Fibulin-3 fragments are prognostic biomarkers for osteoarthritis incidence in overweight and obese women

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Introduction

Biochemical markers of bone, synovium, or cartilage turnover have been proposed as tools for the diagnosis and prognosis of osteoarthritis (OA) and for the monitoring of OA treatment. The discovery of novel OA biomarkers is essential for drug discovery and development, for early diagnosis, and to facilitate individualized treatment to improve outcomes.

The aim of the present study was to evaluate the associations between three Fibulin-3 fragments, originally discovered by proteomics, and the 30 months incidence of radiographic and clinical knee OA among a high-risk group of middle-aged overweight and obese women, free of knee OA at baseline.

Methods

Data of the PROOF study, the first preventive RCT in OA research [1], were used. Women between 50 and 60 years and with a BMI ≥ 27 kg/m^2 were recruited through their general practitioner. At baseline, all women were free of radiographic and clinical knee OA, free of severe disabling comorbidities, without inflammatory rheumatic diseases, and not under treatment for knee compaints. Using binary logistic regression, the associations between baseline concentrations of three Fibuline-3 fragments (Fib3-1, Fib3-2 and Fib3-3) from serum and incidence of medial joint space narrowing (JSN), lateral JSN, Kellgren&Lawrence ≥ 2, the 'clinical and radiographic ACR-critera', and of chronic knee pain (knee pain in the last 12 months and on most days of the last month).

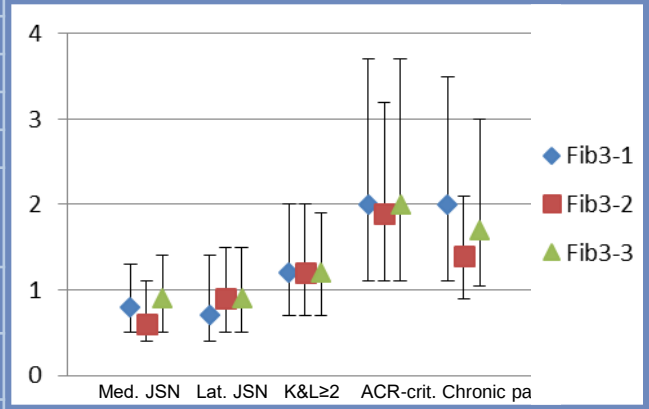
Results

Complete follow-up and baseline Fibulin-3 concentrations were available for 241 women. See Table 1 for baseline characteristics. Adjusted odds ratio's (ORs) for all three Fibuline-3 fragments and all outcomes are given in Figure 1. When adjusted for the other Fibuline-3 fragments, only Fib3-1 showed a significant adjusted odds ratio for incidence of the ACR-criteria (OR 3.21 95% CI: [1.19-8.70]) and for chronic pain (OR 3.05 95% CI: [1.20-7.71]).

Table 1. Baseline characteristics

Age (yr)	55.9 ± 3.2
BMI (kg/m^2)	31.7 ± 3.6
Postmenopausal status	70%
Western ethnicity	96%
WOMAC pain (0-100)	6.1 ± 10.2
WOMAC function (0-100)	5.9 ± 9.7
WOMAC stiffness (0-100)	11.6 ± 17.4
Kellgren & Lawrence grade 1 uni- and bilateral	57% 24% and 33%
Varus alignment uni- and bilateral	50% 19% and 30%
Mild symptoms uni- and bilateral	41% 24% and 17%
OA in other joints	23%

Adjusted odds ratio's for baseline Fibulin-3 Concentrations and knee OA measures after 30 months



Conclusion: Baseline Fibulin-3 fragments were associated with the incidence of clinical knee OA after 30 months in middle-aged overweight and obese women, free of OA at baseline. Therewith, they meet the criteria for a prognostic biomarker according to the BIPED biomarker classification for OA.

[1] Runhaar et al. Prevention of knee osteoarthritis in overweight females; the first preventive randomized controlled trial in osteoarthritis research. American Journal of Medicine (2015).

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