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Synovitis: a potential predictive factor of structural progression of medial tibiofemoral knee osteoarthritis – results of a 1 year longitudinal arthroscopic study in 422 patients

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Summary

Objective: To evaluate the prevalence of synovitis in painful medial tibiofemoral knee osteoarthritis (OA) and to evaluate correlation between synovitis and the structural severity and progression of tibiofemoral cartilage damage.

Design: *Study*: multicenter, longitudinal, 1-year duration. *Patients*: primary painful knee OA (ACR criteria) of the medial tibiofemoral compartment, with pain of the signal knee on at least 30 days in the past 2 months, medial joint space width $\geq$ 2 mm, at least 10% of one cartilage surface of the medial compartment affected by superficial fibrillation or worse at baseline arthroscopy. *Arthroscopic parameters*: knee arthroscopy under local anesthesia was performed and videorecorded at entry and after 1 year. Medial chondropathy was scored by using Société Française d'Arthroscopie (SFA) score (0–100) and reader's overall assessment (VAS score, 100 mm). Progression of medial chondropathy was defined by a change in SFA and VAS scores over 4.5 and 8.0 mm after 1 year, respectively. Medial perimeniscal synovium was scored as normal (few translucent and slender villi, fine vascular network), reactive (proliferation of opaque villi), or inflammatory (hypervascularization and/or proliferation of hypertrophic and hyperemic villi). Medial chondropathy and synovitis were scored by a single reader blind to chronology of paired videotapes.

Results: Four hundred and twenty-two patients were enrolled (mean age: 61 years, females: 59%, body mass index: 31, mean disease duration: 4 years) and completed the 1-year study. Synovial abnormalities were present in 50% of the patients with reactive and inflammatory aspects in 29% and 21% of the patients, respectively. Patients with a reactive or inflammatory medial synovium had a more severe medial chondropathy. The worsening in medial chondropathy after 1 year was statistically more severe in the group of patients with an inflammatory perimeniscal synovial membrane at baseline compared to patients with normal and reactive aspects, with no difference between these two latter groups. The odds ratio for progression in VAS score after 1 year was 3.11 (95% CI [1.07, 5.69]) for patients with inflammatory synovium at baseline compared to patients with normal synovium.

Conclusions: This study suggests that abnormalities of the medial perimeniscal synovium are a common feature of painful medial knee OA, associated with more severe medial chondropathy. It also suggests that an inflammatory aspect of the medial perimeniscal synovium could be considered as a predictive factor of subsequent increased degradation of medial chondropathy.

Key words: Knee osteoarthritis, Arthroscopy, Chondropathy, Synovitis.

Introduction

Osteoarthritis (OA) contributes greatly to overall disability in the community[1], with knee OA the greatest contributor. The pain and gradual loss of joint function characteristic of OA are associated with progressive loss of articular cartilage, formation of osteophytes and joint remodeling. However, OA is no longer considered a "degenerative" or "wear and tear" disease but is now recognized to involve dynamic biological and biochemical processes. The role of cytokines in the progression of OA has received particular attention because of the degree of the interaction between articular cartilage and synovium in this pathology[2]. Chondrocytes and synovial cells are targeted by cytokines such as interleukin-1 (IL-1) and tumor necrosis factor alpha (TNFα) to produce matrix proteases and to suppress the synthesis of collagen and proteoglycan[3–6]. Chronic inflammatory changes with production of proinflammatory cytokines are a feature of early[7] and advanced[7,8] knee OA. The low grade synovitis may contribute to the progression of chondropathy by accelerating the catabolism of articular cartilage.

Cartilage breakdown and synovial abnormalities can be assessed by magnetic resonance imaging (MRI)[9,10]. However, arthroscopy still remains the gold standard for the assessment of these two intra-articular structures because it provides a direct and magnified evaluation of them. Thus, alongside the use of arthroscopy as a diagnostic or therapeutic procedure in knee disorders, a further function of knee arthroscopy, performed under local anesthesia on an outpatient basis, has been proposed: the monitoring and follow-up of knee chondropathy and synovitis conducted for research purposes on patients suffering from knee OA[11–13]. The development of this arthroscopic outcome measurement of chondropathy and

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synovitis has become possible with the establishment of systems for scoring the severity of chondral and synovial lesions[14–20].

In a previous arthroscopic longitudinal study of 46 patients suffering from patellofemoral chondropathy, we found after 6 months a statistically significant correlation between the progression of patellofemoral chondropathy and the presence and amount of synovitis at baseline[12]. However, the small sample size of the study and the characteristics of the recruited patients, i.e., post-traumatic patellofemoral chondropathy, deny any definite conclusions for patients suffering from primary knee OA.

In 2003, we published a large multicenter, randomized, double-blind study aimed at comparing arthroscopically the potential structure-modifying effect of tenidap sodium vs piroxicam in medial knee OA[21]. This 1-year study failed to demonstrate any difference between the treatment arms with regard to the structural progression of medial knee OA as measured by radiography and arthroscopy. Arthroscopy did, however, appear more sensitive in detecting disease progression than the weight-bearing radiographs in extended position. Since the arthroscopic aspects of synovial membrane were also collected by the central reader, it gave us the opportunity to analyze interrelation between synovitis and cartilage damage.

The present arthroscopic study was conducted in this large population of patients suffering from medial knee OA. It aimed to evaluate the prevalence of synovitis and correlation between structural severity of cartilaginous damage and synovitis, and to analyze whether synovitis could be considered as a predictive factor of structural progression of knee OA.

Materials and methods

This study is derived from a large randomized study comparing tenidap sodium and piroxicam[21], in which inclusion/exclusion criteria and study design were the following.

PATIENTS

Inclusion criteria: patients with clinical involvement of the medial tibiofemoral compartment of the knee (pain localized at the medial part of the knee) and satisfying the American College of Rheumatology criteria for knee OA[22]: pain in the signal knee and either A or all the items under B (A = tibiofemoral osteophytes present on knee X-ray, B = (i) morning stiffness if present lasts less than 30 min, (ii) crepitus present on active motion, (iii) synovial fluid collected in the last year with at least two of the following features: clear, viscous, white blood cell count <2000/ml). Other criteria for eligibility were: (1) age: 45–75 years, (2) body mass index (BMI): 25–50, (3) active disease defined by pain of any duration in the signal knee on at least 30 days in the last 2 months and which might benefit from joint lavage, (4) ambulatory patient, (5) radiological joint space of 2 mm or greater at the narrowest point of the medial compartment of the signal joint on weight-bearing radiographs with knee fully extended, (6) no lesion requiring surgery (e.g., of meniscus, cartilage or ligament) at screening arthroscopy, or likely to require surgery during study period, (7) presence of chondropathy of the medial compartment at entry, approved by central reader of video made during screening arthroscopy; for approval, at least 10% of one articular surface of the medial compartment (femoral condyle or tibial plateau) had to be affected by superficial fibrillation or worse; if 90% or greater of both surfaces showed absence of cartilage, the patient was not eligible.

Exclusion criteria were the following: (1) knee OA secondary to other bone or joint disease, (2) initial diagnosis of knee OA made by a physician more than 10 years previously, (3) any of the following procedures prior to the screening arthroscopy: injury to joint and arthroscopy within 2 months prior to entry, intra-articular injection within 3 months, intra-articular surgery including meniscal trimming within 2 years, osteotomy within 3 years, (4) any chronic inflammatory joint disease, including rheumatoid arthritis, ankylosing spondylitis and crystal arthropathies, (5) treatment with corticosteroids (oral, intravenous, intramuscular) in last 3 months, previous tenidap treatment in last 4 months and piroxicam within 1 month.

STUDY DESIGN

This longitudinal, prospective, multicenter study of 1-year duration involved 45 centers in Europe, America and Australia. The study was conducted according to the Declaration of Helsinki (Revised Hong Kong 1989) and received ethics approval at each center. Each patient gave written, informed consent prior to recruitment. Arthroscopy videotapes were sent to central reader (Xavier Ayral, Cochin, Paris) for quality control and assessment of the arthroscopic inclusion criteria. After satisfaction of all entry criteria, patients were randomized equally to one of the three study groups (tenidap 40 mg, tenidap 120 mg, piroxicam 20 mg). Rescue treatment by paracetamol was dispensed as required. This study failed to demonstrate a structural modification[21]. The development of such compound (tenidap) is currently no more developed.

DATA COLLECTION IN THE PRESENT STUDY

At baseline

Demographic data. Demographic data were noted, including age, sex, BMI, and disease duration.

Symptomatic severity of OA. Symptomatic severity of OA was assessed, before arthroscopy, using the following variables: Western Ontario and McMaster Universities (WOMAC) global and its three subscales: pain, stiffness, physical function measured using a five-point Likert scale (none, mild, moderate, severe, very severe)[23], patient and physician assessment of global status measured using a five-point Likert scale.

Radiological variables. Radiological evaluation consisted of bilateral anteroposterior weight-bearing knee radiographs with the knees fully extended. The severity of OA of the medial tibiofemoral compartment was evaluated by a single investigator using Kellgren and Lawrence grading[24] and by measuring the joint space width in millimeters at the narrowest point of the medial compartment, using a 10× lupe scaled to 0.1 mm.

At baseline and after 12 months

Arthroscopy. Arthroscopy of the knee was performed under local anesthesia, without tourniquet hemostasis, with

a standard knee arthroscope or with a smaller arthroscope (2.7 mm), having both a 30° fore oblique lens, using the lateral infrapatellar approach. Usually, the same size of arthroscope was used at entry and after 12 months. Arthroscopic exploration was combined with joint lavage, the volume of which consisted of 1 l of normal saline. Only the exploration of the medial compartment was recorded on a VHS videotape (Sony, Tokyo, Japan). Videorecording of articular cartilage surface of the femoral condyle and tibial plateau was standardized as previously reported[20]. Almost all centers had only one arthroscopist who performed all procedures. Prior to screening their first patient, a center had to provide a videotape to the central reader demonstrating successful use of the required technique. During the study, all screening videotapes were sent to the central reader for confirmation of eligibility and feedback to the arthroscopist.

Evaluation of medial tibiofemoral chondropathy. Two scoring methods were used: the overall assessment of the investigator[14] and the Société Française d'Arthroscopie (SFA) scoring system[15,16].

The overall assessment of chondropathy uses a 100 mm VAS in which 0 indicates the absence of chondropathy and 100 the most severe chondropathy. One VAS is used for each articular surface, i.e., medial femoral condyle and medial tibial plateau. A VAS score is calculated for the medial tibiofemoral compartment by averaging the VAS scores from the medial condyle and plateau.

In the SFA scoring system, the first step consists of reporting on an articular diagram of the knee, the observed chondropathy with three main baseline variables: (1) location: medial femur and medial tibia, (2) depth based on the classification of chondropathy proposed by Beguin and Locker[25], in which grade 0 indicates normal cartilage, grade I swelling and/or softening, grade II superficial fibrillations, grade III deep fibrillations down to bone, and grade IV exposure of subchondral bone, (3) extent from 0% to 100% of the involved articular surface. Extent of lesions is estimated by the investigator as a percentage of the whole articular surface and is reported on a special form.

The composite index of severity of chondropathy of the medial compartment takes into account location, depth, and extent of cartilage lesions of the compartment. It is called the SFA score, which is a continuous variable, between 0 and 100, obtained as follows: SFA score = extent (%) of grade I lesions $\times$ 0.14 + extent (%) of grade II lesions $\times$ 0.34 + extent (%) of grade III lesions $\times$ 0.65 + extent (%) of grade IV lesions $\times$ 1.00. For the medial compartment, the extent (%) of grades 0–IV corresponds to the mean value of the extent of the grade of the two articular surfaces of the compartment, i.e., medial femoral condyle and tibial plateau.

Evaluation of medial perimeniscal synovium. The medial perimeniscal synovium is the thin fringe of synovium covering the attachment of joint capsule along the periphery of medial meniscus. Three aspects of increasing intensity of synovial macroscopic abnormalities have been defined by Watanabe *et al.*[26]. Normal synovium involves few translucent and slender villi formations with a fine vascular network clearly seen. The reactive aspect shows a proliferation of opaque villi formations of enhanced number. These villi show a normal morphology or appear somewhat thicker and squat (aspect of "cut grass"). The vascular network cannot be seen due to loss of translucence. In the inflammatory aspect, there is hypervascularization of the synovial membrane and/or proliferation of hypertrophic and hyperemic villi formations. This aspect is similar to inflammatory joint diseases but may occur in knee OA. The perimeniscal area is a small area and the aspect of the corresponding synovial membrane is homogenous, either normal, reactive or inflammatory, without a patchy distribution.

STUDY SCHEDULE

Arthroscopic evaluations were performed at entry and after 1 year, and videorecorded on two separate videotapes. The paired arthroscopy videotapes of each patient were analyzed by one investigator (XA) using a blind procedure in which the investigator was unaware of the patient's identity and unaware of the chronology of the arthroscopy videotapes.

STATISTICAL ANALYSIS

In the cross-sectional study, statistical analyses were performed to assess the prevalence of the different synovial aspects in painful knee OA and to evaluate relations between the three synovial aspects and the severity of medial chondropathy. The comparisons for SFA score and for VAS score at baseline were based on one-way ANOVA.

In the longitudinal study, statistical analyses were performed to evaluate relations between the three synovial aspects at baseline and the arthroscopic progression of medial chondropathy after 1 year. The comparisons for change in SFA score and for change in VAS score after 1 year were based on one-way ANOVA. Based on the reported results of intra-observer reliability of the arthroscopic quantification of chondral lesions by the central reader[11], a change of over 4.5 for the SFA score and over 8.0 mm for the VAS score can be considered as worsening related to disease progression (called "progressors") and not related to the variability of the measurement. The comparisons for % progressors were based on logistic regression.

Results

PATIENTS CHARACTERISTICS

Four hundred and twenty-two patients were enrolled and completed the 1-year study. Their baseline characteristics are summarized in Table I.

CROSS-SECTIONAL STUDY

Prevalence of synovitis

Synovial abnormalities (called "synovitis") were present in 212 patients over 422 (50%), with 123 patients (29%) with a reactive aspect and 89 (21%) with an inflammatory aspect of the medial perimeniscal synovium (Table I).

Relation between synovitis and medial chondropathy

Patients with a reactive or inflammatory medial perimeniscal synovium had a more severe medial chondropathy (assessed by the SFA and the VAS scores) than patients with a normal synovium, with a tendency for a more severe chondropathy in the inflammatory group compared to the reactive group (Table II).

Table I
Baseline characteristics (n = 422)

Demographic data	m ± SD
Age (years)	61.2 ± 7.7
Sex (F%/M%)	59/41
BMI	30.5 ± 4.7
Disease duration (years)	3.7 ± 2.9
Clinical activity	
WOMAC global (0–100)	40.4 ± 17.1
WOMAC pain (0–100)	38.4 ± 18.6
WOMAC stiffness (0–100)	40.3 ± 22.2
WOMAC function (0–100)	41.9 ± 18.1
Patient assessment (0–100)	52.1 ± 18.9
Physician assessment (0–100)	51.6 ± 17.4
Radiological severity	
Joint space width (mm)	3.9 ± 1.4
Kellgren and Lawrence grading (0–IV)	2.1 ± 0.8
0 (%)	4
I (%)	8
II (%)	61
III (%)	24
IV (%)	3
Arthroscopic severity	
Medial chondropathy	
SFA score (0–100)	34.8 ± 19.6
Overall assessment (100 mm VAS)	38.4 ± 18.0
Medial perimeniscal synovium	
Synovium (normal/reactive/inflammatory)	210/123/89
Synovitis (no/yes)	210/212

LONGITUDINAL STUDY

Change of medial chondropathy after 1 year

There was a statistically significant worsening in medial chondropathy after 1 year by using the SFA and the VAS scores (Table III).

Relationship between synovial aspects at baseline and progression of medial chondropathy after 1 year

The worsening in medial chondropathy after 1 year was statistically more severe in the group of patients with an inflammatory perimeniscal synovial membrane at baseline compared to patients with normal and reactive aspects, with no difference between these two latter groups. This difference was found by using continuous variables (SFA score and VAS score) and categorical variables (% of progressors) to quantify chondropathy change (Table IV). The odds ratio for progression in SFA score was 2.58 (95% CI of [1.37, 4.85]) for inflammatory synovium compared to normal and was 1.11 (95% CI of [0.57, 2.17]) for reactive synovium compared to normal. The odds ratio for progression in VAS score was 3.11 (95% CI of [1.07, 5.69]) for inflammatory synovium compared to normal and was 1.01 (95% CI of [0.52, 1.97]) for reactive synovium compared to normal.

Discussion

This large prospective study confirms that arthroscopic abnormalities of the medial perimeniscal synovial membrane, i.e., reactive and inflammatory aspects, are frequent in painful medial knee OA and associated with more severe chondropathy than normal synovium. This study suggests also that an inflammatory aspect of the medial perimeniscal synovium could be predictive of subsequent increased degradation of medial chondropathy.

The present study derived from a randomized study comparing arthroscopically the structural effect of tenidap sodium, 40 or 120 mg daily, and piroxicam 20 mg daily on articular cartilage, with 494 completers after 1 year[21]. This previous study was not initially designed for synovium examination and only 422 patients had suitable videorecording of medial perimeniscal synovium on paired videotapes at entry and after 1 year. One could argue that difference in non-steroidal anti-inflammatory drugs (NSAIDs) and dosage could interfere with the analysis of cartilage progression. However, in the ''tenidap study'', the intragroup arthroscopic deterioration of chondropathy after 1 year was low, but statistically significant in the three study groups, but there was no statistically significant difference between treatment groups for the change in SFA and VAS scores after 1 year. For this reason, we considered that we were allowed to pool the patients together for synovial examination.

Regardless of clinical diagnosis (OA or various types of arthritis), Linblad and Hedfors[27] found a profound articular variation in the macroscopic signs of inflammatory activity as seen at arthroscopy, with the highest inflammatory changes of the synovial membrane always confined to the area surrounding the cartilage lesions. For these authors, the area of the synovial membrane near the cartilage seems to be crucial in the initiation as well as in the modulation of synovitis, irrespective of diagnosis. Thus, focusing the evaluation of synovial membrane on the medial perimeniscal synovium in medial tibiofemoral knee OA was considered adequate. Since videorecording of arthroscopy exploration was limited to the medial tibiofemoral compartment, we were unable to analyze relation between the medial perimeniscal synovium aspect, on one hand, and synovial aspects and cartilage lesions or progression of cartilage lesions in patellofemoral and lateral tibiofemoral compartments, on the other hand. However, since the inflammatory areas of synovium are usually adjacent to damaged articular cartilage in OA (focal synovitis), it seems unlikely that the evolution of patellofemoral and lateral tibiofemoral compartments influences the medial perimeniscal synovium. Moreover, patients included in this study were suffering from medial knee OA and not from lateral or patellofemoral knee OA.

Table II
Cross-sectional study: comparison of the severity of medial chondropathy with regard to synovial aspects (n = 422)

Chondropathy (day 0)	Medial perimeniscal synovium (day 0)			*P**	*P***	*P****
	Normal (*n* = 210)	Reactive (*n* = 123)	Inflammatory (*n* = 89)			
SFA score (0–100)	29.7 ± 18.6	38.0 ± 20.2	42.1 ± 17.8	<0.0001	<0.0001	0.1665
VAS score (100 mm)	34.1 ± 16.8	41.0 ± 19.2	44.8 ± 16.7	0.0003	<0.0001	0.1341

P-value: ANOVA. **P*-value of reactive synovium vs normal synovium. ***P*-value of inflammatory synovium vs normal synovium. ****P*-value of inflammatory synovium vs reactive synovium.

Table III
Longitudinal study: change in medial chondropathy after 1 year (n = 422)

Severity of medial chondropathy	At entry (m ± SD)	After 1 year (m ± SD)	Change after 1 year (m ± SD)	P*
SFA score (0–100)	34.8 ± 19.6	36.5 ± 20.0	1.7 ± 4.9	<0.0001
VAS score (100 mm)	38.4 ± 18.0	41.2 ± 19.3	2.8 ± 6.4	<0.0001

*Student's paired *t* test.

It should be noted that we did not perform synovial biopsies in this study to compare the microscopic inflammatory features with the macroscopic synovial abnormalities. However, previous studies comparing arthroscopic and histological examinations have found a close correlation between macroscopic and microscopic findings[27–29]. Linblad and Hedfors[27] found in 10 OA patients that the macroscopic variation of inflammatory intensity of the synovial membrane was significantly correlated to a microscopic variation of the immunohistopathologic patterns. Biopsies sampled from macroscopically intensely inflamed areas, showing formation of highly vascularized hyperemic villi (corresponding to our "inflammatory aspect") comprised in all cases foci of T lymphocytes displaying a picture previously thought characteristic of rheumatoid arthritis. In contrast, in tissues sampled within the same joint from areas with macroscopic signs of slight or no inflammation, the microscopic examination revealed a non-proliferated lining layer and sublining but a few infiltrating lymphocytes, thus showing a histopathologic picture usually perceived as either normal or characteristic of OA.

One limitation of the study is that intra- and inter-observer reliability of the qualitative method for synovium evaluation has not been investigated, neither in the present study, nor in the previous study evaluating patellofemoral chondropathy[12], even though the central reader of arthroscopy videotapes was the same in both studies (XA).

In our previous study[12], we analyzed synovial abnormalities in 59 painful patellofemoral chondropathy, induced by direct trauma (54%) or by overuse (46%) in young patients (36 years old) with mild patellofemoral chondropathy (SFA score: 7, VAS score: 11 mm). In this population of patients, which could be considered as early OA, reactive and inflammatory synovial aspects were pooled together and were present in 16 (27%) of the patients. In the present study, synovial abnormalities were more frequent since they were present in 50% of the patients, with an inflammatory aspect in 21%. The disease duration was the same in both studies (4 years) and cannot explain this difference between prevalence of synovial abnormalities. The major difference between the two populations is a more severe chondropathy in the medial tibiofemoral group (SFA score: 35, VAS score: 38 mm). Different authors have reported a significant correlation between synovitis and severity of chondropathy in knee OA[7,8,27]. Most authors consider synovitis in OA as a secondary phenomenon related to cartilage and bone alteration and induced by the release of degradative compounds from the extracellular matrix of hyaline cartilage and the presence of microcrystals in the synovial fluid and the synovium[3,30,31]. Schumacher *et al.*[8] examined 150 knees in consecutive autopsies that included 30 patients with severe OA and 78 with no or minimal OA. Only 12 of 78 synovial membranes from patients with minimal or no OA had either lining cell proliferation or lymphocyte infiltration, compared to 36 of 78 knees from patients with moderate or severe OA. Smith *et al.*[7] confirmed arthroscopically that the most marked changes in synovial tissues of the knee joint are seen with advanced grades of OA, but they also pointed out that chronic inflammatory changes are present in synovial membrane from patients with early OA. The greater the articular cartilage breakdown, the greater the synovial reaction. This picture is illustrated by the result of our cross-sectional study showing a parallel increase of chondropathy and synovitis. However, the difference in cartilage damage between synovium groups was small suggesting that other factors than the tibiofemoral chondropathy could play a role in synovium aspects.

The most interesting finding of the present study is that the presence of inflammatory synovium at baseline could be predictive of structural progression of cartilage lesions. This data was suggested by our previous longitudinal study with an arthroscopic 6-months follow-up of 46 patellofemoral chondropathies, but with no distinction between the inflammatory and the reactive aspect of synovium at baseline[12]. In 422 medial knee OA, we found the presence of inflammatory perimeniscal synovium to be predictive of a more important worsening of medial chondropathy after 1 year compared to patients with normal and reactive synovium, with no difference between these two latter

Table IV
Longitudinal study: relationship between the aspect of medial perimeniscal membrane at baseline and the evolution of medial chondropathy after 1 year (n = 422)

Medial chondropathy (change after 1 year)	Medial perimeniscal synovium at baseline			P*	P**	P***
	Normal (n = 210)	Reactive (n = 123)	Inflammatory (n = 89)			
SFA score (0–100)	1.4 ± 3.7	1.3 ± 5.6	3.1 ± 6.2	0.7323	0.0535	0.0427
VAS score (100 mm)	2.2 ± 5.1	2.1 ± 6.6	5.0 ± 8.1	0.8844	0.0055	0.0084
%SFA score progressors†	11.9%	13.0%	25.8%	0.7675	0.0033	0.0192
%VAS score progressors‡	12.9%	13.0%	31.5%	0.9684	0.0002	0.0014

P-value: ANOVA, for change in SFA score and VAS score; exact *P*-values based odds ratios derived from logistic regression, for comparing % progressors. **P*-value of reactive synovium vs normal synovium. ***P*-value of inflammatory synovium vs normal synovium. ****P*-value of inflammatory synovium vs reactive synovium.

†% of patients with (final SFA score − baseline SFA score) > 4.5.

‡% of patients with (final VAS score − baseline VAS score) > 8.0 mm.

groups. The presence of a more severe chondropathy at baseline in the inflammatory group compared to normal group could be a confounding factor for cartilage damage progression; conversely, the absence of statistically significant difference of severity of chondropathy at baseline between the reactive and inflammatory groups suggests that the inflammatory aspect of the synovium could be a potential predictive factor of progression of chondropathy. This arthroscopic inflammatory aspect corresponds to the most inflammatory immunohistopathologic pattern for Linblad and Hedfors[27]. The role of cytokines in the progression of OA has received particular attention because of the degree of the interaction between articular cartilage and synovium in this pathology. Chondrocytes and synovial cells are targeted by cytokines such as IL-1 and TNFα to produce matrix proteases and to suppress the synthesis of collagen and proteoglycan[3]. In the triangular relationship among severity of chondropathy, synovitis and progression of chondropathy, synovitis may contribute to the progression of chondropathy by a direct deleterious effect on cartilage. However, it could also be suggested that synovitis is just a marker for advanced and/or active cartilage breakdown, without a catabolic effect on cartilage. In practice, detection of inflammatory synovium at arthroscopy near area of chondropathy suggests active cartilage breakdown requiring an appropriate treatment and a thorough follow-up.

It should be noted that the results of this longitudinal study were obtained in patients treated continuously with an NSAID (tenidap 40 or 120 mg, or piroxicam 20 mg) during the 1-year duration of the study. In the absence of a long-term anti-inflammatory treatment, would have been the progression of chondropathy more important in the inflammatory group? Could we imagine that a long-term treatment with an NSAID might slow structural progression of painful OA with recognized inflammatory synovitis? In the absence of a placebo group in the multicenter study comparing tenidap sodium vs piroxicam[21], we are unable to conclude. Further studies are required.

If we consider that inflammatory synovium is a potential predictive factor of structural progression in OA, its recognition with non-invasive methods would be of interest in order to initiate appropriate therapies in clinical practice and to select patients at higher risk of cartilage degradation in clinical trials evaluating potential structure-modifying drugs. Different authors reported a correlation between knee effusion and the presence of synovitis at arthroscopy[12,28], even though no correlation was found between synovitis and the level of pain or functional impairment[12]. However, it should be pointed out that these arthroscopic studies evaluate exclusively painful patients, which could induce a systematic bias in the analysis of correlation between pain and synovial reaction. At this time, knee effusion seems to be a simple clinical signal of a flare of the disease, i.e., a clinical signal of a probable intra-articular inflammatory process with a potential risk of accelerated cartilage degradation[32]. In clinical research, the use of ultrasonography and MRI will permit to detect and to follow non-invasively OA patients with a synovial reaction and will permit to reanalyze correlation between synovitis and clinical parameters in painful and painless OA patients.

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