

Analysis of the association between chondrocalcinosis and osteoarthritis: a community based study

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Abstract

Objectives—To analyse the association between chondrocalcinosis and osteoarthritis (OA) of the hands and knees in an unselected elderly rural population.

Methods—A community based cross sectional study was performed in individuals randomly selected from a previous epidemiological survey on the prevalence of chondrocalcinosis in people older than 60 years from Osona county, Catalonia, northeastern Spain. Radiological OA (grade 2 or more of Kellgren's classification) was evaluated in 26 individuals with chondrocalcinosis and in 104 controls. A total of 18 articular areas of both knees (medial and lateral tibiofemoral compartments) and hands (first, second and third metacarpophalangeal (MCP), first carpometacarpal, trapezium-scaphoid, radiocarpal and distal radioulnar joints) were studied.

Results—Radiological changes of OA in the knees were more common in subjects with chondrocalcinosis than in those without it, with an odds ratio adjusted for age and gender (aOR) of 4.3 (95% confidence interval (CI) 1.6 to 11.8, $p = 0.005$). OA was also more frequent in almost all areas of the hands in individuals with chondrocalcinosis, though the difference reached statistical significance only in the MCP joints (aOR 3.1; 95% CI 1.1 to 8.8; $p = 0.033$). However, taking into account the side and the different joint compartments analysed, the association between chondrocalcinosis and OA was significant only in the lateral tibiofemoral compartment and the left MCP joints.

Conclusions—In an elderly population unselected for their rheumatic complaints, there was a real association between OA and chondrocalcinosis. This association was particularly relevant in the lateral tibiofemoral compartment of the knee and in the first three left MCP joints.

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Chondrocalcinosis, defined by its characteristic radiological calcifications that result usually from the articular deposition of calcium pyrophosphate dihydrate crystals,¹ has been found to affect from 8 to 10 percent of individuals aged 60 and older.^{2,3} Since its first

description, a subchondral arthropathy resembling that of idiopathic osteoarthritis (OA) has been recognised in patients with chondrocalcinosis.^{4,5} Some authors have found that, in addition to the radiological features, the distribution of joints affected in pyrophosphate arthropathy differs from that observed in primary OA;⁶⁻⁸ however, other investigators have not found important differences between the two arthropathies.⁹ Furthermore, it is not unusual in daily practice to diagnose, by radiographic examination, isolated chondrocalcinosis that lacks clinical expression.^{3,4}

Thus discrepancies remain regarding the frequency and nature of the association between chondrocalcinosis and OA. Most investigators conclude that the frequency of OA is increased in individuals with chondrocalcinosis,^{2,8-13} whereas others have not confirmed this association.^{14,15} However, the variable methodology and criteria used to evaluate the presence of OA, in addition to the different methods of selection of the populations studied, make the results of previously published work inconclusive.

The aim of this study was to investigate the association between chondrocalcinosis and osteoarthritis. A case series of chondrocalcinosis was selected from a previous community based cross sectional study and, as a reference group, a sample of subjects without chondrocalcinosis was assembled from the same study.³

Patients and methods

In 1993, an epidemiological survey to determine the prevalence of chondrocalcinosis was performed in Osona, a rural area of Catalonia (northeastern Spain). The study methodology has been described previously.³ Briefly, 31 family physicians each selected randomly 10 patients aged 60 years or older during a one week period, regardless of the patients' reasons for seeking medical care. The participation rate was 84%, resulting in a study population of 261 individuals. A questionnaire with clinical and demographic information was completed, in addition to knee (anteroposterior without weight bearing) and hand-wrist (palmar view) radiographs. Only the presence or absence of chondrocalcinosis was evaluated. Twenty seven individuals (10%) had typical calcifications (26 in the knees, 14 in the carpal triangular ligament, seven in other carpal

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locations, and three in the metacarpophalangeal joints).³

In the present study, conducted two years after the aforementioned cross sectional study was completed, the original radiographs were examined for the presence of OA. Because one of the radiographs was not available, 26 cases of chondrocalcinosis were included in our study and 104 individuals without chondrocalcinosis were randomly selected as controls. In each of the cases and controls, radiographic presence of OA was evaluated for the following joints: first, second, and third metacarpophalangeal, first carpometacarpal, trapezium-scapoid, radiocarpal, and inferior radioulnar of both hands, in addition to the medial and lateral tibiofemoral compartments of both knees. Kellgren and Lawrence's¹⁶ graded criteria were used to define the presence of OA. Grade II (the finding of an unequivocal osteophyte) was considered OA, while grades III and IV were considered to be severe OA. The radiographs were read independently by two observers (RS, EK) who were ignorant of the data from the questionnaires. If there was a discrepancy between the conclusions drawn by the observers regarding any radiograph, it was re-examined and a consensus agreed.

STATISTICAL ANALYSIS

Interobserver agreement for each grade in Kellgren and Lawrence's classification criteria of OA was assessed using the weighted κ statistic.¹⁷ Odds ratios with 95% confidence intervals (CI) were used to evaluate the degree of the association between OA and chondrocalcinosis. The χ^2 test was used to determine statistical significance. When an expected frequency of less than five was found in one of the cells, Fischer's exact method was used as the test of statistical significance. Because age

and gender are variables that influence the frequency of chondrocalcinosis and OA, an unconditional logistic regression model was used to obtain estimates of the adjusted odds ratios (aOR) for age and gender. The Hosmer-Lemeshow test was used to test the goodness of fit of the model; first order interactions were tested also.¹⁸ A probability level of less than 0.05 was considered statistically significant for all tests of significance in the analysis. All statistical calculations were performed using the program STATA.¹⁹

Results

Individuals with chondrocalcinosis (19 women/seven men) had an average age of 73 (SD 5.9) years, while that of the control group (50 women/54 men) was 67.7 (6.9) years ($p < 0.001$). The proportion of individuals who consulted their primary care physician for rheumatic problems was similar among cases and controls (15.4% *v* 12.5%).

The degree of agreement among the two observers in the diagnosis of OA was high, with a weighted κ estimator greater than 0.6 in all the joints studied, with the exception of the first left metacarpophalangeal, for which κ was 0.53. The highest rate of agreement was obtained for the third right metacarpophalangeal joint (κ 0.82).

Table 1 shows the frequency of OA in each of the joints studied, for both patients with chondrocalcinosis and controls, together with crude odds ratios (OR) and those adjusted for age and gender (aOR). Knee OA (radiographic changes of grade 2 or greater in one or more of the four compartments analysed) was more frequently found in individuals with chondrocalcinosis than in controls (aOR 4.3; 95% CI 1.6 to 11.8). If only severe OA (grade 3 or 4) was considered, the association was weaker, although still significant (aOR 3; 95% CI 1.1 to 8.1). When the association between OA and chondrocalcinosis was analysed separately for the two tibiofemoral compartments, a positive significant association was observed for the lateral compartment (aOR 5.5; 95% CI 2 to 14.9), but not the medial compartment (aOR 1.9; 95% CI 0.7 to 5). In addition, the involvement of the lateral compartment without involvement of the medial side was more frequent in individuals with chondrocalcinosis than in the controls (aOR 4.8; 95% CI 1.3 to 17.4). When all the evaluated compartments of the knee were included, an increased frequency of OA was observed among those with chondrocalcinosis (table 2).

Table 1 Presence of osteoarthritis (OA) in the joints analysed: number of patients diagnosed with OA in the whole group, distribution of OA among patients with chondrocalcinosis and among controls, and crude (OR) and age and gender adjusted (aOR) odds ratios with 95% confidence intervals (CI)

	Whole group (n = 130)*	Chondrocalcinosis (n = 26)*	Controls (n = 104)*	OR (95% CI)	aOR (95% CI)
Overall knee (≥ 2)†	55 (42.3)	18 (69.2)	37 (35.6)	4.1 (1.6 to 10)	4.3 (1.6 to 11.8)
Lateral knee	37 (28.5)	16 (61.5)	21 (20.2)	6.3 (2.5 to 15.7)	5.5 (2 to 14.9)
Medial knee	40 (30.8)	11 (42.3)	29 (27.9)	1.9 (0.8 to 4.6)	1.9 (0.7 to 5)
Severe OA knee (≥ 3)‡	33 (25.4)	11 (42.3)	22 (21.1)	2.7 (1.1 to 6.7)	3 (1.1 to 8.1)
Global MCP	60 (46.5)	18 (69.2)	42 (40.8)	3.3 (1.3 to 8)	3.1 (1.1 to 8.8)
1st right MCP	27 (20.9)	8 (30.8)	19 (18.5)	2 (0.8 to 5.1)	2.6 (0.8 to 7.9)
2nd right MCP	26 (20.2)	10 (38.5)	16 (15.5)	3.4 (1.3 to 8.7)	2.2 (0.8 to 6.4)
3rd right MCP	30 (23.3)	8 (30.8)	22 (21.4)	1.6 (0.6 to 4.2)	2.5 (0.7 to 8.3)
1st left MCP	15 (11.5)	7 (26.9)	8 (7.7)	4.4 (1.4 to 13.3)	4 (1.1 to 14.5)
2nd left MCP	22 (16.9)	9 (34.6)	13 (12.5)	3.7 (1.4 to 9.9)	3.6 (1.1 to 11.3)
3rd left MCP	22 (16.9)	7 (26.9)	15 (14.4)	2.2 (0.8 to 6)	4.7 (1.3 to 17.2)
2nd or 3rd MCP	47 (36.4)	15 (57.7)	32 (31)	3 (1.3 to 7.2)	3.1 (1.1 to 8.7)
2nd or 3rd severe MCP	29 (22.5)	9 (34.6)	20 (19.4)	2.2 (0.9 to 5.6)	2.3 (0.7 to 7.2)
Right FCM	38 (29.7)	11 (42.3)	27 (26.5)	2 (0.8 to 4.9)	1.7 (0.6 to 4.5)
Left FCM	43 (33.1)	13 (50)	30 (28.8)	2.5 (1 to 5.9)	2.3 (0.9 to 6)
Right trapezium-scapoid	11 (8.6)	5 (19.2)	6 (5.9)	3.8 (1.1 to 13)	1.9 (0.4 to 8.1)
Left trapezium-scapoid	10 (7.7)	5 (19.2)	5 (4.8)	4.7 (1.3 to 16.7)	3.4 (0.8 to 14)
Right radioulnar	12 (9.4)	2 (7.7)	10 (9.8)	0.8	0.7 (0.1 to 4.6)
Left radioulnar	7 (5.4)	3 (11.5)	4 (3.9)	3.3 (0.7 to 14.1)	2.6 (0.4 to 16)

*Values in parentheses are percentages of the value of n for the column.

†Grade 2 or superior according to Kellgren's criteria; ‡grade 3 or superior according to Kellgren's criteria.

MCP = metacarpophalangeal; FCM = first carpometacarpal.

Table 2 Frequency of knee osteoarthritis (OA) in the medial and lateral compartments

	Chondrocalcinosis	Controls
Subjects	26	104
No of compartments	104	416
OA in any compartment	38.5% (40/104)	15.8% (66/416)
OA in lateral compartment	46% (24/52)	13% (27/208)
OA in medial compartment	30% (16/52)	19% (39/208)

Of the 104 femorotibial compartments analysed in the individuals with chondrocalcinosis, 69 showed evidence of chondrocalcinosis. Table 3 shows that OA was as frequent in those compartments with chondrocalcinosis as in those without it.

Individuals with chondrocalcinosis had more OA than the controls in almost all articular areas of the hand (table 1). However, the difference was statistically significant only for the metacarpophalangeal joints. Metacarpophalangeal OA (defined as the presence of OA in at least one of the six metacarpophalangeals studied in each case) was significantly more frequent in subjects who had chondrocalcinosis than in those who did not (aOR 3.1; 95% CI 1.1 to 8.8). This association was also evident when the first metacarpophalangeal joint of both hands was excluded—that is to say, when the presence of OA was analysed only for the second or third metacarpophalangeal (aOR 3.1; 95% CI 1.1 to 8.7). Both associations were also observed when the relation between OA and chondrocalcinosis was evaluated regarding the number of metacarpophalangeal joints analysed (data not shown). Severe OA of the second or third metacarpophalangeal joints was more frequent among people with chondrocalcinosis, though the difference was not statistically significant.

When a separate analysis was made for each of the metacarpophalangeal joints, the positive association between OA and chondrocalcinosis was present only in the left hand (table 1). OA in the trapezium-scaphoid, first carpometacarpal and distal radioulnar joints was slightly more frequent in the group with chondrocalcinosis, but the differences were not significant. Only two subjects had radiocarpal OA; neither of the two had chondrocalcinosis.

Discussion

The results of this study show that individuals with chondrocalcinosis had more osteoarthritic changes in their hands and knees than those without chondrocalcinosis. However, the magnitude of the association between OA and chondrocalcinosis varied depending on the articular areas analysed. The association was particularly strong in the lateral compartment of the knee, and in the first three metacarpophalangeal joints of the left hand.

The relation between OA and chondrocalcinosis has been studied previously. In one study of 338 biopsy specimens of the knee, chondrocalcinosis was six times more frequent in osteoarthritic knees than in those that were non-osteoarthritic, after adjusting for age and gender.¹² Almost all the radiographic studies⁷⁻¹¹

agree that OA is more frequent in those individuals that have chondrocalcinosis than in those that do not. However, homogeneity does not exist between studies regarding the articular areas evaluated, the criteria used to define OA, or the statistical methods used. Moreover, these studies compared the frequency of OA between a group of patients with chondrocalcinosis (previously selected for their rheumatic complaints) with a non-rheumatic 'control' population without chondrocalcinosis—a circumstance that could result in a bias of the real association between both entities. In this respect, we are aware of only one previous study on the association between OA and chondrocalcinosis of the knees, carried out in a representative sample of the general population of Framingham.² This large study included more than 1400 individuals older than 63 years, and a weak but significant positive association was observed between the two diseases (relative risk = 1.5). Using the same diagnostic criteria and with a population having characteristics similar to those of the Framingham population (table 4), we have also found an association between OA of the knee and chondrocalcinosis (aOR 4.3). Had we used the relative risk as the measure of association, the estimate of risk would have been similar to that of the Framingham study (relative risk of 2). Notably in our study, as in the Framingham survey,² the association between chondrocalcinosis and severe OA was not stronger than that observed between chondrocalcinosis and mild OA.

When we analysed the association of OA and chondrocalcinosis in both tibiofemoral compartments (not evaluated in the previous studies), we found that such association was stronger in the lateral compartment. This finding has not been observed in idiopathic OA, where the medial compartment is affected commonly, and the isolated involvement of the lateral compartment is rare.²⁰

Although Resnick *et al*⁸ concluded that in patients with chondrocalcinosis the medial compartment was the area most affected by OA, two radiographic studies comparing the knees of subjects with chondrocalcinosis with those of subjects with idiopathic OA^{9 21} showed that the involvement of the medial compartment in patients with chondrocalcinosis was less evident than that of patients with OA. Moreover, in one of the studies²¹ osteophytes were more frequently identified in the lateral compartment than in the medial side. More recently, in a large study of knee radiographic patterns of OA patients, it was found that the involvement of the lateral tibiofemoral side had

Table 3 Relationship between the presence of osteoarthritis (OA) and radiographic chondrocalcinosis in the femorotibial compartments of subjects with chondrocalcinosis (26 subjects, 104 compartments)

	Compartments with chondrocalcinosis (n = 69)	Compartments without chondrocalcinosis (n = 35)
OA	26 (38%)	14 (40%)
No OA	43 (62%)	21 (60%)

Table 4 Comparison of population characteristics of Osona and Framingham

	Framingham	Osona
Number of subjects	1402	261
Age (yr) (mean (range))	73 (63-93)	68 (60-88)
Sex ratio (M/F)	1.4	1.2
Chondrocalcinosis (No (%))	114 (8)	27 (10)
Knee OA (%)		
With chondrocalc.	51.8	69.2
Without chondrocalc.	31.1	35.6

a greater degree of association with chondrocalcinosis.²²

This is the first study in which the association between OA and chondrocalcinosis has been analysed in several articular areas of the hand in an unselected population. As in previous studies,⁶⁻⁹ we have found a statistically significant association between metacarpophalangeal OA and chondrocalcinosis, especially for the second and third joints. The fact that the association was significant only when the left hand was analysed is curious and unexpected, although this finding could be explained by the population included in our study. Metacarpophalangeal OA is frequent in the rural Spanish population,²³ and is most probably related to repetitive manual labour.²³⁻²⁴ As this type of lesion is predominant in the right hand,²³⁻²⁵ the degree of association between OA and chondrocalcinosis could be masked by this phenomenon and therefore be less evident than in the left or non-dominant hand.

The present study has several limitations. First, as the 'cases' were pre-existing we can establish an association, but cannot be certain about its directionality: that is to say, it is not clear whether the pyrophosphate deposits are the predisposing factor that triggers the articular lesion, or the consequence of the degenerating process in the articular cartilage.²⁶ Second, lateral knee radiographs were not taken. These projections are required to evaluate the patellofemoral compartment that is said to be affected, characteristically and in isolation, in chondrocalcinosis,⁸⁻²¹ though this was not confirmed in a recent study.²⁷ Third, analysis of the femorotibial compartments without radiographs during weight bearing makes it more difficult to detect definite joint space narrowing; however, evaluation of the less involved compartment is problematic in the weight bearing projection.²⁰⁻²⁷ We believe, nevertheless, that these limitations have not influenced the nature of the results of our study. The absence of radiocarpal OA in the present patients is somewhat surprising, especially as Resnick *et al*²⁸ found it to be characteristic of chondrocalcinosis. Our findings may be explained by the fact that the presence of typical osteophytes was required in our definition of OA, while joint space narrowing and subchondral sclerosis are the most frequent radiological signs of radiocarpal OA.²⁸ As Felson *et al*² suggested, an overdiagnosis of OA in subjects with chondrocalcinosis (information bias) cannot be discarded; however, as the κ estimator was high and the observers assessed the joints independently, we believe that information bias was unlikely in this study. Finally, the sample size was relatively small, thus there was insufficient power to study the association in several joints or in subgroups of subjects.

We conclude that there was an association between osteoarthritis and chondrocalcinosis in an elderly population sample selected independently of rheumatic complaints. People with chondrocalcinosis had a greater prevalence of osteoarthritis in the knees, especially

in the lateral compartment. In addition, osteoarthritis in the first three metacarpophalangeal joints of the left or non-dominant hand was more frequent in people with chondrocalcinosis than in those without it.

We dedicate this article to the late Dr Maria Ant3nia Branc3s.

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