The association between baseline quadriceps strength and worsening of WOMAC function score

Sex	N Per Tertile (% with Progression)	Tertile of Strength	Odds Ratio	95% CI	p-value
Men	274 (6.5)	High	(Referent)		
	277 (5.5)	Middle	0.69	(0.32, 1.46)	0.3145
	277 (6.1)	Low	0.68	(0.34, 1.42)	0.3241
Women	437 (4.4)	High	(Referent)		
	432 (4.2)	Middle	0.97	(0.49, 1.92)	0.9308
	425 (6.4)	Low	1.58	(0.82, 3.03)	0.1685

Conclusions: Quadriceps weakness was not associated with an increased risk for worsening of knee pain severity or worsening self-reported physical function over 30 months in either men or women. For the goals of minimizing risk for impairments and functional limitations, these data do not appear to support the importance of maintaining adequate quadriceps strength in men and women with or at increased risk for knee OA.

3
SERUM OPIOID MONITORING IN OSTEOARTHRITIS PATIENTS WITH CHRONIC PAIN: THE SEARCH FOR SENSITIVE BIOMARKERS

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Background: Osteoarthritis (OA), a common, minimally inflammatory rheumatological syndrome characterized by chronic joint pain and dysfunction, the primary symptom of OA is pain that is seen as entirely linked with function, with physical movements triggering pain, while pain, in turn, causes limitations in physical function. Chronic pain has been associated with augmented circulating catecholamines (CAs) and bradykinin. The presence of natural antibodies (NA) regarding specificity and have gained increasing attention in proteome analysis for developing, monitoring and effective treatment of OA.
Objectives: The objective of the study was to test of natural antibodies against serum proteins relevant to pain (dopamine DA, adrenaline AD, noradrenaline NA, bradykinin BK) expression on chronic osteoarthritis pain.
Methods: We evaluated 75 individuals with chronic pain (>3 months) due to OA. Pain was moderate to severe (>4 of 10), as self-assessed with Likert scale (0 to 10) using a daily pain diary for 2 wk before outpatient screening assessment. The clinical diagnosis of OA was further confirmed using Kellgren and Lawrence radiographic scoring criteria. 75 healthy individuals without OA or other pain syndromes, of similar age and body mass index (BMI), were evaluated as control subjects Table 1. We compared circulating concentrations of NA against CAs, BK in the using express ELISA protocol (INR).
Results: We detected significantly higher concentrations of DA-IgG and BK-IgG in OA patients compared with healthy control. In addition, we found significant relationships between serum DA-IgG and BK-IgG in patients with chronic, moderate to severe OA pain. Elevated DA-IgG was significantly correlated with BK-IgG ($r = 0.91$; $P < 0.005$) and VAS ($r = 0.75$; $P < 0.001$) in OA patients. There were no statistically significant differences in mea values for NA to AD and NA in OA patients, compared with healthy control subjects.
Conclusions: Evaluated together DA-IgG and BK-IgG, they can give important information about immune system functioning, especially relating to pain and vascular homeostasis. High throughput technology has made major contributions to the study autoantigen-antibody systems as serological markers of pain in OA. Quick and easy to perform ELISA test for detect DA-IgG/BK-IgG can be routinely used in clinical laboratories. Our results have potential applications for controlling unwanted pain and future response to therapy in OA patients.

Table 1. Baseline characteristics

Age (yr)	54±8.8	51±11.1
BMI (kg/m^2)	26±2.5	26±3.3
Duration of OA (yr)	13.0±9.8	
Pain (visual analog) scores	5.46±2.15	0.00±0.00
Beck Depression Index	5.56±5.69	1.00±1.86

4
OSTEOPONTIN LEVEL IN SYNOVIAL FLUID IS ASSOCIATED WITH THE SEVERITY OF KNEE JOINT PAIN

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Purpose: Osteopontin (OPN) is an O-glycosylated phosphoprotein which is synthesized in a variety of tissues and cells including chondrocytes and synoviocytes. Accumulating data indicated that OPN is involved in the process of inflammation, immunity, and bone metabolism. OPN knockout mice have already been created and shown that cartilage degradation is accelerated in the absence of OPN. Human studies revealed that OPN protein level increased in the synovial fluid from the patients suffering from OA and RA. These data strongly suggest that OPN is involved in joint homeostasis and in the pathogenesis of arthritis. However, the molecular functions of OPN in these processes are not yet extensively studied. Here we report that synovial fluid OPN level is associated with the severity of joint pain.
Methods: This study was approved by the Ethics Committee of this institute. All patients included in this study gave their full, written, informed consent for participation prior to the operative procedure. Tissue samples (synovial fluid and synovial membrane) were obtained from the patients who underwent anterior cruciate ligament reconstruction (ACL-R) or total knee arthroplasty (TKA) from January 2009 till October 2010 in our hospital (OA: 27 samples, female: 22 male: 5, range 51–90 year-old, average 77 year-old, ACL-R: 17 samples, female: 4 male: 13, range 18–47 year-old, average 27 year-old). OPN mRNA expressed in synovial membrane was quantified by RT-QPCR (Roche, Light Cycler 480, Germany). Total OPN protein levels in synovial fluid were quantified using OPN/OPN N-half ELISA kit (IBL, Japan) and compared them with clinical parameters such as Lysholm score (ACL-R), visual analogue scale (VAS, TKA), serum C-reactive protein (CRP) level, and macroscopic observation of cartilage degradation.
Results and Discussion: As previously reported, OPN mRNA expression level in synovial membrane and OPN protein level in synovial fluid were significantly increased in OA if compared with those of ACL-R.
In the ACL-R group, OPN protein level in synovial fluid was gradually decreased after the injury. We found that OPN protein level in synovial fluid was POSITIVELY associated with the severity of joint pain (Lysholm Score) although it was not statistically significant. Since OPN acts as a pro-inflammatory cytokines by enhancing migration, survival, phagocytosis, and pro-inflammatory cytokine production of macrophages, we hypothesized that OPN induces joint pain by promoting inflammation in the joint. To test this hypothesis, we investigated the correlation of OPN protein level in synovial fluid with serum CRP level. However, we did not observe any correlation between these two. Further analysis is required to elucidate if our hypothesis is correct or not. Since accelerated degradation of articular cartilage is observed in OPN knockout mice, we next investigated the correlation of OPN protein level in synovial fluid with the macroscopic observation of cartilage degradation. However, we also did not observe any correlation between these two parameters.
In the TKA group, most interestingly, OPN protein level in synovial fluid was NEGATIVELY correlated with the severity of joint pain (VAS) in OA patients ($R = -0.469$) but not with the serum CRP level by Pearson product-moment correlation coefficient analysis. These data represent stark contrast to those of ACL-R group, and further analyses is required to elucidate the roles of OPN in the regulation of knee joint pain.
Conclusions: Osteopontin level in synovial fluid was associated with the severity of joint pain. In the ACL-R group, it is POSITIVELY associated with the severity of joint pain, however, NEGATIVELY correlated in the TKA group.

5
IDENTIFYING PAIN VULNERABILITY PHENOTYPES IN OSTEOARTHRITIS

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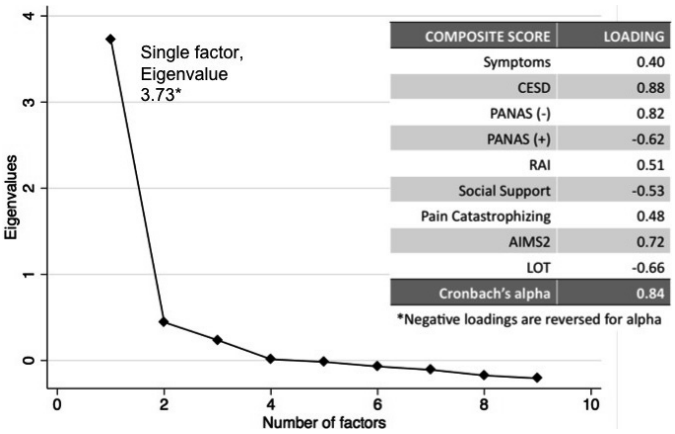
Purpose: Joint symptoms do not correlate perfectly with structural damage in osteoarthritis (OA), and it is known that psychosocial issues,

such as depression, can increase an individual's experience of pain. We used factor analysis to determine the relationships among symptomatic and psychosocial variables in a community-based sample with and without OA.

Methods: We used data from individuals who were both enrolled in both the Johnston County OA Project and the separately funded Arthritis, Coping, & Emotion (ACE) study (data collected 1999–2005, n = 2239). This sample was approximately 1/3 male and African American, with mean age of 65±11 years, body mass index 30±7 kg/m2, and 13±11 years of education. Half had radiographic OA (defined as a Kellgren-Lawrence grade ≥2) of at least one hip or knee. Symptomatic data were available for 9 joint sites: the lower back and bilateral hands, knees, hips, and feet, and were graded as none, mild, moderate, or severe "on most days." The 7 validated psychosocial scales used were: the Centers for Epidemiological Studies Depression Scale (CES-D), Positive and Negative Affect Scale (PANAS), Rheumatology Attitudes Index (RAI), Social Support, Pain Catastrophizing Helplessness Subscale, Arthritis Impact Measurement Scale 2 Tension and Anxiety Subscale (AIMS2), and Life Orientation Test (LOT). Symptomatic data and the 7 scales were individually factor analyzed and appropriate composite scores were constructed. Higher order factor analysis was used to determine the relationships among these 8 composite scores. Cronbach's alpha was calculated as a measure of reliability and internal consistency. Analyses stratified by gender, race (African American vs. Caucasian), age (<55, 55–65, 65–75, 75+ years), body mass index (BMI, <25, 25 to <30, 30+ kg/meter squared), education (less than, equal to, or more than 12 years) and by radiographic OA status in the hip or knee were performed to determine any subgroup differences.

Results: Analysis of each of the individual scales resulted in a single factor (all alphas >0.79) with the exception of the PANAS, which, as expected, had 2 factors (alpha 0.90) reflecting positive and negative affect characteristics. Symptoms from 9 joint sites also loaded onto a single factor (alpha 0.86). Higher order factor analysis using composite scores for each of these factors produced a single factor with an eigenvalue of 3.73 (See figure, due to missing values in individual scales, n = 1332, loadings 0.40–0.88, alpha 0.84). Dropping each score individually did not substantially change the alpha. Consistent results (factor loading pattern and alpha) were obtained when stratified by gender, race, age, BMI, education, or OA status.



COMPOSITE SCORE	LOADING
Symptoms	0.40
CESD	0.88
PANAS (-)	0.82
PANAS (+)	-0.62
RAI	0.51
Social Support	-0.53
Pain Catastrophizing	0.48
AIMS2	0.72
LOT	-0.66
Cronbach's alpha	0.84

*Negative loadings are reversed for alpha

Figure: Screeplot of higher order factor and table of loadings of each scale onto this factor. *The eigenvalue represents the amount of information contained in a factor, while loadings represent the association between the individual scores and the factor.

Conclusions: This analysis suggests that there is a single latent variable underlying musculoskeletal symptoms and a variety of psychosocial variables representing depression, anxiety, optimism, social support, and helplessness. The results were similar for subgroups of gender, race, age, BMI, education, and radiographic OA status. Addressing psychosocial components of the pain experience will be important for successful treatment in conditions leading to chronic musculoskeletal pain, such as OA.

6

A NOVEL TECHNOLOGY TO DECREASE KNEE PAIN AND JOINT LOAD IN EARLY-ONSET KNEE OSTEOARTHRITIS

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Purpose: To examine the effect of un-weighted exercise on knee pain and knee loading in an overweight early-onset knee osteoarthritis (OA) population. Research has demonstrated that body weight is the number one modifiable risk factor associated with the onset and progression of knee OA. However, exercise programs that aim to initiate weight loss and improve pain and function in knee OA often increase loading on the knee joint, contributing to exacerbation of symptoms and progression of the disease. The introduction of a new treadmill that allows the participant to walk un-weighted (the G-Trainer, Alter-G Inc., Menlo Park CA), utilizes a technology called Lower Body Positive Pressure (LBPP), and now enables our research team to study the relationship between body weight, knee pain and knee loading via knee acceleration during exercise.

Methods: Participants with radiographically-confirmed early-onset knee OA were recruited to walk on the treadmill for a period of 25 minutes at a speed of 1.4 m/s. Subjects completed two walking sessions (one full weight-bearing and one un-weighted session), which occurred 1 week apart and were randomized in order. Subjects also completed two full weight-bearing walking sessions (at a self-selected speed) on a walkway. Measures included knee pain (via Visual Analog Scale) and knee joint acceleration (via tri-axial accelerometry).

Results: Twenty-two overweight/obese patients (mean (SD) age 53.7 (5.9) yrs; mean (SD) BMI 33.6 (6.4) kg/m^2) completed the treadmill and walkway walking sessions. The mean level of un-weighting for pain relief was 12.3% of body weight. There was a significant difference in knee pain between full weight-bearing treadmill walking and un-weighted treadmill walking sessions ($p < 0.05$). Higher levels of un-weighting during treadmill walking resulted in lower levels of knee acceleration ($p < 0.05$). Similar speeds were seen for treadmill walking and fast walking on the walkway; however knee acceleration was significantly lower during treadmill walking ($p < 0.05$).

Conclusions: A mean un-weighting of 12.3% of body weight was sufficient to decrease subjects' pain while attenuating knee joint acceleration. This level of weight loss (12% of body weight) is a realistic value for overweight/obese patients suffering from knee pain due to knee OA. The LBPP technology used by the G-trainer treadmill may help to conserve the joint by limiting knee acceleration, while allowing patients to successfully complete exercise programs targeting weight loss and improved function. Future research should be directed at establishing the efficacy of this technology in the treatment of knee OA and other musculoskeletal disorders of the lower extremity.

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PROGNOSIS OF CARTILAGE LOSS BY ANALYZING MAGNETIC RESONANCE IMAGING OF THE TIBIA TRABECULAR BONE STRUCTURE

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Purpose: Degradation of the articular cartilage and overall bone remodeling are the main effects of Osteoarthritis (OA) progression. Magnetic resonance imaging (MRI) has helped experts to diagnose OA by providing methods for quantification the multiple components of the knee joint and detecting early tissue changes. A recent advance in OA quantification is the automatic measurement of the cartilage volume using MRI scans. We analyzed MRI scans to investigate the feasibility of predicting the rapid/slow progressors of tibial cartilage loss by a fully automatic quantification of the trabecular tibia bone structure.

Methods: The longitudinal study included 159 subjects from a community-based, non-treatment study. The data set consisted of 268 knee MRI, after exclusion of scans due to the subjects that dropped out in the follow-up or to acquisition errors. The population characteristics were: age 56±16, Body Mass Index 26±4, 47% female, and 19% with radiographic OA (Kellgren Lawrence grade, KLG > 1). The KLG was determined from load-bearing radiographs in semi-flexed position using the SynaFlex (Synarc). MRI scans were acquired using a Turbo 3D T1