Serum concentrations of cartilage oligomeric matrix protein and bone sialoprotein in hip osteoarthritis: A one year prospective study

Thierry Conrozier, Tore Saxne, Charles Shan Sei Fan, Pierre Mathieu, Anne-Marie Tron, Dick Heinegård, Eric Vignon

Abstract

Objective—To evaluate serum concentrations of cartilage oligomeric matrix protein (COMP) and bone sialoprotein (BSP) as predictors of disease progression in hip osteoarthritis (OA).

Methods—Forty eight consecutive patients, referred to hospital for symptomatic hip OA, (ACR criteria) were monitored in a one year prospective trial with radiographs and serum samples. The radiographs were graded for joint space narrowing, osteophytes, and sclerosis and the joint space width was measured by a digitised image analyser. Serum COMP and BSP were quantified by immunoassays.

Results—The COMP concentrations at baseline correlated with the joint space width at entry and with its yearly mean narrowing (r = 0.38, p = 0.002) but not with joint space narrowing grade progression. The concentrations were higher in patients with bilateral hip OA (p = 0.03). The serum BSP concentrations at baseline were unrelated to OA progression but correlated inversely to the osteophyte grade (r = −0.36, p = 0.004) and sclerosis grade (r = −0.42, p = 0.0004).

Conclusion—Serum COMP seems to be a surrogate marker of OA and may be of interest for the detection of patients at risk of rapidly progressing disease in hip OA. Serum BSP changes seem to reflect alterations in the subchondral bone turnover in hip OA. Measurement of joint space width using a digitised image analyser is a sensitive way of assessing OA progression that facilitates evaluation of tissue markers in relation to anatomical changes in the joint.

Osteoarthritis (OA) is characterised by cartilage destruction and subchondral bone changes. Assessment of the anatomical progression of joint damage is of major importance, especially when potentially disease modifying drugs are developed and efficacy in OA needs to be assessed. For optimal therapeutic intervention it is also highly relevant to be able to identify the patients at highest risk for progressive tissue destruction.

Cartilage oligomeric matrix protein (COMP) and bone sialoprotein (BSP) have been shown to have potential as prognostic markers of OA progression. COMP is a non-collagenous protein primarily isolated from the extracellular matrix of cartilage although the protein is not unique to this tissue. Thus, it has been found in bone and equine tendons and in human knee joint meniscus. Furthermore, synovial cells can in vitro be stimulated to COMP production by transforming growth factor β (TGFβ). COMP is a large, Mr 435 kDa, acidic protein consisting of five subunits united close to their N-termini forming a bouquet-like structure. COMP is preferentially located in the superficial, interterritorial matrix. The COMP concentrations are higher in synovial fluid than in serum, which suggests that it is locally produced in the joints. High concentrations of COMP have been detected in synovial fluid after knee trauma and increased serum COMP concentrations have been indicated to predict severe destruction in large joints in patients with rheumatoid arthritis. In knee OA, changes in serum COMP concentrations have been shown to predict joint space narrowing progression, and to correlate with the bone scintigraphic uptake of technetium diphosphonate.

BSP is a bone specific non-collagenous matrix macromolecule, polydisperse in size with an average Mr of 52 500. The protein is enriched in the immediate subchondral layer of bone. It is increased in serum in patients with early radiographic signs of knee OA and in synovial fluid after knee trauma. In RA, BSP is increased in serum compared with healthy controls and synovial fluid concentrations correlate significantly to degree of knee joint damage. Serum concentrations show a similar variation, although not a significant association.

A quantitative assessment of OA changes (that is, articular cartilage thickness, osteophytes, sclerosis, and cysts) is important in defining correlates in the evaluation of these new molecular markers. Anatomical changes can be visualised using plain radiographs or magnetic resonance imaging (MRI). MRI is a promising method but precise and reproducible measurements of cartilage and bone features are still in the developmental stage and are not fully validated. On the other hand, it seems that conventional radiography may be the most suitable method to assess articular cartilage thickness of the hips and knees in long term follow up studies. The most widely used method for radiographic evaluation of OA progression remains the Kellgren and
Lawrence (KL) grading scale,\(^2\) which has been considered the “gold standard” for diagnosis and assessment of the progression of the condition. Alternatives to the KL scale are needed for evaluation of OA progression and particularly cartilage destruction.\(^1\) The separate grading of different radiographic OA lesions has been used to improve sensitivity and reduce interobserver variability,\(^2\)--\(^4\) but an accurate measure of progression requires direct measurement of joint space narrowing. New techniques have therefore been designed to quantitatively and reproducibly assess knee and hip joint space.\(^5\)--\(^8\) Examples of such measures include special devices for microfocal radiography\(^9\) and semiautomated digitised image analysers in combination with rigorous standardisation of the radiological procedure.\(^10\)

The use of a computer image analysis system has been demonstrated to improve both sensitivity and reproducibility of the measurements.\(^11\)--\(^13\) The purpose of this study was to evaluate serum concentrations of COMP and BSP as possible predictors of OA progression as determined by both semi-quantitative grading and automated measurement of radiographic changes in hip OA.

**Methods**

**CLINICAL DATA**

Forty-eight patients (25 women and 23 men) referred to the department of rheumatology with symptomatic hip OA were recruited to this one-year prospective study. All fulfilled the ACR criteria for hip OA.\(^14\) Only patients with superior femoral head migration (suprolateral, superointermediate, and superomedial) were selected because of the difficulties for inferior or medial joint space narrowing (JSN) to be measured. Exclusion criteria were: total loss of radiographic joint space making it not measurable; total hip arthroplasty needed in the next 12 months; and hip OA secondary to alternative arthropathies (that is, infectious or inflammatory arthritis, hip injury, aseptic osteonecrosis, congenital abnormality such as congenital dislocation of the hip). At entry all patients underwent a full clinical history and examination to obtain the following information: height, weight, body mass index (BMI), disease duration and date of diagnosis, risk of hip joint overwork with regard to professional or sport activities (for example, regular heavy lifting or strenuous walking and running), clinical presence of polyarticular OA involvement (Heberden or Bouchard’s nodes, clinical evidence of spine or knee OA), smoking status. At entry and 12 months later, patients were asked for pain and function (using Lequesne’s index\(^15\)) and a pain evaluation on a 100 mm visual analogue scale (VAS) and current treatment (non-steroidal anti-inflammatory drugs (NSAIDs) and symptomatic slow acting drugs for OA (SYSADOA)).

**RADIOGRAPHIC DATA**

At each visit patients underwent radiography of the pelvis, by the same radiologist during the whole study, using an identical radiological procedure. Anteroposterior radiographs of the pelvis, by the same radiologist during the whole study, using an identical radiological procedure. Anteroposterior radiographs of the

<table>
<thead>
<tr>
<th>Joint space narrowing</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 no narrowing</td>
<td></td>
</tr>
<tr>
<td>1 mild or doubtful narrowing (&lt;33%)</td>
<td></td>
</tr>
<tr>
<td>2 moderate narrowing (34–66%)</td>
<td></td>
</tr>
<tr>
<td>3 severe narrowing (&gt;66% but no complete narrowing)</td>
<td></td>
</tr>
<tr>
<td>4 complete narrowing (100%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Osteophytes (acetabulum and/or femoral head)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 no osteophyte</td>
<td></td>
</tr>
<tr>
<td>1 mild osteophyte</td>
<td></td>
</tr>
<tr>
<td>2 moderate osteophyte</td>
<td></td>
</tr>
<tr>
<td>3 large osteophyte</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sclerosis</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 no or doubtful sclerosis</td>
<td></td>
</tr>
<tr>
<td>1 evidence of sclerosis</td>
<td></td>
</tr>
</tbody>
</table>

The sepa-rate grading of different radiographic OA lesions has been used to improve sensitivity and reduce interobserver variability,\(^2\)--\(^4\) but an accurate measure of progression requires direct measurement of joint space narrowing. New techniques have therefore been designed to quantitatively and reproducibly assess knee and hip joint space.\(^5\)--\(^8\) Examples of such measures include special devices for microfocal radiography\(^9\) and semiautomated digitised image analysers in combination with rigorous standardisation of the radiological procedure.\(^10\)

The use of a computer image analysis system has been demonstrated to improve both sensitivity and reproducibility of the measurements.\(^11\)--\(^13\) The purpose of this study was to evaluate serum concentrations of COMP and BSP as possible predictors of OA progression as determined by both semi-quantitative grading and automated measurement of radiographic changes in hip OA.

**Methods**

**CLINICAL DATA**

Forty-eight patients (25 women and 23 men) referred to the department of rheumatology with symptomatic hip OA were recruited to this one-year prospective study. All fulfilled the ACR criteria for hip OA.\(^14\) Only patients with superior femoral head migration (suprolateral, superointermediate, and superomedial) were selected because of the difficulties for inferior or medial joint space narrowing (JSN) to be measured. Exclusion criteria were: total loss of radiographic joint space making it not measurable; total hip arthroplasty needed in the next 12 months; and hip OA secondary to alternative arthropathies (that is, infectious or inflammatory arthritis, hip injury, aseptic osteonecrosis, congenital abnormality such as congenital dislocation of the hip). At entry all patients underwent a full clinical history and examination to obtain the following information: height, weight, body mass index (BMI), disease duration and date of diagnosis, risk of hip joint overwork with regard to professional or sport activities (for example, regular heavy lifting or strenuous walking and running), clinical presence of polyarticular OA involvement (Heberden or Bouchard’s nodes, clinical evidence of spine or knee OA), smoking status. At entry and 12 months later, patients were asked for pain and function (using Lequesne’s index\(^15\)) and a pain evaluation on a 100 mm visual analogue scale (VAS) and current treatment (non-steroidal anti-inflammatory drugs (NSAIDs) and symptomatic slow acting drugs for OA (SYSADOA)).

**RADIOGRAPHIC DATA**

At each visit patients underwent radiography of the pelvis, by the same radiologist during the whole study, using an identical radiological procedure. Anteroposterior radiographs of the pelvis, by the same radiologist during the whole study, using an identical radiological procedure. Anteroposterior radiographs of the

<table>
<thead>
<tr>
<th>Joint space narrowing</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 no narrowing</td>
<td></td>
</tr>
<tr>
<td>1 mild or doubtful narrowing (&lt;33%)</td>
<td></td>
</tr>
<tr>
<td>2 moderate narrowing (34–66%)</td>
<td></td>
</tr>
<tr>
<td>3 severe narrowing (&gt;66% but no complete narrowing)</td>
<td></td>
</tr>
<tr>
<td>4 complete narrowing (100%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Osteophytes (acetabulum and/or femoral head)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 no osteophyte</td>
<td></td>
</tr>
<tr>
<td>1 mild osteophyte</td>
<td></td>
</tr>
<tr>
<td>2 moderate osteophyte</td>
<td></td>
</tr>
<tr>
<td>3 large osteophyte</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sclerosis</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 no or doubtful sclerosis</td>
<td></td>
</tr>
<tr>
<td>1 evidence of sclerosis</td>
<td></td>
</tr>
</tbody>
</table>

The sepa-rate grading of different radiographic OA lesions has been used to improve sensitivity and reduce interobserver variability,\(^2\)--\(^4\) but an accurate measure of progression requires direct measurement of joint space narrowing. New techniques have therefore been designed to quantitatively and reproducibly assess knee and hip joint space.\(^5\)--\(^8\) Examples of such measures include special devices for microfocal radiography\(^9\) and semiautomated digitised image analysers in combination with rigorous standardisation of the radiological procedure.\(^10\)

The use of a computer image analysis system has been demonstrated to improve both sensitivity and reproducibility of the measurements.\(^11\)--\(^13\) The purpose of this study was to evaluate serum concentrations of COMP and BSP as possible predictors of OA progression as determined by both semi-quantitative grading and automated measurement of radiographic changes in hip OA.

**Methods**

**CLINICAL DATA**

Forty-eight patients (25 women and 23 men) referred to the department of rheumatology with symptomatic hip OA were recruited to this one-year prospective study. All fulfilled the ACR criteria for hip OA.\(^14\) Only patients with superior femoral head migration (suprolateral, superointermediate, and superomedial) were selected because of the difficulties for inferior or medial joint space narrowing (JSN) to be measured. Exclusion criteria were: total loss of radiographic joint space making it not measurable; total hip arthroplasty needed in the next 12 months; and hip OA secondary to alternative arthropathies (that is, infectious or inflammatory arthritis, hip injury, aseptic osteonecrosis, congenital abnormality such as congenital dislocation of the hip). At entry all patients underwent a full clinical history and examination to obtain the following information: height, weight, body mass index (BMI), disease duration and date of diagnosis, risk of hip joint overwork with regard to professional or sport activities (for example, regular heavy lifting or strenuous walking and running), clinical presence of polyarticular OA involvement (Heberden or Bouchard’s nodes, clinical evidence of spine or knee OA), smoking status. At entry and 12 months later, patients were asked for pain and function (using Lequesne’s index\(^15\)) and a pain evaluation on a 100 mm visual analogue scale (VAS) and current treatment (non-steroidal anti-inflammatory drugs (NSAIDs) and symptomatic slow acting drugs for OA (SYSADOA)).

**RADIOGRAPHIC DATA**

At each visit patients underwent radiography of the pelvis, by the same radiologist during the whole study, using an identical radiological procedure. Anteroposterior radiographs of the pelvis, by the same radiologist during the whole study, using an identical radiological procedure. Anteroposterior radiographs of the
acacetabulum. JSW was obtained by measuring
the inter-bone distance at the narrowest point
of the joint. The radius of the femoral head
(RH) was automatically given by the computer
from three peripheral points drawn using the
mouse. Because two radiographs of the same
subject had to be compared, it was necessary to
look for possible differences in magnification of
the hip, and to make adequate corrections.
This was done by the measurement of the RH
of each film and then by calculating the ratio
RH of the measured film/RH of the reference
film. The intraobserver CV for repeated meas-
urements of the same film was 1.2 %,30 It was
2.9% for measurements of three radiographs of
a single patient, performed by three radiolo-
gists at different days and without a particular
standardised procedure, as described previ-
ously.28 Progression of JSN was calculated in
mm per year, enabling determination of the
yearly mean narrowing of the joint space
(YMN).

BIOLOGICAL DATA
Blood samples were obtained at the baseline
and after one year of follow up. C reactive pro-
tein (CRP) measurements were performed by
immunonephelometry (N Latex CRP mono,
Behringwerke AG, Marburg, Germany) with a
threshold of detection of 5 mg/l. Serum
samples were stored at −30°C until assayed for
COMP and BSP.

Analyses of COMP and BSP were made
without any knowledge of other clinical or
radiographic characteristics of the patients.
Serum concentrations of COMP were mea-
ured by enzyme linked inhibition immunosorb-
ent assay (ELISA) as described.13 Briefly,
human COMP was used for coating the micro-
titre plates and for producing a standard curve
included in each plate. A polyclonal antiserum
raised in a rabbit against bovine COMP was
used as first antibody. Serum samples with
known COMP concentrations were included in
each plate to detect variability. The intra-
assay and interassay variabilities were 5% and
8%, respectively. The BSP assay was per-
formed using an inhibition ELISA as described
previously.15 Briefly, human BSP was used for
coating the microtitre plates and for the stand-
ard curve. A polyclonal antiserum raised in a
rabbit against human BSP was used for detec-
tion of BSP in the serum samples. Serum sam-
plies with known BSP concentrations were included
in each plate. The intra-assay and interassay variabilities were < 10%.

STATISTICAL ANALYSIS
In patients with bilateral hip OA only the most
affected joint was selected for analysis of corre-
lations between biological and radiographic
variable. Correlations between continuous
variables were performed using linear regres-
sion analysis or Spearman test as appropriate.
Relation between continuous and qualitative
variables were studied using analysis of vari-
ance. Factors found to be associated in univariate analysis were then studied using
multivariate analysis and logistic regression
analysis. Student’s paired t test was used to
compare values at baseline and end point.
P Values <0.05 were considered significant.

Results
The demographic and clinical data at entry are
summarised in table 2 and the initial radio-
graphic data are summarised in table 3. The
mean (SD) JSW at entry was 1.8 (1.04) mm
(median: 1.65 mm, range 0.5–4.0). The yearly
mean narrowing was 0.52 (0.45) mm/year
(median 0.49, range 0–2). It was correlated to
JSW at entry (r=0.66, p<0.001).

COMP and BSP at baseline were mean (SD)
7.7 (1.2) µg/ml ( range 5.4–10.5) and mean
(SD) 143.3 (27.3) ng/ml (range 100.8–250.5),
respectively. The mean (SD) CRP was 7.5
(14.6) mg/ml (range <0.2–60). The
COMP concentrations did not vary over time
(mean (SD) 7.6 (1.4) µg/ml at one year
compared with mean (SD) 7.7 (1.0) µg/ml at
eventry, p > 0.05), whereas the BSP concentra-
tions increased during the year of follow up
(mean (SD) 160.0 (36.4) ng/ml at one year
compared with mean (SD) 143 (27.3) ng/ml at
entry, p = 0.01). The COMP and BSP con-
centration at entry correlated significantly (r
= 0.25, p = 0.04).

The COMP concentrations at baseline
correlated with JSW at entry (r = 0.40, p
= 0.001) and to YMN (r = 0.38, p = 0.002) (fig
1). In contrast, after one year COMP concen-
trations did not correlate with YMN, while
the correlation persisted with JSW (r = 0.36,
p = 0.02) . The correlation between COMP at
entry and YMN is also shown in table 4 where
COMP and BSP concentrations at baseline are
grouped according to the tertiles of YMN. In
support of this association, figure 2 shows that
patients with serum COMP at baseline equal
to or above 8.5 µg/ml had a 61.7% higher rate
of narrowing than those with serum COMP
below 8.5 µg/ml (p = 0.022). In contrast, the
variations of serum COMP over time did not
 correlate with YMN. The 10 patients with the
most marked YMN (> 1 mm/year) had

| Table 2 Characteristics of the 48 patients at entry in the study |
|-----------------|-----------------|-----------------|
| Number of patients (female/male) | 48 (25/23) |
| Age at entry in the study (y) | 56.4 (14.1) |
| Age at onset of disease (y) | 51.1 (14.1) |
| Lequesne index | 8.4 (4.3) |
| Pain on the VAS (mm) | 48.2 (25.4) |
| Joint space width (mm) | 1.80 (1.04) |
| Body mass index | 25.8 (4.3) |
| Other OA sites involved (yes/no) | 24/24 |
| Bilateral hip OA (yes/no) | 18/30 |
| Current NSAIDs consumption (yes/no/NA) | 22/19/7 |
| Current SYSDOA consumption (yes/no/NA) | 18/23/7 |
| Hip overwork (yes/no/doubtful) | 14/27/7 |
| Smoking cigarettes (yes/no) | 15/33 |
| Serum COMP (µg/ml) | 7.7 (1.2) |
| Serum BSP (ng/ml) | 143.3 (27.3) |

| NA: not available. Data shown as numbers and mean (SD). |

| Table 3 Radiographic data at entry in the study |
|-----------------|-----------------|-----------------|
| Joint space narrowing grade (0/1/2/3) | 2/11/13/24 |
| Osteophyte grade (0/1/2/3) | 6/28/14/0 |
| Joint space width (SD) (mm) | 1.80 (1.0) |
| Bone response (hypertrophic/atrophic/undeetable) | 38/6/4 |
| Femoral head migration (superolateral/superointermediate/superomedial) | 29/12/7 |
Table 4  Serum COMP and BSP concentrations at baseline according to the rate of progression of joint space narrowing in hip OA.

<table>
<thead>
<tr>
<th>YMN (mm/year)</th>
<th>Number</th>
<th>COMP (µg/ml)</th>
<th>BSP (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.3</td>
<td>16</td>
<td>7.22 (1.12)</td>
<td>136.4 (2.03)</td>
</tr>
<tr>
<td>0.3–0.6</td>
<td>16</td>
<td>7.62 (1.22)</td>
<td>146.2 (3.40)</td>
</tr>
<tr>
<td>&gt;0.6</td>
<td>16</td>
<td>8.31 (1.24)</td>
<td>144.6 (2.71)</td>
</tr>
</tbody>
</table>

Data shown as mean (SD) and ranges.

Discussion

The positive correlation between the COMP concentration at baseline and progression of JSN is the main finding in this study. Such a correlation between a single serum measurement of a tissue marker and future OA progression has not been demonstrated previously for a marker that may reflect cartilage turnover, albeit increasing COMP concentrations have been found to correlate to later disease progression in knee OA. The correlation between serum COMP and anatomical changes in the joint could be that the method for measuring JSN progression, using a computer image analysis, is much more sensitive to small changes than commonly used semi-quantitative grading or inter-bone distance measurement using a ruler. Our data suggest that a serum COMP concentration greater than 8.5 µg/ml is associated with a higher rate of JSN and supports the hypothesis that COMP is a surrogate marker of OA, which could be particularly of interest for the detection of patients at risk of rapidly progressive disease. The finding of higher serum concentrations in patients with bilateral hip OA further supports that COMP in the general circulation reflects joint pathology. The effects on serum concentrations of COMP by putative contribution from extra-articular sources, have to be considered when interpreting changes in the circulating concentrations. However, the contribution from tendon is probably negligible in view of findings that even in race horses, who have exceptionally high COMP concentrations in their tendons, no increase was found in serum during tendinitis. Furthermore, it is not likely that the contribution from the synovial membrane is significant, as COMP concentrations in this tissue from RA and OA patients at joint replacement surgery are below detection level, that is less than 1/100 of the level in cartilage (Saxne T and Heinegård D, unpublished information). Further support for this view has recently been gained in experimental arthritis where increased serum COMP is not seen in the initial phase of arthritis when a marked inflammatory reaction is demonstrable but at a later time point when erosive changes are seen in the cartilage. However, it is tempting to speculate, in view of the findings of Recklies and coworkers, that in certain cases, for example, rapidly progressing forms with a marked synovitis, a contribution from synovial tissue might exist. This might reflect a low grade inflammation of the synovial tissue in certain cases of OA and would be consistent...
with the findings of a predictive value of hyaluronan in serum and also with the recent observation of a correlation between serum CRP and progression of knee OA. However, in this study CRP assay was not performed using a high sensitivity method as done by Conrozier and colleagues. Another important finding in this study is the inverse correlation between serum concentrations of BSP and radiographic features of subchondral bone changes. Thus BSP seems to be a marker of bone turnover in OA in accordance with other findings. The increase in serum concentrations particularly in atrophic OA and its inverse correlation with the radiographic features of bone repair (osteophyte and sclerosis) suggest BSP may preferentially reflect subchondral bone osteopenia. These data are in accord with experimental findings showing BSP synthesis is stimulated by dexamethasone and inhibited by 25OH vitamin D3. In line with previous observations, we also found a significant correlation between serum COMP and BSP, which suggests a linkage between changes in the cartilage and bone turnover in the progressive tissue alterations in OA. The correlation may in part be explained by the much increased localisation of BSP at the cartilage-bone interface, while other bone markers such as osteocalcin appear to be more evenly distributed throughout the bone matrix.

The BSP concentrations did not correlate to radiographic measures of cartilage thickness, which is not unexpected in view of its tissue distribution. Nevertheless it is somewhat at variance with previous observations of increasing serum BSP in early stages of knee OA. However, in the previous study we likewise did not either find a correlation between baseline BSP and JSN. In contrast with previous studies we did not find any correlation between changes in COMP and BSP concentrations over time and progression of OA. On the other hand the previous studies did not show any correlation between baseline values and OA progression. The explanations for these discrepancies are not clear but obviously there might be differences depending on the type of joint examined and also depending on the patient selection and the duration of the follow up. The patients in this study were all referred because of symptomatic OA of the hip, which differs from the Swedish knee OA study as it was a population based study. The duration of the follow up is probably of importance. It was only one year in this study while it reached five years in the knee OA trial. Furthermore most of the patients suffered from severe and advanced disease at inclusion (mean JSW 1.80 mm) and it has been shown that serum COMP concentrations increase during the earliest stages of the condition, then decrease in advanced disease. The progression of JSN was very rapid in 10 of the patients in this study. This explains the high rate of progression in comparison with other reports. Nevertheless the 38 other patients appeared to progress at a rate similar to previously recorded data. The rapidly progressors differed from the other patients only regarding age (69.4 (9) compared with 56.4 (14.1), p=0.02) and COMP concentrations, but not regarding serum CRP at JSN of OA at other sites, and BMI. This may mean that in this study we have selected a subset of patients with severe OA, which might facilitate the identification of tissue morphological changes over a short time interval.

The inverse correlation between serum concentrations of both COMP and BSP and the radiographic severity of OA is a novel finding that extends earlier observations. Thus, lower synovial fluid concentrations of the proteins were seen in advanced knee OA as compared with less advanced stages as determined by a score combining radiographic and arthroscopic observations.

The serum concentrations of COMP and BSP did not correlate to a number of studied demographic as well as clinical variables. This is not surprising, as no close link between such parameters and the tissue process is to be expected. The correlation between COMP and BMI is an exception. This association was not found in knee OA. However, Wolfe found a correlation between CRP and disease severity, and between CRP and BMI in 653 patients with OA of the knee or hip. Furthermore, an association between synovial fluid concentrations of the C-propeptide of type II collagen and BMI has also been reported. Obesity is known to be frequently associated with progressive OA and OA severity but the explanation for an association between overweight and serum markers of OA is presently unclear and additional studies are required to clarify it.

In conclusion, the findings of this study show that serum measurements of tissue derived macromolecules have potential as a tool in studies of the pathophysiology of OA and also for obtaining information on specific tissues including such of prognostic value. The combination of such measurements with sensitive instruments for assessing anatomical changes should facilitate future efforts to elucidate tissue responses and mechanisms of joint destruction in OA.

We are grateful for technical assistance by Mrs Mette Lindell and Mrs Stella Godeau. Grants were obtained from the French Society of Rheumatology, the Laboratoire Cassenne, France, the Swedish Medical Research Council, the Medical Faculty of Lund, the Axon Johnson, Osterlund, Kock, Nanna Svartz, Crafoord and King Gustaf V 80-year Foundations and the Swedish Arthritis Foundation.


Serum concentrations of cartilage oligomeric matrix protein and bone sialoprotein in hip osteoarthritis: A one year prospective study
Thierry Conrozier, Tore Saxne, Charles Shan Sei Fan, Pierre Mathieu, Anne-Marie Tron, Dick Heinegård and Eric Vignon

doi: 10.1136/ard.57.9.527

Updated information and services can be found at:
http://ard.bmj.com/content/57/9/527

These include:
References
This article cites 34 articles, 12 of which you can access for free at:
http://ard.bmj.com/content/57/9/527#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections
- Degenerative joint disease (4641)
- Immunology (including allergy) (5144)
- Musculoskeletal syndromes (4951)
- Osteoarthritis (931)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/