than men with ACL injuries

Roos Current Opinion in Rheumatology 2005
Knee OA-Anatomic Risk Factors

• Larger Q-angle
• Foot pronation
• Increased femoral anteversion
• Genu valgum
• External tibial torsion
• Tibia vara
• Generalized ligamentous laxity
• Tight lateral patellar retinaculum
• Patella alta
• Shallower femoral notch
• Narrower patella
Effects of Estrogen

- Mice with model of induced OA
- Ovariectomy increased degree of cartilage injury
- Due to loss of bone or direct effect on cartilage?
- Does this translate to joint issues for women after menopause?

Sniekers et al. *Arthritis Res Ther* 2010
Muscle Strength

• Quads strength in women was higher in those without OA or few radiographic changes
• Only ½ with OA had OA-related pain
• Impact of strength on development of OA?

Palmieri-Smith et al Am J PM&R 2010
Impact of/Response to Obesity

• More than only increased cartilage loads (increased risk of hand OA)
• Women more likely to demonstrate association between metabolic syndrome and symptomatic OA
• Effect of obesity was greater in women than men for more severe knee OA (K/L grade 2 and 4)
• Link between obesity and OA may be mediated by leptin, especially for women

Batushansky et al Arthritis and Cartilage 2021
Sex/Gender Impact on Pain

**Sex-Based**
- Genetic
- Neurochemical
- Impact of sex steroids
- Systems level (e.g., inflammation, cortical connectivity, midbrain-brainstem connectivity)
- Psychologic (e.g., depression, anxiety)

**Gender-based**
- Psychosocial (e.g., coping, self-efficacy)
- Sociocultural (e.g., gendered expectations, gender role)
- Experiential (e.g., abuse, IPV, familial history)

Mogil *Nat Rev Neurosci* 2012
Knee OA Treatment
Non-Surgical

- Women more likely (than men) to be treated in the 12 months prior to surgery with opioids, non-opioids, injections, physical therapy

Bawa et al *J of Arthroplasty* 2016
Pre-operative Function

- Patients with end-stage OA and waiting for TKA/THA
- Women with significantly poorer health-related QOL scores, self-efficacy (confidence in management of pain, fatigue, etc), and function

Ackerman et al Arthritis Rheum 2005
Metal Hypersensitivity

- Pts referred with painful joint replacements
- Women had higher levels of pain than men
- Women had higher rates and severity of metal sensitization

Caicedo et al JBJS 2017
Quality of Life/Disability

Burden of Musculoskeletal Conditions in the US 2015
OA and Co-morbidities

- HTN, depression, COPD most common co-morbidities for women and men with OA
- Prevalence of each additional condition more common among women
- Women had higher number of co-morbidities

Women, Knee OA, and Mortality

- Increased CVD-related and all-cause mortality for those with OA of the knee
- Women with knee pain and no ROA had a 49% increased risk of dying from all-cause mortality (compared with those with no knee pain/no ROA)
- Women with painful knee ROA had a 97% increase in mortality risk
- Greatest increase in mortality from CVD conditions (pain only HR=3.25, pain and ROA HR=4.19)
- Related to the presence of knee pain, not only radiographic degenerative changes (no increased mortality among those with only radiographic changes)
- No similar findings for those with hand OA

Kluzek et al Ann Rheum Dis 2015
Reported Results Based on Sex

- Evaluation of literature for rotator cuff injuries and OA of the knee
- 31% reported sex-specific analysis
- 30-40% reported based on sex for knee OA studies
- No change over time

Stumpff et al JWH 2020
Future Directions

Continued exploration of the impact of sex/gender on OA
• onset/risk factors/early diagnosis
• prevention
• response to treatment
• impacts on function, co-morbidities, mortality

Requires
• disaggregation of data based on sex/gender
• targeted research/funding regarding OA among women, given differing risks/contributing factors
• enhanced health education in sex/gender to train next generations of clinicians and researchers
Thank You!