1 □ Evaluation and Treatment of Knee Arthritis
John Zebrack, MD
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2 □ Classification of Knee Arthritis
• Non-inflammatory
  –Osteoarthritis
    • Primary
    • Secondary
      –Post-traumatic, dysplasia, neuropathic, Paget’s disease, Septic, Hemorrhagic conditions
  • Inflammatory
    –RA, Psoriatic, Crystalline, Lupus, AS, Lyme

3 □ Osteoarthritis
• Loss of articular cartilage
• Remodeling of subchondral bone
• Formation of osteophytes

4 □ Osteoarthritis
• Leading cause of disability in patients older than 65
• Knee is most commonly affected joint
• Incidence: 12% over 60 years of age

5 □ Osteoarthritis of Knee
• Risk Factors:
  –Advancing age
  –Female sex
  –Genetics
  –Obesity: rising BMIs significant role in increasing number of TKAs annually

6 □ Osteoarthritis of Knee: Genetics
• Genome association study identifies an osteoarthritis susceptibility locus on chromosome 7q22
–30% increased risk of knee OA progression
–Gene encodes a G protein-coupled receptor

Arthritis Rheum, 2010 Feb
Kerkhof et al

7 Long distance running and knee osteoarthritis. A prospective study

The objective of this study was to determine if differences in the progression of knee OA in middle- to older-aged runners exist when compared with healthy nonrunners over nearly 2 decades of serial radiographic observation. Multivariate regression analyses were performed to assess the relationship between runner versus control status and radiographic outcomes using age, gender, BMI, education, and initial radiographic and disability scores among covariates.

Conclusion -distance running among healthy older individuals was not associated with accelerated radiographic OA. These data raise the possibility that severe OA may not be more common among runners.

8 Knee osteoarthritis in 50 former top-level soccer players: comparative study Ann Readapt Med Phys 2008

• Knee osteoarthritis was more common in the football players than in the nonsporting subjects (80% versus 68%), although the difference was not statistically significant. Whereas pain was noted in only six footballers and was observed in 50% of controls.
• Knee osteoarthritis is common in male football players. However, our study shows that the condition is less painful and less likely to cause functional disability (but paradoxically more destructive) than in nonsportsmen.

9 Osteoarthritis of Knee

• Cellular Level
  –Deterioration in the ability of chondrocytes to maintain and restore articular cartilage
  –Chondrocytes undergo age related telomere erosion
Osteoarthritis of Knee

- Cellular Level
  - Deterioration in the ability of chondrocytes to maintain and restore articular cartilage
  - Chondrocytes undergo telomere erosion
  - Loss of proteoglycan content and composition
  - Elevation of proteolytic enzymes (metalloproteinases, nitric oxide synthase) and inflammatory cytokines

- Radiographs:
  - WEIGHT-BEARING x-rays
    - AP, Lateral, flexed PA, and sunrise
  - Joint space narrowing
  - Sclerosis – increased density of subchondral bone
  - Osteophytes

Evaluation of the Knee

- History
  - Often aggravated with activity and relieved by rest
  - Deep aching pain
  - May notice loss of ROM, function, and swelling

- Physical Exam
  - Often reveals loss of ROM, crepitus, tenderness along joint line, an effusion, and some degree of deformity
  - Assess patella tracking and ligament stability
  - Varus or valgus
  - Muscle atrophy
  - Altered gait
  - Check the Hip!

LEG ALIGNMENT

1. Mechanical Axis
2. Neutral
   - 5-7 deg of tibiofemoral valgus
3. Valgus
   - Angle points toward center axis of body
   - Lateral compartment wears
4. Varus
   - Angle points away from center axis
   - Medial compartment wears

WINDSWEPT KNEES

VARUS KNEE

VALGUS KNEE

Imaging
• Radiographs:
  – WEIGHT-BEARING x-rays
    • AP, Lateral, flexed PA, and sunrise
    • Joint space narrowing
    • Sclerosis – increased density of subchondral bone
    • Osteophytes
    • Advanced OA – cysts, loose bodies, joint subluxation, malalignment

17 MRI INDICATIONS
• Acute injury in nonarthritic knee
• History of trauma
• Mechanical symptoms with mild to mod DJD
• Evaluating for secondary causes of OA
  – i.e. tumors

18 SYNOVIAL FLUID ANALYSIS

19 BLOOD ANALYSIS FOR ARTHRITIS

20 NONSURGICAL TREATMENT OF KNEE ARTHRITIS
• Acute Flares
  – Rest
  – Ice
  – Compression
  – Gait Aids
  – Pain Meds
  – Anti-inflammatories
    • NSAID
    • Oral Steroids
    • Injection
      – Corticosteroid
      – Hyaluronic Acid

21 CAUSE OF THE ACUTE FLARES
• Often no obvious trauma, just everyday activity
–Degenerative meniscus tear
–Chondral flaking
–Osteophyte fracture
–Swelling
–Standard acute injuries

22 Nonsurgical Treatment of Knee Arthritis

• AAOS Recommended Treatment
  –Low impact aerobic exercises and strengthening
  –Weight loss for BMI > 25
  –NSAIDS

23 Nonsurgical Treatment of Knee Arthritis

• AAOS Cannot Recommend for OR against
  –Physical therapy
  –Unloader brace
  –Cortisone injections
  –Growth factor or PRP injections

24 Nonsurgical Treatment of Knee Arthritis

• AAOS Cannot Recommend %
  –Acupuncture %
  –Lateral heel wedges %
  –Glucosamine and chondroitin sulfate %
  –Hyaluronic acid injections %

25

Cortisone Injections *
• Double-Blind Placebo-Controlled studies do show that they are effective for approximately 80% of patients with mild to moderate DJD for an average of 10 weeks

26 SURGICAL TREATMENT OF ARTHRITIS: *

Arthroscopy *

Relative Indications:
• Acute onset with mechanical symptoms
• Recent effusion
• Loose bodies, normal mechanical alignment
• Isolated cartilage flap, meniscus tears, unicompartamental
• Isolated full thickness defect without global DJD
  — Cartilage Restorative Procedures %
  • %

— %
  • %

27 Stem Cell Injections with Arthroscopy

• Adult human mesenchymal stem cells delivered via intra-articular injection to the knee following partial medial meniscectomy: a randomized, double-blind, controlled study
  — 55 patients w APM given either high dose stems cells, low dose stems, or control
  — Increased meniscal volume by MRI in 24% group A and 6% group B

• Vangsness et al. JBJS, 2014 %
  • %

28 Can a Meniscus Really Regenerate with Stem Cells?

• At one year only 14% had increased meniscal volume and only 9% of patients at two years
• There was no statistical difference between the three groups in the overall progression of arthritis
• Interesting finding is the pain scores was significantly improved at two years in the MSC groups, possibly due to anti-inflammatory property
29 Surgical Treatment of Arthritis
   • Osteotomy
     –Correct malalignment
   • Partial Knee Replacement
     –Specific patterns
   • Total Knee Replacement

30 Optimizing Outcome for TKA
   • Modifiable Risk Factors associated with readmissions
     –Active tobacco use: any product
     –S aureus colonization: mupirocin
     –High BMI: >40
     –Diabetes mellitus: HbA1c > 8.0
     –Hypothyroidism
     –Drug and alcohol dependency
     –Depression
     –Nutritional deficiencies
     –Cardiovascular disease
     –Physical de-conditioning and fall risk

31 Patient Factors during hospitalization for Re-admission after TKA
   • Discharge to a nursing facility
   • Length of stay
   • Blood transfusion
   • Heart disease
   • Renal failure
   • Infection
   • DVT and PE
   • Hospital and Surgeon volume

32 Are patients willing and able to modify their risks before
surgery?

- Morbid obesity, smoking, and poorly controlled diabetes
- 58% improved and 42% ultimately met specific goals

DeFroda et al.
RI Med J (2013)

### Gene Therapy

- Recent work showed that localized gene therapy with use of a small adeno-associated virus (AAV) resulted in sustained transgene expression after a single intra-articular injection
- Control gene expression by selective use of promoters to “turn on” and “turn off” genes
- Approved use in several human clinical trials

### Mesenchymal Stem Cells

- Functional difference in MSCs isolated from patients with OA compared to those without OA
- Theory is exposure to elevated proinflammatory cytokines
- Suggested that interventions using MSCs to regenerate cartilage are feasible

### Mesenchymal Stem Cells

- Second look arthroscopic findings from IA stem cell injections observed significant improvement at 2 years in patients > 65 years
  - Koh et al. Knee Surg Sports 2013
- Experimental animal models with direct IA injection showed lower degree of cartilage degeneration, osteophyte formation, and subchondral sclerosis compared to controls
  - Singh et al. Bone Joint Res. 2014

### Mesenchymal Stem Cells

- Systematic review and meta-analysis
  - 7 randomized controlled and controlled clinical trials
Mesenchymal Stem Cells

• Systematic review and meta-analysis
  –7 randomized controlled and controlled clinical trials

–Quality of evidence was rated as low %
–No significant effect on pain %
–Potentially effective but inconclusive %
–Need further studies and clinical trials %

Tanezumab

• IgG monoclonal antibody that targets NGF
• Recent studies showed significant improvement in pain and function of knee OA
• Drug does have adverse side effects
• Considered safe and well tolerated, patients responded better compared to oxycodone or placebo