Hand osteoarthritis patients characteristics according to the existence of a hormone replacement therapy

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Summary

Background: Hand osteoarthritis (hand OA) mostly occurs in women around the time of menopause, but its relationship with sexual hormones remains a controversial issue. The eventual influence of hormone replacement therapy (HRT) on the incidence and progression of hand OA is still debated.

Objective: To assess whether HRT influences the occurrence and disease activity of hand OA.

Methods: Epidemiological prospective cross-sectional study. Patients: Menopausal women, aged 50–75, consulting for painful hand OA, for another rheumatic condition with hand OA or controls (no disease of the upper limbs). Eligibility criteria: hand OA [American College Rheumatology (ACR) criteria] with X-ray evidence. Patients with 'painful' hand OA defined by a Dreiser's functional index score ≥6 and pain on VAS ≥35 mm. Study parameters: Demographics, personal histories and gynecologic data for patients and controls including the administration of HRT (+) or not (−). For patients, description and symptom activity of hand OA. Statistics: Descriptive analysis in the studied population and in subsets taking into account treatment and disease activity factors.

Results: 711 women were studied: 238 with 'painful' hand OA, 240 with 'quiescent' and 233 controls. Baseline characteristics were similar for patients and controls except for age (patients were older). HRT+ patients were younger (−5 years) (P<0.0001), slightly taller (P<0.0045) and more often cigarettes smokers (P<0.012) than HRT− patients. They did not differ in gynecologic characteristics with the exception that the women in the HRT+ group had been menopausal for a shorter period of time, probably because of their younger age. There were no differences between HRT+ and HRT− patients, whatever the symptom activity, on the characteristics of hand OA: Dreiser's index scores were, respectively, 11.3±3.8 vs 12.3±4.5 in 'painful' patients, 3.6±2.5 vs 3.7±2.7 in 'quiescent' patients. Pain on VAS showed no difference between the two groups.

Conclusion: Few differences were found between hand OA patients receiving HRT or not. HRT did not seem to influence the severity or the symptom activity of hand OA. Further prospective studies are required in order to evaluate the exact effect of HRT on hand OA.

Introduction

Hand osteoarthritis (hand OA) commonly affects women, with peak onset around the time of menopause.1–6 The reasons for the predominance of hand OA with or without generalized osteoarthritis in women are not yet elucidated. Some authors have stated that hormonal factors could be responsible,3–5 but the exact relationship between hand OA and sexual hormones is still controversial.

Experimentally, estrogens have been found to protect male mice with increased susceptibility to OA but have worsened lesions in meniscectomized rabbits, while tamoxifen improved these lesions (in 2). Recently, it has been shown that biomechanical properties of the cartilage were altered in ovariectomized sheep, but not in sheep treated by estradiol implants.6

Clinically, works published in this field give conflicting results. Cauley et al. did not find any correlation between serum levels of various male and female sexual hormones and radiological severity of hand OA in 229 women.7 Schouten et al. did not find any increased risk in developing OA of the distal interphalangeal joints (DIP) in hysterectomized women compared with naturally menopausal women.8 He did observe, however, a statistically significant relationship between the occurrence of Heberden's nodes and both the age at menopause and the duration of the fertile period. Spector et al. reported an increased relative risk to develop OA of the knee and trapezometacarpal joints in hysterectomized women compared to agematched controls.9

Studies concerning a protective effect of hormone replacement therapy (HRT) show contradictory results. Laroché et al., in a case report, find a protective effect of estrogen/progesterone treatment.10 Oliveria et al. did not find any protective action of estrogens on hand OA in 16

Key words: Hand osteoarthritis, Hormone replacement therapy, Disease severity, Disease activity.
Zhang et al. does not report any protective effect of estrogens on radiological lesions of hand OA assessed on X-rays taken at an 11-year interval in 407 women. Conversely, Spector et al. report a protective effect of current HRT (≥12 months) with respect to knee (odds ratio (OR)=0.31, 95% confidence interval (CI): 0.11;0.93) and distal interphalangeal (DIP) OA (OR=0.48, 95% CI: 0.17;1.42). In their recent review, Felson and Nevitt have commented on the possible effect of estrogens on OA.

We conducted this study to investigate the potential influence of HRT on the occurrence of hand OA and on its clinical severity.

**Methods and patients**

This was a prospective cross-sectional multicenter epidemiologic study conducted in all areas of France by 250 rheumatologists who recruited women affected by hand OA or controls, receiving HRT (HRT+) or not (HRT-).

**Patients**

Each rheumatologist selected three patients as follows: women consulting for painful hand OA (‘painful’ hand OA group), women known to be affected by hand OA but consulting for another rheumatological condition (‘quiescent’ hand OA) and women without hand OA (‘control’). In order to insure a well-balanced recruitment of either HRT+ or HRT- women, rheumatologists were divided into two groups: one selected exclusively women receiving HRT and the other only women without any hormonal therapy.

**Eligibility criteria**

Consecutive menopausal patients (at least 6 months without menses), aged 50–75 years, consulting a rheumatologist. Hand OA patients needed to fulfill the American College of Rheumatology (ACR) criteria for the reporting of hand OA (Classification tree format) and had to show X-ray features of hand OA on standard plain radiographs of both hands. In a previous work, differences have been observed with regard to OA history and clinical presentation between patients affected by ‘painful’ hand OA and patients affected by a ‘quiescent’ hand OA. Therefore, each investigator was asked to select a ‘painful’ and a ‘quiescent’ patient. The cut-off was determined by a value of Dreiser’s functional index (a validated 10-item investigator-administered questionnaire) (and see in this issue the paper by Dreiser) global score of 6 and a level of pain (during the previous 24 h) rated on a VAS at 35 mm. ‘Painful’ hand OA patients were defined by (1) a Dreiser’s functional index score ≥6 and (2) a spontaneous pain on VAS ≥35 mm and ‘quiescent’ hand OA patients respectively by (1) a functional index score <6 and (2) pain on VAS <35 mm. Excluded from both groups were patients presenting with a monoarticular post-traumatic hand OA.

**Study parameters**

For each case or control, the investigator collected the following information: (1) demographic data (age, height, weight), (2) medical history including cigarette smoking, history of hand OA in the family, the existence of radiologically documented OA at other sites, and (3) gynecological data including the age at first menses, number of pregnancies, age at menopause, time since menopause, existence of HRT (past >6 months duration or current) and, for HRT+ patients the type of treatment administered from the various HRTs available today. In addition, data for hand OA patients were collected including: values of Dreiser’s functional index score, global spontaneous pain on VAS, handedness, delay since first symptoms, number of painful flares during the past 12 months, number of osteoarthritic joints, number of painful joints at the time of the visit, and number of joints with nodes (Heberden and/or Bouchard) reported on a sketch of both hands, and, if applicable, current professional occupation and sports activity.

**Results**

**Study population**

A total of 711 women were studied: 238 ‘painful’ hand OA patients, 240 ‘quiescent’ hand OA patients and 233 controls.

There were no differences in eligibility criteria between the two groups of hand OA patients: the majority fulfilled both the clinical ACR criteria and the X-ray features requirement for the definition of hand OA (Table I). Approximately half of the patients or controls received HRT (current or past >6 months).

**Demographic data**

The results appear in Table II. Mean age was comparable in the ‘painful’ and ‘quiescent’ hand OA groups. On the other hand, controls were a little younger than hand OA patients, this difference being significant vs the ‘quiescent’ hand OA group (adjusted mean age 61.6 versus 63.9 years, P<0.001). The most important difference with regard to age was that HRT+ patients were five years older than HRT+ patients (65.2 years vs 60.3, P<0.0001). Maybe consequently, other statistically significant differences were
Table I

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Painful hand OA (33.5)</th>
<th>Quiescent hand OA (33.8)</th>
<th>Controls (32.8)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (%)</td>
<td>238</td>
<td>240</td>
<td>233</td>
<td>711</td>
</tr>
<tr>
<td>ACR criteria for hand OA definition</td>
<td>209</td>
<td>198</td>
<td></td>
<td>407</td>
</tr>
<tr>
<td>X-ray &lt;1 year</td>
<td>204</td>
<td>190</td>
<td></td>
<td>394</td>
</tr>
<tr>
<td>Dreiser's index ≥6</td>
<td>206</td>
<td></td>
<td></td>
<td>394</td>
</tr>
<tr>
<td>Pain on VAS ≥35 mm</td>
<td></td>
<td></td>
<td></td>
<td>394</td>
</tr>
<tr>
<td>HRT current past</td>
<td>91 (38.2)</td>
<td>85 (35.4)</td>
<td>91 (39.1)</td>
<td>267 (37.1)</td>
</tr>
<tr>
<td>none</td>
<td>121 (50.8)</td>
<td>132 (55.0)</td>
<td>132 (55.7)</td>
<td>385</td>
</tr>
</tbody>
</table>

HRT=Hormone replacement therapy.

Table II

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Painful hand OA (50.8)</th>
<th>Quiescent hand OA (55.0)</th>
<th>Controls (55.7)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients HRT+</td>
<td>117</td>
<td>121</td>
<td>108</td>
<td>346</td>
</tr>
<tr>
<td>HRT-</td>
<td>121</td>
<td>108</td>
<td>132</td>
<td>361</td>
</tr>
<tr>
<td>Age (years)</td>
<td>60.4±6.0</td>
<td>65.2±8.7</td>
<td>62.2±6.0</td>
<td>67.7±8.3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>62.1±9.5</td>
<td>62.4±10.0</td>
<td>62.4±9.3</td>
<td>64.6±10.2</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>168±5.8</td>
<td>159.0±5.8</td>
<td>160.2±6.6†*</td>
<td>159.3±5.1</td>
</tr>
<tr>
<td>Cigarette smoking (current or past)</td>
<td>18 (15.4%)‡</td>
<td>19 (15.7%)‡</td>
<td>21 (19.4%)‡*</td>
<td>23 (22.8%)‡*</td>
</tr>
</tbody>
</table>

*Statistically significant difference between HRT+ and HRT- patients: mean age higher in the HRT- group (P<0.0001).
†Statistically significant difference between HRT+ and HRT- patients: women receiving HRT were taller (P<0.0045).
‡Statistically significant difference between HRT+ and HRT- patients: more cigarette smokers in women receiving HRT (19% vs 11.2%, P<0.012).

Table III

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Painful hand OA (50.8)</th>
<th>Quiescent hand OA (55.0)</th>
<th>Controls (55.7)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural menopause</td>
<td>101 (88.8%)</td>
<td>103 (88.8%)</td>
<td>103 (88.8%)</td>
<td>307</td>
</tr>
<tr>
<td>Surgical menopause</td>
<td>16</td>
<td>12</td>
<td>17</td>
<td>45</td>
</tr>
<tr>
<td>Medical menopause</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Number of pregnancies</td>
<td>2.2±1.3</td>
<td>2.0±1.2</td>
<td>2.3±1.5</td>
<td>2.0±1.2</td>
</tr>
<tr>
<td>Type of HRT (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estrogen</td>
<td>15 (13.6)</td>
<td>16 (16.2)</td>
<td>10 (10.3)</td>
<td></td>
</tr>
<tr>
<td>Combined estrogen and progesterone</td>
<td>61 (56)</td>
<td>57 (57.6)</td>
<td>53 (54.6)</td>
<td></td>
</tr>
<tr>
<td>Alternate estrogen and progesterone</td>
<td>35 (31.8)</td>
<td>26 (28.3)</td>
<td>33 (34)</td>
<td></td>
</tr>
<tr>
<td>Progesterone</td>
<td>3 (2.8)</td>
<td>4 (4)</td>
<td>5 (5.2)</td>
<td></td>
</tr>
</tbody>
</table>

*Statistically significant difference between HRT+ and HRT- patients: time since menopause was shorter in the HRT+ group than in the HRT- group.

GYNECOLOGIC CHARACTERISTICS

Table III summarizes these data. 'Painful' and 'quiescent' patients and controls were comparable for all collected gynaecological parameters. Mean age at first menses was 13 years, mean age at menopause was 50 years. Natural menopause occurred in 88% of the studied women, surgical menopause accounting for the remaining 12%. The different types of HRT (estrogens, combined estrogen/progesterone, alternating estrogen and progesterone, progesterone alone) were equally distributed in the three groups. The only difference observed between HRT+ and
HRT+ patients concerned the time since menopause, which was shorter in HRT+ patients. This was not unexpected, since these women were five years younger than HRT− patients.

CHARACTERISTICS OF HAND OA

Table IV provides the results. 96% of the patients were right-handed with no difference between symptom-related groups, nor between HRT+ and HRT− patients. Almost 73% of the patients had OA at other sites (hip, knee, spine) with no differences observed between ‘painful’ and ‘quiescent’ groups, nor between HRT+ and HRT− patients. There was a significant difference between controls and hand OA patients concerning the existence of a previous history of hand OA, 22% of controls vs 68% of hand OA patients reporting a familial history of hand OA. No difference in family history was found between the two groups of hand OA patients (P<0.266). In 80% of hand OA patients, it was the mother who had a history of hand OA, which was expected.

No difference was observed between ‘painful’ and ‘quiescent’ patients for the other characteristics of hand OA, with the exception of the percentage of erosive OA which was significantly higher in the ‘painful’ group (P<0.001). The other differences concerned the level of symptomatic activity which was obviously and by definition more severe in the ‘painful’ group (more patients experiencing a greater number of flares during the previous year, higher values of Dreiser’s index score and pain on VAS, higher number of painful joints). It can be noted that HRT+ patients had more past or current sports activity than HRT− patients regardless of symptom activity of hand OA.

No other significant differences were observed between HRT+ and HRT− patients. The values of the Dreiser’s index score were comparable: Dreiser’s index scored respectively 11.3±3.8 vs 12.3±4.5 in ‘painful’ patients, 3.6±2.5 vs 3.7±2.7 in quiescent patients, as were those of pain on VAS. The percentages of patients with erosive OA were higher in both HRT+ and HRT− ‘painful’ patients compared to ‘quiescent’ patients (P<0.001) and slightly higher in HRT+ vs HRT− ‘painful’ patients (44% vs 38%) but not in the overall HRT+ vs HRT− sample comparison. The mean number of osteoarthritic joints, painful joints at visit and nodal joints were comparable in the ‘painful’ and ‘quiescent’ groups of patients.

Discussion

The present prospective cross-sectional epidemiological study was aimed at studying the characteristics of hand OA patients according to the administration of HRT or not, and at assessing whether or not HRT influenced the occurrence and severity of hand OA. One limitation of this work is that it was not a longitudinal study.

In this study, we found no difference between HRT+ and HRT− patients with regard to the characteristics of hand OA.

Patients were selected according to validated criteria for the reporting of hand OA15 and divided into two groups with regard to symptom severity (Dreiser’s index score and pain on VAS values). In addition, a control group was selected to ascertain whether some possible differences observed were related to HRT and not to the OA condition. It was decided to separate prior to the study the rheumatologists selecting women (case or control) receiving HRT or not. Half of the rheumatologists had to recruit HRT+ patients and control subjects while the other half had to recruit HRT− patients and control subjects. This was done in order to make sure there would be the same proportions of HRT+ patients and control subjects while the other half had to recruit HRT− patients and control subjects. This was done in order to make sure there would be the same proportions of HRT+ or HRT− patients and to ensure a random selection of patients and avoid bias in the recruitment of HRT+ hand OA patients. However, selection bias might have occurred since this was a cross-sectional study and conducted in rheumatology practice. The results should be interpreted keeping in mind this distinction between participating rheumatologists.

Except for age, patients and controls had comparable demographic and gynecological data. Family history of hand OA was more frequent in hand OA patients, which was expected.
There were important significant differences between 'painful' and 'quiescent' hand OA patients concerning all the parameters of severity and symptom activity of hand OA, such as, by definition, the Dreiser's functional index score and pain on VAS values, the number of painful flares during the 12 previous months, the percentage of patients with erosive OA, the number of painful joints and the number of joints affected by OA. This means that the distinction of patients into 'painful' or 'quiescent' groups is clinically relevant, and should be considered in future epidemiological studies.

When we compared HRT+ patients to HRT-, the only differences concerned some demographic and gynaecological parameters: HRT+ patients were five years younger, taller, more often cigarette smokers, and had a shorter time since menopause at study entry. All these parameters may be related to the younger age, since nowadays HRT seems to be more systematically prescribed around the time of menopause. However, no difference was found between HRT+ and HRT- patients with regard to the characteristics of hand OA. The use of HRT was not associated with reduced severity or symptoms of hand OA in this study. The time since first symptoms, the number of flares during the past 12 months, the percentages of erosive OA, the level of pain (VAS) and the value of the Dreiser's functional index score were similar in hand OA patients whatever the hormone therapy and the symptom activity of hand OA. Therefore the existence of HRT (whatever the type of treatment) does not seem to have influenced the symptoms and structural course of hand OA in the studied population. A possible bias may have occurred in the recruitment of hand OA patients receiving HRT, resulting in the selection of a subset of HRT+ women. This bias seems unlikely, since HRT+ patients and controls were comparable for all parameters except age.

Conclusion

The results of this study do not support the hypothesis of a beneficial effect of HRT on prevention or stabilization of hand OA. This conflicts with results of some previous studies. We do not explain the absence of a beneficial influence of HRT on hand OA severity or symptom activity in this population. However, we recommend that future prospective longitudinal studies be conducted in order to assess clearly if HRT is of benefit to prevent or stabilize hand OA and if there are clinical parameters predictive of a good response to this treatment.

References