techniques including chemical exchange saturation transfer (CEST) can be used to visualize microstructural and biochemical changes to the cartilage matrix even before morphological damage is visible^{2,3}. CEST is a promising technique based on detecting the chemical exchange between bulk water protons and protons bound to solutes. This technique renders the possibility to function as a biomarker for glycosaminoglycan (GAG/gag) content for instance in cartilage of joints.

Objectives: The aim of the study was to compare glycosaminoglycan chemical exchange saturation transfer (gagCEST) of knee cartilage with intraoperative results for the assessment of early osteoarthritis (OA) and to define gagCEST values for the differentiation between healthy and degenerated cartilage.

Methods: Patients with cartilage lesions or moderate OA were preoperatively examined using 3T Magnetic Resonance Imaging (MRI). In this prospective study, regions of interest (ROIs) were examined by a sagittal gagCEST analysis and a morphological high-resolution three-dimensional, fat-saturated proton-density space sequence. Cartilage lesions were identified arthroscopically, graded by the International Cartilage Repair Society (ICRS) score in 42 defined ROIs per patient and consecutively compared with mean gagCEST values using analysis of variance and Spearman's rank correlation test. Receiver operating characteristics (ROC) curves were applied to identify gagCEST threshold values to differentiate between the ICRS grades.a

Results: Twenty-one patients with cartilage lesions or moderate OA were examined. The imaging assessment consisted of a total of 882 ROIs which were examined and graduated in ICRS score 0 (67.3%), 1 (25.2%), 2 (6.2%) and the merged ICRS 3 and 4 (1.0%). gagCEST values decreased with increasing grade of cartilage damage with a negative correlation between gagCEST values and ICRS scores. A gagCEST value threshold of 3.55% was identified to differentiate between ICRS score 0 (normal) and all other grades.

Conclusion: Conclusions. gagCEST reflects the content of glycosaminoglycan and might provide a diagnostic tool for the detection of early knee-joint cartilage damage and for the non-invasive subtle differentiation between ICRS grades by MRI even at early stages in clinical practice.

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OP0110

A COHORT STUDY ON THE BIDIRECTIONAL RELATIONSHIP BETWEEN PERIODONTITIS AND OSTEOARTHRITIS OVER A 15-YEAR FOLLOW-UP

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Background: Recently, osteoarthritis has been proposed to be driven by complement-mediated inflammatory cascades. That is, in addition to the conventional degenerative model, our knowledge of osteoarthritis pathogenesis has been expanded with an inflammation-dependent theory.

Objectives: To identify the relationship between osteoarthritis and periodontitis.

Methods: 144,788 periodontitis patients and 144,788 propensity score-matched controls without history of periodontitis were enrolled in this cohort study. A Cox proportional hazard model was used to estimate the risk of osteoarthritis. Survival analysis was utilized to assess the time-dependent effect of periodontitis on osteoarthritis. Age and gender were stratified to identify susceptible subgroups. A symmetrical case-control analysis was designed to determine the relationship between periodontitis and history of osteoarthritis.

Results: Patients with periodontitis had higher risk of osteoarthritis (HR =1.15, 95% CI =1.12-1.17, P < 0.001) and severe osteoarthritis that led to total knee/hip replacement (HR =1.12, 95% CI =1.03-1.21, P < 0.01) than controls, which was time-dependent (log-rank test P < 0.01). The effect of periodontitis on osteoarthritis was significant in both genders and age subgroups over 30 years old (all P < 0.001). Among them, females (HR=1.27, 95% CI = 1.13-1.42, P < 0.001) and patients aged over 51 (HR= 1.21, 95% CI =1.10-1.33, P < 0.001) with periodontitis were predisposed to severe osteoarthritis that led to total knee/hip replacement. In addition, periodontitis patients were more likely to have a history of osteoarthritis (OR = 1.11, 95% CI = 1.06 - 1.17, P < 0.001).

Conclusion: These findings suggest a bidirectional relationship between osteoarthritis and periodontitis. Patients with periodontitis presented with a higher risk of osteoarthritis, including severe osteoarthritis that led to total knee/hip replacement. Likewise, periodontitis was more likely to develop following osteoarthritis.

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OP0111

PLASMA PROTEOMICS IDENTIFIES CRTAC1 AS BIOMARKER FOR OSTEOARTHRITIS SEVERITY AND PROGRESSION

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Background: Accurate biomarkers for diagnosis and prediction of osteoarthritis (OA) are needed. In addition, biomarkers have the potential to serve as a measure of the different pathological processes underlying OA. Here, we report on a proteomics screen targeted at two important pathways thought to underlie the etiology of OA: the inflammation and metabolic pathways.

Objectives: The aim of this study was to identify a robust biomarker for OA severity and progression.

Methods: We used data from the Rotterdam Study, a population based prospective study with participants aged 45 and older. The participants in this study underwent blood measurement at baseline and radiographic measurements at baseline as well as after a mean follow-up time of 5 years. We measured 184 proteins (inflammation and cardiometabolic panel) in plasma from 3,517 participants in the Rotterdam Study using the Olink platform.

We estimated the association for all available proteomic biomarkers with OA in knee, hip and hand in 2 ways: 1) Cross-sectionally in all joints, where we analyzed severity of OA by adding up KL-scores of both joints (knee and hip OA), and all joints of the left and right hand (total amount of joints=30); 2) Longitudinally in Knee and Hip, defining cases of progression of OA as an increase with at least 1 unit in KL-grade per person, excluding progressing from KL0 to KL1. We analyzed the relationship with multivariate regression

Figure 1. Forest plot for significantly associated proteins with severity of Hand OA

models using generalized linear models with binomial link function. In model 1 we adjusted for age, sex and cell counts, in model 2 we additionally adjusted for BMI. We report effect estimate(beta) per standard deviation (SD) change in protein levels with 95% Confidence Interval (CI) and nominal p-value (significance level<0.05) for each protein. All statistical analyses were performed in R version 3.5.2.

Results: We found in total 56 proteins that were significantly associated with one or more OA-outcomes at nominal level. Figure 1 illustrates the 19 significant associations for severity of hand OA ordered by significance level (most significant at top). We observed a very robust association between the level of circulating Cartilage acidic protein 1 (CRTAC1) and severity of OA in the knee ($\beta=0.16$, 95%CI 0.09-0.23, $p=0.000013$, FDR-corrected $P=0.0011$) hand ($\beta=0.086$, 95%CI 0.03-0.14, $p=0.00085$, FDR-corrected $P=0.0252$), while a similar trend was seen in hip ($\beta=0.08$, 95%CI -0.02-0.18, $p=0.12$), although power in hip was limited in our study. The association with CRTAC1 was also found for progression in knee ($\beta=0.21$, 95%CI 0.03-0.36, $p=0.0156$, FDR-corrected $P>0.2$) and hip ($\beta=0.18$, 95%CI -0.01-0.38, $p=0.0624$, FDR-corrected $P>0.9$). These associations were independent of BMI. Among the findings were several other promising biomarkers, e.g. MMP-10, which we observed to be associated with severity of hand OA ($\beta=-0.09$, 95%CI -0.15- -0.04, $p=0.00067$, FDR-corrected $P=0.0383$) and progression of knee OA ($\beta=-0.24$, 95%CI -0.42- -0.06, $p=0.0073$, FDR-corrected $P>0.1$). Additionally, COMP, a well-known biomarker for OA, was also found significant for OA severity in hand ($\beta=0.10$, 95%CI 0.05-0.16, $p<0.001$, FDR-corrected $P=0.0043$) and knee ($\beta=0.09$, 95%CI 0.02-0.17, $p=0.01$, FDR-corrected $P>0.2$).

Conclusion: We identified the CRTAC1 protein as a robust, promising biomarker for osteoarthritis severity and progression. This protein is a glycosylated extracellular matrix protein that is found in the interterritorial matrix of articular deep zone cartilage. This protein can also be used to distinguish chondrocytes from osteoblasts and mesenchymal stem cells in culture. This suggests that CRTAC1-levels reflects a cartilage-specific process in the joint. Such a biomarker might be useful for targeting the right patients for clinical trials and designing novel therapies for OA.

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OP0112 FACTORS ASSOCIATED WITH OSTEOPOROSIS CARE OF MEN: A REAL-LIFE STUDY ON A NATION-WIDE DATASET

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Background: Male osteoporosis is associated with an important clinical and economic burden worldwide. Notwithstanding that, undertreatment of men with osteoporosis is common. Understanding the factors associated with less osteoporosis care utilization might help define future intervention to improve access of men to osteoporosis care.

Objectives: The aim of the study was to describe the factors associated with osteoporosis care in men.

Methods: We conducted a retrospective analysis of a nation-wide cohort (DeFRA-Calculator database). DeFRA-Calculator is a tool that estimates the fracture risk considering clinical and densitometric risk factors, including the presence of prior hip or vertebral and non-vertebral or non-hip fractures. We compared the clinical characteristics of male individuals with an age matched cohort of women. Propensity score generation with 2:1 matching for female and male patients was performed matching the cohorts for age, generating propensity estimates with a logistic regression model.

Results: We analyzed a sample of 4,902 men at high risk of osteoporosis. We found that the factors associated to osteoporosis care utilization in men were: the presence of comorbidities (OR 1.939, 95% CI 1.799-2.090), adjuvant hormonal therapy for prostate cancer (OR 1.482, 95% CI 1.315-1.670), the presence of vertebral or hip fractures (OR 1.490, 95% CI 1.378-1.611) and glucocorticoid treatment (OR 2.573, 95% CI 2.274-2.832) (Table 1)

Conclusion: We found that men accessed osteoporosis care with more severe osteoporosis and/or with a diagnosis of secondary osteoporosis. Male osteoporosis remains largely underdiagnosed with a dramatic latency in osteoporosis care utilization compared to women.

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Table 1. Clinical and densitometric characteristics of the study population and age-matched cohort of women

	Men (n=4,902)	Women (n=9,804)	OR (95% CI) – p value
Age (±SD)	65.1 (±14.2)	65.1 (±14.2)	NS
BMI (±SD)	25.31 (±4.91)	24.07 (±4.85)	<0.0001
Lumbar spine T-score (±SD)	-2.13 (±1.37)	-2.51 (±1.15)	<0.0001
Osteoporosis at lumbar spine (%)	2,601 (53.1%)	5,948 (60.7%)	0.733 (0.684-0.785)
Femoral neck T-score (±SD)	-1.93 (±1.04)	-2.19 (±0.91)	<0.0001
Osteoporosis at femoral neck (%)	1,412 (28.8%)	3,936 (40.1%)	0.603 (0.560-0.649)
% 10-year risk of fracture (±SD)	22.77 (±21.05)	20.26 (±4.85)	<0.0001
Family history of fragility fracture (%)	891 (18.2%)	2,379 (24.3%)	0.693 (0.636-0.756)
Secondary osteoporosis (%)	2,415 (49.3%)	3,092 (31.5%)	2.108 (1.965-2.262)
Glucocorticoids ≥5 mg/day >3 months (%)	768 (17.4%)	694 (7.7%)	2.573 (2.274-2.832)
Glucocorticoids ≥5 mg/day ≥3 months <12 months (%)	74 (2.0%)	72 (0.9%)	2.357 (1.700-3.267)
Glucocorticoids ≥5 mg/day ≥12 months (%)	119 (3.2%)	138 (1.6%)	1.977 (1.543-2.534)
Adjuvant hormonal therapy for breast cancer or prostate cancer (%)	495 (12.0%)	766 (8.4%)	1.482 (1.315-1.670)
Comorbidities (%)	1,778 (36.3%)	2,225 (22.7%)	1.939 (1.799-2.090)
Rheumatoid arthritis (%)	303 (8.8%)	511 (6.3%)	1.439 (1.241-1.668)
Psoriatic arthritis (%)	59 (1.9%)	103 (1.3)	1.390 (1.006-1.919)
Systemic lupus erythematosus (%)	22 (0.7%)	77 (1.0%)	0.693 (0.431-1.115)
Systemic sclerosis (%)	9 (0.3%)	60 (0.8%)	0.364 (0.180-0.734)
Other rheumatic diseases (%)	173 (5.2%)	310 (3.9%)	1.354 (1.119-1.638)
Inflammatory bowel diseases (%)	144 (2.7%)	126 (1.6%)	2.773 (2.175-3.534)
Chronic obstructive pulmonary disease (%)	281 (8.3%)	277 (3.5%)	2.461 (2.074-2.920)
Diabetes (%)	441 (12.4%)	478 (5.9%)	2.238 (1.954-2.564)
Neurological diseases (%)	236 (7.0%)	260 (3.3%)	2.202 (1.837-2.639)
HIV infection (%)	110 (3.4%)	23 (0.3%)	11.603 (7.389-18.221)
Vertebral or hip fractures (%)	1,434 (29.3%)	2,130 (21.7%)	1.490 (1.378-1.611)
Non-vertebral, non-hip fractures (%)	534 (10.9%)	1,477 (15.1%)	0.689 (0.620-0.766)

OP0113 FEMALE REPRODUCTIVE FACTORS AND RISK OF JOINT REPLACEMENT ARTHROPLASTY OF KNEE AND HIP DUE TO OSTEOARTHRITIS IN POSTMENOPAUSAL WOMEN: A NATIONWIDE COHORT STUDY OF 1.36 MILLION WOMEN

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Background: Previous studies on the link between female reproductive factors and osteoarthritis (OA) have shown conflicting results.

Objectives: This study attempted to explore the association between reproductive factors and joint replacement arthroplasty of knee (TKRA) and hip (THRA) in a large nationwide population-based cohort of postmenopausal women.

Methods: 1,218,257 subjects who participated in national health examination in 2009 were included in the study. The study outcomes is incident THRA or TKRA