CONCISE REPORT

Relationship between Heberden's nodes and underlying radiographic changes of osteoarthritis

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Objective: To determine whether clinically determined Heberden's nodes (HN) and Bouchard's nodes (BN) are associated with underlying individual radiographic changes of osteoarthritis (OA).

Methods: 232 index patients with symptomatic large joint and/or hand OA, and 257 of their first degree relatives were included. HN were graded 0–2; BN were scored as present/absent. Joint space narrowing (JSN) and osteophyte (OST) were each scored 0–3 using the OARSI atlas. A weighted κ test was used to examine intraobserver reproducibility. Odds ratio (OR) was estimated for the relationship between nodes and associated JSN and OST.

Results: The adjusted OR of HN for underlying JSN in the same digit was 1.72 (95% CI 1.47 to 2.02), whereas for OST it was higher at 5.15 (95% CI 4.37 to 6.08). A similar trend was seen with BN and underlying OA, with OST having a higher OR (OR = 2.98, 95% CI 2.55 to 3.47) than JSN (OR = 1.62, 95% CI 1.37 to 1.91).

Conclusion: There is a positive relationship between HN/BN and underlying radiographic changes of OA, especially OST. Nodes do appear to link pathologically to OA in interphalangeal joints.

Heberden's nodes (HN) and Bouchard's nodes (BN) are firm swellings over the superolateral and dorsal aspects of distal and proximal interphalangeal joints respectively.[1 2] Despite their prevalence the pathogenesis of nodes remains unclear, although bony outgrowth[3] and endochondral ossification of marginal hypertrophic fibrocartilage[4 5] are implicated in their aetiology. Nevertheless, it is widely held that nodes are associated with hand osteoarthritis (OA),[5–7] that they are a marker for systemic predisposition to generalised OA,[6 7] and that they reflect the presence of underlying osteophyte (OST).[4 5] However, the link between HN and underlying interphalangeal OA has been questioned in one study of middle-aged female twins,[8] in which a poor correlation was found between HN and underlying radiographic OST, assessed on a 0–3 scale using a radiographic atlas.[9] In contrast, a more recent study[10] of 71 subjects with hand OA showed a reasonable correlation between HN and radiographic OA in the corresponding joint, assessed using the global Kellgren and Lawrence scale.[11] Thus the postulated association between nodes and underlying OA is in doubt.

We therefore undertook a cross sectional study of women and men with HN to determine whether nodes are associated with radiographic OA of the corresponding joint. Unlike previous studies[8 10] we assessed individual radiographic features of OST and joint space narrowing (JSN) and investigated the influence of sex, age, and body mass index (BMI) on the relationship.

METHODS

Participants

The study was approved by the local research ethics committee. Participants were patients referred to a hospital rheumatology clinic because of symptomatic large joint and/or hand OA, together with their first degree relatives, who were identified for a nodal OA genetic study.[12] Cross sectional data on these participants were collected.

Clinical and radiographic assessment

HN were determined by clinical inspection and palpation for firm/hard posterolateral rounded swellings and/or joined dorsal bars, irrespective of any tenderness or symptom reporting, and classified for each finger of both hands as: grade 0 = no firm/hard swelling; grade 1 = unilateral (posterolateral) firm/hard swelling; and grade 2 = bilateral (posterolateral) firm/hard swellings. BN were similarly determined by inspection and palpation and classified as present or absent, because a previous study in our unit showed poorer agreement for BN than HN.[13] Assessments were undertaken by two trained nurses. To determine interobserver variation, both metrologists scored the same 20 subjects, selected to show a range of scores, 1 week apart. Height and weight, and thus BMI (kg/m^2), were recorded for each subject.

Hand radiographs were dorsal-palmar, both hands on one film, centred on the 3rd metacarpal heads (Agfa film, 50 kV, 4 mA/s). The thumb metacarpophalangeal joint, the thumb interphalangeal joint, and the index, middle, ring, and little finger distal interphalangeal (DIP) joints, and proximal interphalangeal joints were graded for JSN (0—3) and OST (0–3) using the OARSI atlas.[14] Radiographs were read by a single observer who was unaware of the clinical scores. To examine reproducibility a sample of 20 radiographs, selected to show a range of values, was re-read by the same observer who was unaware of the initial scores.

Statistical analysis

The relationship between HN/BN and JSN/OST was examined using odds ratio (OR). To calculate the OR, HN and BN were defined based on severity grade $\geqslant$1 and JSN and OST were defined based on radiographic grade $\geqslant$1. In addition, the ORs for HN grades 0, 1, and 2 were calculated. Stratified analyses were undertaken to examine the influence of age, sex, and BMI on the relationship. A logistic regression model was used to calculate the OR adjusted for age, sex, and BMI (aOR). To best fit the model, age was dichotomised as $<$65 years and $\geqslant$65 years, and BMI as $<$25 kg/m^2 and $\geqslant$25 kg/m^2. All statistical calculations were performed on SPSS version 11.0 for Windows (SPSS, Chicago IL, USA).

Abbreviations: aOR, adjusted odds ratio; BMI, body mass index; BN, Bouchard's nodes; CI, confidence interval; DIP, distal interphalangeal; HN, Heberden's nodes; JSN, joint space narrowing; OA, osteoarthritis; OR, odds ratio; OST, osteophyte

Table 1 Characteristics of patients

Characteristic	Men	Women	p Value
Number of patients	85	404	
Age	65.8 (1.0)	65.7 (0.5)	0.96
Height (cm)	171.9 (0.7)	159.2 (0.3)	0.00
Weight (kg)	78.1 (1.3)	67.1 (0.7)	0.00
Body mass index (kg/m^2)	26.4 (0.4)	26.4 (0.2)	0.99
Heberden's node severity	10.2 (0.6)	11.3 (0.2)	0.07
Bouchard's node severity	2.6 (0.3)	2.9 (0.1)	0.25
Summated DIP JSN score	7.9 (0.7)	11.3 (0.3)	0.00
Summated DIP OST score	12.2 (0.7)	12.3 (0.4)	0.93
Summated PIP JSN score	3.7 (0.4)	4.5 (0.2)	0.13
Summated PIP OST score	3.7 (0.4)	4.5 (0.2)	0.13

Results are shown as mean (SEM).
DIP, distal interphalangeal joint; PIP, proximal interphalangeal joint; JSN, joint space narrowing; OST, osteophyte.

RESULTS

Characteristics of participants

A total of 489 subjects (404 women, 85 men) with finger nodes were studied, including 232 index patients and 257 of their affected siblings, parents, or offspring. Forty three per cent had current symptoms in one or both hands. Table 1 provides demographic details.

Odds ratios between HN/BN and underlying radiographic features

Interobserver reproducibility for specific HN and BN was good (κ values 0.6–0.8 and 0.5–0.7, respectively). Values of κ for radiographic features varied from 0.3 to 0.8, depending upon the joints assessed. Table 2 shows the OR and 95% confidence intervals (CIs) of HN for their underlying radiographic change. The aOR of HN (grade ⩾1) for underlying joint space narrowing was 1.72 (95% CI 1.47 to 2.02). The aOR for underlying OST was much stronger at 5.15 (95% CI 4.37 to 6.08). More severe HN (grade 2) had a higher predictive value for JSN (aOR = 1.96, 95% CI 1.77 to 2.17) than the nodes of grade 1 (aOR = 0.96, 95% CI 0.81 to 1.14). In contrast, the severity of HN did not significantly affect predictive values for OST (aOR = 3.53, 95% CI 2.94 to 4.24 for grade 1 *v* aOR = 2.90, 95% CI 2.60 to 3.22 for grade 2).

A similar statistically significant association was found for BN and underlying radiographic change (table 3). The aOR was higher for OST (aOR = 2.98; 95% CI 2.55 to 3.47) than for JSN (aOR = 1.62; 95% CI 1.37 to 1.91).

The aORs (95% CI) of HN and BN for underlying OST, given the effects of JSN, were 4.92 (4.16 to 5.80) and 2.87 (2.39 to 3.24), respectively. The aORs (95% CI) of HN and BN for underlying JSN, given the effects of OST, were 1.52 (1.28 to 1.79) and 1.37 (1.15 to 1.63). Hence the node, as a clinical marker, is associated with underlying individual radiographic features independently, with higher predictive value for OST than for JSN. There was no statistically significant influence of age, sex, or BMI on this relationship, as 95% CIs overlapped between strata (tables 2 and 3).

DISCUSSION

This study shows that in a mixed population of men and women with a broad age range, digital nodes are associated with underlying radiographic changes of interphalangeal OA, as suggested previously.[4] This association is stronger for OST and is not significantly influenced by sex, age, or BMI.

The higher OR observed between HN or BN and OST suggests that the main association is with OST. Interestingly, more marked HN (grade = 2) with dorsolateral swelling on both radial and ulnar aspects were a better predictor of JSN than unilateral swellings, but this was not so for OST (table 2). Because nodes evolve slowly to reach their maximum size, this suggests that radiographic JSN manifests later in the course of node development and that established nodes affecting both aspects of the joint are a good clinical marker for this change. However, a prospective study is required to confirm this. The stronger relationships between nodes and radiographic changes seen at DIP joints might be explained anatomically. The presence of lateral bands over proximal interphalangeal joints may influence osteophyte growth making it less distinct than at DIP joints.

The different conclusions from our study and those of Cicuttini *et al*[8] may be accounted for in part by the populations studied. Cicuttini *et al* studied middle-aged female twins with a mean age of 56 years, whereas we studied both women and men with a mean age of 66 years. Such a demographic difference might result in our population having more patients with fully established nodes. If nodes do form by endochondral ossification then a temporal difference might be expected, in that new (radiolucent) fibrocartilage might form a palpable swelling some time before calcification and ossification make it apparent on radiographs.

There are several caveats to this study. Firstly, index patients were recruited through hospital referral with symptomatic OA and their relatives were recruited subsequently. It was not a random population sample and thus is subject to selection bias. Secondly, it was cross sectional; only a prospective study can document the temporal relationship between nodes and OA changes. Thirdly, nodes were scored clinically and OA changes examined by radiographs using a single view. Although reproducibility for nodes was good the reproducibility for radiographic scores varied according to joint site and might have influenced the results.

Table 2 Heberden's nodes and underlying radiographic changes of OA

	Sex		Age (years)		BMI (kg/m^2)		
	Men	Women	<65	⩾65	<25	⩾25	aOR
JSN							
HN=0	1	1	1	1	1	1	1
HN=1	1.15 (0.79 to 1.69)	0.96 (0.79 to 1.15)	0.93 (0.73 to 1.19)	0.94 (0.74 to 1.20)	0.86 (0.65 to 1.13)	1.10 (0.89(to 1.37)	0.96 (0.81 to 1.14)
HN=2	3.26 (2.10 to 5.06)	4.21 (3.38 to 5.25)	3.57 (2.70 to 4.74)	4.10 (3.11 to 5.41)	4.63 (3.31 to 6.44)	3.86 (3.03 to 4.95)	1.96 (1.77 to 2.17)
HN⩾1	1.74 (1.22 to 2.47)	1.81 (1.53 to 2.15)	1.65 (1.33 to 2.05)	1.77 (1.42 to 2.21)	1.76 (1.37 to 2.27)	1.88 (1.54 to 2.28)	1.72 (1.47 to 2.02)
Osteophyte							
HN=0	1	1	1	1	1	1	1
HN=1	4.26 (2.74 to 6.61)	3.61 (2.97 to 4.38)	3.27 (2.54 to 4.21)	3.81 (2.95 to 4.92)	3.39 (2.55 to 4.51)	3.89 (3.09 to 4.91)	3.53 (2.94 to 4.24)
HN=2	7.09 (4.12 to 12.20)	8.91 (7.14 to 11.14)	6.95 (5.22 to 9.25)	9.46 (6.99 to 12.80)	9.04 (6.53 to 12.52)	8.50 (6.46 to 11.17)	2.90 (2.60 to 3.22)
HN⩾1	5.17 (3.48 to 7.70)	5.42 (4.55 to 6.46)	4.54 (3.62 to 5.69)	5.67 (4.50 to 7.15)	5.27 (4.07 to 6.84)	5.43 (4.41 to 6.69)	5.15 (4.37 to 6.08)

Results are shown as odds ratio (95% confidence interval).
JSN, joint space narrowing. Joint space narrowing and osteophyte were defined based on a radiographic grade ⩾1 from the scale 0–3; HN, Heberden's nodes were graded based on the scale 0–2; aOR, adjusted odds ratio by age (<65 years *v* ⩾65 years), sex (female *v* male), body mass index (normal (<25 kg/m^2) *v* overweight (⩾25 kg/m^2)).

Table 3 Bouchard's nodes and underlying radiographic changes of OA

	Sex		Age (years)		BMI (kg/m^2)		
	Men	Women	<65	≥65	<25	≥25	aOR
JSN							
BN=0	1	1	1	1	1	1	1
BN=1	2.75 (1.83 to 4.18)	1.57 (1.27 to 1.81)	1.15 (0.87 to 1.50)	1.98 (1.60 to 2.45)	1.77 (1.37 to 2.28)	1.64 (1.32 to 2.03)	1.62 (1.37 to 1.91)
Osteophyte							
BN=0	1	1	1	1	1	1	1
BN=1	3.09 (2.13 to 4.47)	2.96 (2.52 to 3.47)	2.69 (2.10 to 3.44)	3.17 (2.61 to 3.85)	2.98 (2.35 to 3.78)	2.98 (2.46 to 3.61)	2.98 (2.55 to 3.47)

Results are shown as odds ratio (95% confidence interval).
JSN, joint space narrowing. Joint space narrowing and osteophyte were defined based on radiographic grade ≥1 from the scale 0–3; BN, Bouchard's nodes were measured as present (1) or absent (0); aOR, adjusted odds ratio by age (<65 years *v* ≥65 years), sex (female *v* male), body mass index (normal (<25 kg/m^2) *v* overweight (≥25 kg/m^2)).

Furthermore, a single dorsal-palmar radiograph might be expected to be sensitive for lateral but not dorsal OST. In future studies, it would be preferable to employ more sensitive imaging such as magnetic resonance imaging or high resolution ultrasound to assess both joint and periarticular tissues in more than one plane. Indeed, the results of a recent magnetic resonance imaging study of patients with HN[15] show consistent and prominent abnormalities of collateral ligaments in affected DIP joints, with more variable abnormalities of all other joint structures, thus emphasising the importance of non-cartilage tissues in pathogenesis.

In conclusion we have demonstrated a positive relationship between HN, BN, and underlying radiographic change. This association is stronger for OST, suggesting that nodes do appear to be linked pathologically to changes in underlying joints. These findings may have implications for genetic studies of hand OA in suggesting that the presence of HN and BN may be taken as clinical markers of predisposition to underlying interphalangeal OA.

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