

The Relationship of Denuded Subchondral Bone to Incident Frequent Knee Pain

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Introduction

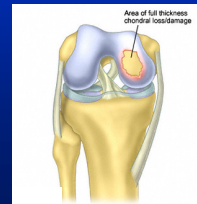
- Chief complaint in knee osteoarthritis (OA) is pain
- Anatomical sources of pain unclear
- Although cartilage aneural, other tissue pathology (e.g. bone, menisci, ligaments, capsule, synovium, muscle) accompanying cartilage loss may contribute

Introduction

- Bone is a primary candidate as a pain generator in OA:
 - Its load-bearing function during weight-bearing activities
 - Prior studies reveal bone marrow lesion/pain relationship
 - With full thickness defects in articular cartilage, subchondral bone is exposed
- Relationship between proportion of bone exposed and pain has not been examined

Introduction

- State of art imaging methods allow quantification of denuded subchondral bone
 - Bone not covered by cartilage, expressed as
 - Surface area, or
 - Percent of total area of subchondral bone that is uncovered
 - Specific to each joint surface (tibial, femoral, patellar)



Hypothesis

Among persons with knee OA, in knees without frequent knee pain at baseline, percent denuded subchondral bone at baseline predicts development of frequent knee pain at 2 years.

Methods-Overview

- Longitudinal natural history study of community-recruited cohort, MAK-2
- All participants had knee OA in at least one knee
- %denuded subchondral bone assessed at baseline
- Frequent knee pain status assessed at baseline and 2 years later

Methods

Inclusion criteria

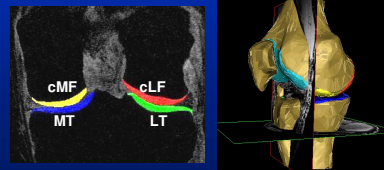
- definite tibiofemoral osteophytes (\geq K/L 2) in one or both knees
- $>$ a little difficulty (Likert scale) with two or more WOMAC physical function scale items

Exclusion criteria

- systemic, inflammatory arthritis
- secondary OA
- any steroid use in previous 3 months
- MRI exclusions (pacemaker, artificial valve, aneurysm clip or shunt, stent, implanted device, ocular metallic fragment)

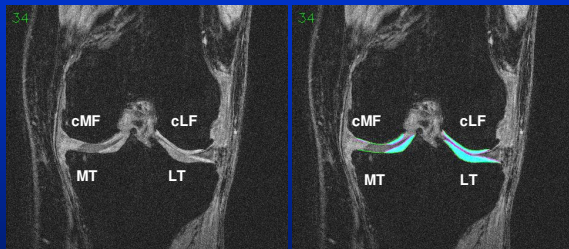
MRI Acquisition and Segmentation

- Acquisition of coronal 1.5 mm FLASHwe MR images at 1.5 and 3.0T at baseline
- Segmentation of tibial, weight-bearing femoral, and patellar cartilage using proprietary software (Chondrometrics GmbH, Ainring, Germany)



Plates:
MT = medial tibia cMF = medial weight-bearing femur
LT = lateral tibia cLF = lateral weight-bearing femur

MRI Acquisition and Segmentation



Plates:
MT = medial tibia cMF = medial weight-bearing femur
LT = lateral tibia cLF = lateral weight-bearing femur

Methods-MRI Computation

- Computation of total area of subchondral bone, cartilage surface area, cartilage-covered area of bone, and denuded area of bone using Chondrometrics software
- QC by one expert
- Reliability:
 - Graichen H, Arthritis Rheum, 2004
 - Burgkart R, Arthritis Rheum 2003
 - Burgkart R, Arthritis Rheum 2001

Methods

Frequent Knee Pain

- Assessed at baseline and 2 yrs later
- “Did you have pain in or around your knee for most days in the past month?” (yes or no)
- Specific to each knee, right and left

Statistical Analysis

- Analysis included knees without frequent knee pain at baseline
- Percent denuded subchondral bone calculated as $(dAB/tAB) \times 100$, for surface(s) of interest
- Logistic regression with GEE used to estimate odds ratios (OR) associated with baseline %denuded subchondral bone for baseline-to-2-year incident frequent knee pain

Statistical Analysis

- Analyses adjusted for age, gender, BMI, and further adjusted for maximal bone marrow lesion score (WORMS) in the same compartment
- Adjusted OR presented are per 10 percentile point increase in %denuded subchondral bone

Results

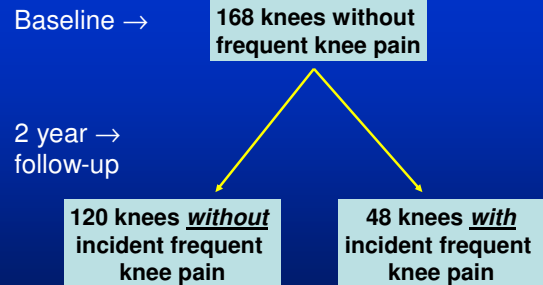
- 168 knees from 117 persons were without frequent knee pain at baseline
- Age, mean (S.D.), years 68.5 (11.4)
- BMI, mean (S.D.), kg/m² 28.8 (5.2)
- Women 86/117 (74%)

Results

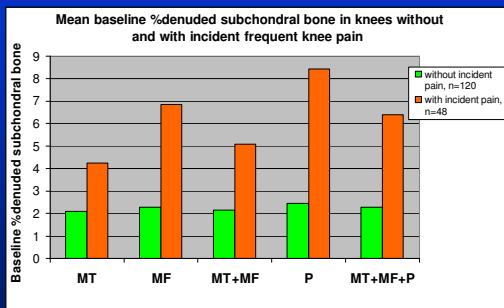
- Medial compartment involvement more common (only 10% with definite lateral OA)
- K/L grade

0	5 knees
1	18
2	75
3	56
4	14
- Alignment
 - 73 neutral limbs (within 2° of 0°)
 - 43 valgus limbs (>2° in the valgus direction)
 - 52 varus limbs (>2° in the varus direction)

Results



Results



MT=medial tibia, MF=weightbearing medial femur, MT+MF=medial compartment, P=patella, MT+MF+P=medial compartment +patella

Odds ratios for baseline-to-two-year incident frequent knee pain associated with baseline %denuded subchondral bone

%Denuded bone, surface examined	Age, gender, BMI-adjusted OR* (95% CI)
Medial tibia	1.38 (0.97, 1.98)
Weight-bearing medial femur	1.32 (1.04, 1.68)
Medial tibia + medial femur	1.39 (1.03, 1.86)
Patella	1.68 (1.14, 2.46)
Medial tibia + medial femur + patella	2.22 (1.39, 3.54)

*OR per 10 percentile point increase in %denuded bone at baseline

Odds ratios for baseline-to-two-year incident frequent knee pain associated with baseline %denuded subchondral bone

%Denuded bone, surface examined	Age, gender, BMI-adjusted OR* (95% CI)	Age, gender, BMI, BML-adjusted OR* (95% CI)
Medial tibia	1.38 (0.97, 1.98)	1.22 (0.83, 1.79)
Weight-bearing medial femur	1.32 (1.04, 1.68)	1.25 (0.95, 1.63)
Medial tibia + medial femur	1.39 (1.03, 1.86)	1.26 (0.90, 1.75)
Patella	1.68 (1.14, 2.46)	1.46 (0.95, 2.23)
Medial tibia + medial femur + patella	2.22 (1.39, 3.54)	2.14 (1.29, 3.54)

*OR per 10 percentile point increase in %denuded bone at baseline

Summary

Among persons with knee OA, in knees without frequent pain at baseline, percent denuded subchondral bone predicted development of frequent knee pain at 2 year follow-up.

Discussion

- First study to investigate relationship between denuded subchondral bone and pain
- Among the first to investigate relationship between quantitative assessment of bone pathology and pain
- Stronger relationship with pain was found when we considered percent denuded bone from both medial and patellar surfaces

Discussion

- Frequent knee pain commonly used measure
- Additional measures of pain experience may provide further insight
- Larger sample size will increase power to detect relationships for individual plates

Conclusion

- These results support that exposure of subchondral bone may be a source of pain in knee OA

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