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The Bristol 'OA500 study': progression and impact of the disease after 8 years

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Summary

Objective: To study the natural history of peripheral joint osteoarthritis (OA) and assess its impact over eight years in a prospective study of 500 patients.

Methods: 500 consecutive patients with peripheral joint OA were recruited from a hospital-based rheumatology clinic. All were invited for review 3 and 8 years after entry. Joint sites involved, pain severity, change in index joints, global change in the condition, use of medication, surgery and walking aids were all recorded at each visit, and after eight years disability was assessed by the health assessment questionnaire (HAQ) and anxiety and depression by the Hospital anxiety and depression scale (HAD).

Results: At eight-year review, 349 patients were seen: 90% of those remaining alive. Outcome was heterogeneous. Sixty patients (17.2%) reported worsening in all three subjective parameters (pain, index joint and global change) compared with 22 (6.3%) who improved in all three parameters. Using this definition of worsening or improvement, strong baseline predictors of clinical outcome did not emerge. For further description, the group was split according to the index joint sites involved at entry to the study, there being 111 with knee OA alone, 87 with hand and knee OA, 72 with hand disease alone, and 29 with hip disease alone. Forty-four percent of those with lone hand disease at entry had acquired significant knee or hip OA 8 years later. The mean HAQ and HAD scores at 8 years were high, especially in those with knee disease, indicating significant disability as a result of the disease. Those with knee or knee and hand disease had the worst outcome in all parameters recorded. The data showed a general decrease in use of NSAIDs over the eight years, but an increase in utilization of analgesics, surgery (especially for hip disease) and walking aids.

Conclusions: Patients with peripheral joint OA of sufficient severity to lead to hospital referral have a heterogeneous, but generally bad outcome over 8 years, the disease resulting in high levels of physical disability, anxiety and depression, with a high level of utilization of healthcare resources, including joint replacement, drugs and walking aids. The results were consistent with previous suggestions that peripheral joint OA in older people is characterized by the slow acquisition of new joint sites. Progression and outcome may depend on a complex set of psychosocial factors, as well as biological ones. © 2000 OsteoArthritis Research Society International

Key words: Osteoarthritis, Knee, Progression, Outcome.

Introduction

Osteoarthritis (OA) is a common condition, often said to be one of the main causes of pain and disability in older people, and the most frequent of the rheumatic diseases.[1,2] However, until recently, relatively little was known either about the natural history of the condition, or the impact of the disease on individuals. To address this problem, and to see if subsets of the disease could be clearly defined, the 'Bristol OA500 study' was established in the late 1980s.[3,4] It describes a prospective cohort of 500 people with peripheral joint osteoarthritis, ascertained through a hospital-based rheumatology clinic. The basic demography of the group has been described,[3] 3-year follow-up data

reported,[4] and the radiographic progression of knee joint OA in people in this cohort has been presented.[5] The data obtained from the cohort have contributed to the growing body of information that suggests that OA subsets are best defined according to the main joint site(s) affected.[3,6]

We here report the clinical outcomes of a proportion of this cohort after eight years of study, according to the main site(s) involved at entry. The data reported in this paper are clinical, and largely concerned with the impact of the condition on people, use of medical resources, acquisition of new joint sites of involvement and intercurrent disease, as well as possible predictors of outcome. Radiographic data, and more detailed clinical findings on the knee and hand joints (the most commonly affected sites) will be submitted for publication elsewhere.

Patients and methods

As reported previously, 500 consecutive patients with peripheral joint OA were recruited from a hospital-based rheumatology clinic.[3] Three and 8 years later all patients were invited to attend a follow-up clinic, and they were re-examined by one of two observers (JC or MT). Information obtained in the same way at each visit (0, 3 and 8 years) included self-reported pain severity (none, mild,

moderate or severe), reported change in the index joint (better, same, worse*),* and reported change in the overall condition of their osteoarthritis (better, same or worse than when first seen), use of analgesics or non-steroidal anti-inflammatory drugs (NSAIDs), any surgery for their arthritis, the use of walking aids, and the main joint sites with OA.

At each visit, an attempt was made to record which peripheral joints were worst affected by osteoarthritis (no attempt was made to assess spinal disease). When the cohort was first seen, radiographs of all painful joints were obtained and PAD classified one or two joint sites as the 'index' joints on the basis of their being the joints with both radiographic evidence of definite OA (Kellgren and Lawrence grade 2 or more) and identified by the patient as causing the most problems. They were then interviewed and examined fully by a single observer (JC). At the subsequent 3 and 8 year reviews, JC or MT recorded the three worst affected joint sites through a combination of identification of those sites by the patient as causing use-related pain which also had physical signs consistent with a diagnosis of OA (crepitus and bony swelling at the knee, Hebereden's nodes on two or more distal inter-phalangeal joints, or painful restriction of internal rotation at the hip). Radiographs were not used to classify the joint sites affected at 3 and 8 year visits, and no more specific criteria were applied. Cases were then analyzed by 'index joint' at baseline.

In addition to this longitudinal data, other cross-sectional data was obtained at the 8-year review to assess outcome. All patients seen at that time point filled in both the health assessment questionnaire (HAQ, 7), and hospital anxiety and depression scale (HAD, 8), and they were also asked about any intercurrent diseases.

STATISTICAL ANALYSIS

A chi-squared test was used to test for an association between patient reported outcomes (better, same, worse) and categorical baseline variables and an analysis of variance was used to test for differences in continuous variables with respect to patient reported outcomes. To test for differences in reported pain and global change at different time points in the different patient groups, the Kruskal-Wallis test was used.

A chi-squared test was used to look for between group differences in the numbers of patients using different health care resources, and a one way analysis of variance for differences in the health status of the different groups at 8 years.

Results

At entry, the cohort consisted of 342 women (mean age 65.3 years) and 158 men (mean age 59.7). The most commonly involved sites were the knees, hands and hips, hip disease standing out as being present in a younger, predominantly male group in comparison with other joint sites.[3] The mean disease duration reported by patients at entry was 9.8 years (range 1–23). After 3 years, 415 of the original cohort were available for review, and an overall worsening of pain and disability were reported.[4]

After 8 years we were able to review a total of 349 of the original 500 patients (70%), the remaining 151 either having died (113=22.6%), been lost to follow-up (30=6%), or refused to take part (8=1.6%). The only difference in baseline demographic data between those who had died or were lost to follow up and the whole group was in age, the 349 available for follow up being significantly younger at entry than the remainder. Those available for follow-up included 241 women and 108 men, and their worst reported joint at follow up was: knee 149 (43.1%), hand 72 (20.8%), hip 39 (11.3%), others (including spine) in 86 (24.9%) (data missing in 3 cases). Overall global worsening of the condition over eight years was reported in 216 compared with 62 who said that their arthritis was the same as eight years previously, and 67 (19.4%) who claimed that it had improved.

The three subjective indices of change over 8 years (change in pain, change in index joints and global change) were then combined in an attempt to define which patients clearly improved or worsened over the 8 years. This overall measure of change, which was predetermined, is described as the 'primary outcome measure' in the remainder of this manuscript. Twenty-two (6.3%) described improvement in the primary outcome measure, compared with 60 (17.2%) who described worsening. In the remainder there were many different discrepancies in change in these three measures. Discussions with patients and the metrologists (JC and MT) suggest that there was great variation in pain, in particular over time.

Several baseline variables were examined as possible predictors of change in the primary outcome measure. There were no statistically significant relationships (at the 5% level) between outcome and sex, occupation at entry (either repetitive, non-manual, light manual or heavy manual), hypertension, family history of OA, the presence of rheumatoid factor, worst joint affected (as described above), age, and body mass index. A statistically significant association was found with respect to drug usage at baseline (P=0.017). Those patients using NSAIDS at entry were more likely to report an improvement than those that were not (approximately 24% compared to 12%). A significant relationship was also found between disease duration and patients reported outcome (P=0.007). Patients reporting a worsening in their condition had, on average, a disease duration of approximately five years greater than those patients that reported an improvement.

The data set was then examined to allow a comparison of outcome and change in patient groups, defined by the index joint site(s) affected at entry, to allow a clear description of what happened to these patients, according to the most widely accepted and clinically useful means of describing subsets of the condition. The main patterns at entry were lone involvement of one or both knees, hands or hips, and the combination of hand and knee disease[3]—and these are the patterns that have been included in the subsequent data (the very small number of patients whose main problem affected another joint, such as the ankle or elbow, have been omitted from this analysis).

Of the 349 patients who were seen after eight years, 299 fitted into one of the four defined patterns of disease distribution at entry, and had data recorded at entry and three years (Table I). This represents 59% of the original cohort of 500, or 77.3% of the 387 remaining alive at the time of the 8-year review. At entry, 111 (37%) had OA of one or both knees only, 87 (29%) had OA in both their knees and hands, 72 (24%) had hand disease only (interphalangeal joints, thumb base, or both), and 29 (10%) had isolated OA in one or both hips. The demographic data shown on these patients shows that, as expected from the entry data, those with hip disease were younger and had a greater male preponderance than the other three groups.

Table I
Demographic data on the 299 patients with common patterns of joint involvement at entry and full clinical data available at entry, 3 and 8 years

	Joint site(s) affected at entry			
	Knee alone	Hand alone	Hip alone	Knee and hand
Number	111	72	29	87
% female	59%	86%	9%	86%
Age at entry	60	59	50	64
Mean (SD)	10.7	9.4	12.1	9.3

Change in pain and global rating of the osteoarthritis by the patients is shown in Table II. Those with combined knee and hand disease at entry reported significantly greater intensities of pain at all times than other groups, and appeared to show more worsening of the condition as well. The data also indicate a steady deterioration in the groups overall, with those with knee involvement (either lone or in combination with the hand) faring worse.

Table 3 shows some of the data on the use of drugs (analgesics and NSAIDs), walking aids, and surgical interventions for OA in the four groups of patients. There was an overall trend to less use of NSAIDs and greater dependence on simple analgesics, but a steady rise in the need for walking aids, and the provision of surgical interventions, even in those with lone hand disease at entry. This may be related to the acquisition of OA in lower limb joints, because, as shown in Table IV, 44% of those with lone hand disease had apparently acquired significant knee or hip OA 8 years later. Table III also shows that a much higher proportion of those with hip disease came to surgery than those with knee involvement and that those with lone hip disease used significantly less drugs than those with knee or knee and hand disease. It appears from Table 4

that as many of those with lone knee OA at entry developed hand disease after 8 years (33%) as vice-versa, and that an even higher percentage of those with lone hip disease at entry developed knee disease subsequently (45%), however, it must also be noted that a separate analysis to look for evidence of acquisition of new joint sites between the 3- and 8-year observation time points showed no statistical evidence of this trend, so the data presented in Table IV could be due to the different criteria used to assess joint involvement at entry and 8 years.

Those patients in the lone knee OA group that had knee replacement surgery in the 8-year follow up period did not show any significant improvement either in self reported pain or in the primary outcome measure when compared with those that did not have surgery. Of those that had surgery, 70% reported a worsening of their condition compared with 61% that did not have surgery; 26% reported no or mild pain at eight years compared with 27% that did not have surgery. A similar relative lack of improvement in the primary outcome measure was shown in those patients with lone hip OA that had hip replacement surgery over the eight year follow up period. However, this was based on a relatively small sample.

The mean HAQ score was greater than one in all groups at 8 years, except for those with lone hand disease at entry (Table V). The recorded HAD scores also suggest that many of the patients in this study were suffering from a lot of anxiety, depression, or both when the follow-up data were collected. Those with a combination of knee and hand disease at entry had significantly higher HAQ and HAD (depression) scores at 8 years than those in any of the other groups.

Some of the reported disability and use of interventions such as walking aids could be related to ageing and intercurrent disease, rather than OA. We therefore enquired about intercurrent disease. There was a high

Table II
Reported changes in pain and overall condition at 3 and 8 years for each group as defined by index joint at entry—note that the numbers in each column are not always the same for each joint group because of some missing values

		Joint sites affected			
		Knee alone	Hand alone	Hip alone	Knee and hand
Reported pain					
Entry	None	5 (5%)	7 (10%)	2 (7%)	3 (3%)
	Mild	39 (35%)	29 (41%)	14 (48%)	20 (23%)
	Moderate	39 (35%)	28 (39%)	9 (31%)	33 (38%)
	Severe	28 (25%)	7 (10%)	4 (10%)	30 (35%)*
3-Year	None	4 (4%)	3 (5%)	1 (4%)	2 (2%)
	Mild	29 (28%)	25 (40%)	14 (50%)	18 (22%)
	Moderate	54 (51%)	29 (46%)	9 (32%)	38 (46%)
	Severe	18 (17%)	6 (10%)	4 (14%)	24 (29%)*
8-Year	None	3 (3%)	6 (8%)	1 (3%)	2 (2%)
	Mild	27 (25%)	26 (36%)	10 (34%)	9 (10%)
	Moderate	50 (45%)	27 (38%)	14 (48%)	43 (50%)
	Severe	30 (27%)	13 (18%)	4 (14%)	32 (37%)*
Reported change					
3-Year	Better	26 (25%)	15 (23%)	11 (39%)	13 (16%)
	Same	28 (27%)	18 (28%)	5 (18%)	13 (16%)
	Worse	51 (49%)	31 (48%)	12 (43%)	56 (68%)†
8-Year	Better	22 (20%)	19 (27%)	6 (21%)	12 (14%)
	Same	19 (17%)	14 (20%)	7 (25%)	13 (15%)
	Worse	69 (63%)	38 (54%)	15 (54%)	60 (71%)

*$P<0.005$, †$P<0.05$ (Kruskal–Wallis test).

Table III
Numbers of patients in each group using drugs (analgesics or NSAIDs), walking aids, or coming to surgery for osteoarthritis at entry and after 3 and 8 years (with omission of missing values as in Table 2)

	Joint sites affected				
	Knee alone	Hand alone	Hip alone	Knee and hand	Total
Number using walking aids					
Entry	36 (33%)	2 (3%)	9 (32%)	23 (27%)	70
3-Year	47 (45%)	3 (5%)	8 (29%)	34 (41%)	92
8-Year	70 (63%)	13 (18%)	12 (41%)	53 (61%)	148
Number using drugs					
Entry					
Analgesic	40 (36%)	21 (30%)	15 (52%)	35 (41%)	111
NSAIDs	61 (55%)	41 (58%)	13 (45%)	52 (61%)	167
3-Year					
Analgesic	64 (61%)	24 (38%)	12 (43%)	51 (62%)	151*
NSAIDs	50 (48%)	23 (37%)	10 (36%)	43 (52%)	126
8-Year					
Analgesic	64 (59%)	39 (54%)	13 (45%)	65 (75%)	181*
NSAIDs	56 (51%)	21 (29%)	11 (38%)	31 (36%)	119
Surgery					
By 3-year	15 (14%)	5 (8%)	9 (32%)	17 (21%)	46
By 8-year	36 (33%)	13 (18%)	14 (48%)	30 (34%)	93

*Chi-square test shows significantly less analgesic use in patients with hip disease than in those with knee or knee and hand disease ($P<0.01$).

Table IV
Numbers (%) of patients reporting osteoarthritis at additional sites after 8 years

	Joint site affected at entry			
	Knee alone	Hand alone	Hip alone	Knee and hand
Additional joint sites (by 8-year visit)				
Knees	—	24 (33%)	13 (45%)	—
Hips	20 (18%)	8 (11%)	—	15 (17%)
Hands	36 (33%)	—	7 (24%)	—

prevalence of co-morbid conditions, over 30% of older patients complaining of cardiovascular, respiratory or gastrointestinal disorders, but we could find no differences between groups.

Discussion

Most studies reporting on the natural history of OA have been concerned with radiographic rather than clinical change,[9,10,11] and studies of the impact of the condition in terms of disability or quality of life have mostly studied groups before and after surgical intervention.[12,13] However, from the patient's point of view it is obvious that pain, disability and quality of life are more important than radiographic outcome, and the data that we reported after three years of follow-up of this cohort showed a discrepancy between radiographic and clinical change, indicating that it may be inappropriate to use radiographic changes as a surrogate for patient outcomes in OA.[4] In this report we have concentrated therefore, on the clinical changes in this group of patients, there being virtually no comparable published data on the outcome of osteoarthritis in patients whose condition is sufficiently severe to lead to referral to a hospital based rheumatology clinic. The main conclusion that can be drawn from the outcome of the group as a whole is that peripheral joint OA is a condition that causes persistent but variable pain, and severe disability in many patients. However, the clinical outcome is obviously very heterogeneous, some patients reporting improvement. Reported improvement could be due to the ability of some patients to adapt better to the condition over time, or to changing needs and aspirations, rather than genuine improvement in disease, and the data presented does not allow us to speculate on the cause.

The variability of self-reported changes in pain, index joint condition and global assessment were striking; most patients showing no consistent change over time; and only a minority reporting either improvement or worsening on our chosen primary outcome measure. This is consistent with other recent data that suggest that pain and disability are as dependent on psychosocial variables as they are on the condition of the joint[14,15] and would imply that the assessment of impact at any single time point will always be clouded by other dependent variables, such as social isolation, which are not recorded in this study, and generally ignored in the assessment of OA,[16] as well as variations in adaptation and illness related behaviours.[17,18] We also acknowledge the fact that review at an arbitrary time point 8 years after entry to the study might not reflect what is going on over the whole time period of the study.

One of our main aims when first setting up this study, was to find factors that might predict the outcome, but few

Table V
The impact of disease on the four groups of patients described, as recorded at the 8-year visit by self reported HAQ and anxiety and depression scores (HAD)

	Joint site affected			
	Knee alone	Hand alone	Hip alone	Knee and hand
HAQ				
Mean	1.32	0.84	1.07	1.60
Std dev.	0.77	0.73	0.76	0.78*
HAD (anxiety)				
Mean	7.23	6.29	7.90	7.57
Std dev.	4.22	4.24	4.89	4.57
HAD (depression)				
Mean	5.81	4.31	5.59	5.46
Std dev.	3.78	3.41	3.31	3.39†

One way ANOVA tests showed that those with knee or knee and hand disease were significantly more disabled (*$P=0.0001$) and depressed (†$P=0.05$) than other groups.

such factors have emerged clearly either from the three or eight year data. However, we accept that the chosen outcome measures in this study were crude, limiting our ability to detect predictors. It is interesting to note the negative findings; there being no association between age, sex, occupation or body mass index and change in the primary outcome measure for example; the apparent discrepancy between this finding and some other data might be in part due to the fact that we were concentrating on clinical, rather than radiographic changes. The fact that patients with a longer disease duration were more likely to report worsening probably reflects the slowly progressive nature of the condition, which is apparent from other data in this study (addition of new joint sites). The only other association found, that those taking non-steroidal anti-inflammatory drugs (NSAIDs) at entry were more likely to report improvement is difficult to interpret, but would suggest that NSAIDs usage should not be considered as necessarily deleterious to the progression of the arthritis. The chief, negative conclusion that we have to make from this part of the study is that the key causes and predictors of the heterogeneity of outcome for patients with osteoarthritis of their peripheral joints remain largely unexplained, and should be studied further. However, a further important caveat to this conclusion is the size of the study, as it may not have the power to detect some associations between baseline factors and outcomes, particularly as relatively small numbers clearly got better or worse.

After 8 years of follow-up, some of the conclusions that we came to from the previous cross-sectional study of this cohort appear to have been substantiated. The co-existence of hand and knee disease, and the important observation that peripheral joint OA is characterized by the slow acquisition of new joint sites over time, inferred from the first cross-sectional report[3] has again been suggested by these data. However, the ways in which the presence or absence of OA was defined in this study presents a major limitation to this interpretation—the change in methods and change in observers over time could have affected classification of joints as having or not having OA. When the study was first established there were no published clinical criteria for the definition or classification of OA, and although the clinical definitions used in the 3 and 8 year follow-up are consistent with the ACR criteria,[19] the lack of

formal standardization of the observations means that the findings presented in Table 4 must be interpreted with great caution.

The main new conclusions that can be drawn from the 8-year data, analyzed according to the main joint sites affected at entry, are: (1) that those with knee disease (either with or without hand disease) became more disabled and were more likely to suffer severe pain than those with lone hip or hand disease at entry, and that they were using more drugs and walking aids than the other groups; (2) that those with hip disease were more likely to come to surgery than those with knee disease, in spite of less pain and disability than the knee group; (3) that over the 8 years there has been a trend to less use of NSAIDs and more use of simple analgesics; (4) that the overall impact of the disease is very great in terms of the overall degree of both physical and psychological disability, as well as the use of drugs and walking aids, and that most of this impact is likely to be due to the OA.

We were interested by the finding that although surgery was more likely to be for hip replacement than knee replacement, those with knee disease appeared to have considerably more pain and disability after 8 years than the younger patients with hip disease. There are many possible reasons for this, including age, intercurrent diseases and OA at other joint sites. We also accept that the inclusion of those who had undergone surgery during the study in the final analyses could be a source of criticism.

We elected to analyze the data according to the main joint site(s) affected at entry because this is the most conventional and clinically valuable means of subsetting patients with peripheral joint OA[6] of immediate and obvious relevance to those providing health services, as well as those who have the condition. Our ability to hold this cohort together (thanks largely to SB) meant that relatively large numbers were available for data analysis at all three time points within the four main patterns of OA described in the first report. Furthermore, the fact that we were able to review 90% of those remaining alive at the time of the 8-year review (349 of the 387 patients) reduces the likelihood of our results being affected by loss of those with the most severe disability or other confounding factors. Caveats to the interpretation of the data include the fact that it is essentially an observational study of a highly selected group of patients, we also recognize that the numbers in the subgroups are relatively small, particularly those with hip disease. In addition, over the 8 years that we have followed these patients they have aged, acquired OA at new joint sites and developed intercurrent diseases. As we have no control or comparator group in the study, we cannot be certain about how much of their significant burden of pain, disability, anxiety and depression is due to these other factors, rather than to their osteoarthritis. We chose the HAQ and HAD as ways of assessing the outcome in terms of burden of physical or psychological disability respectively, as these are standard measures, widely used. The scores (in each case a higher score means more disability) for physical disability, anxiety and depression are all much higher than that which would be expected in such an age group.[7,8] Furthermore, the mean scores for the HAQ were >1 in all except the hand alone group, indicating significant levels of physical disability, and the high use of walking aids and surgery for OA suggest that arthritis was the main cause of these patient problems. It is unfortunate that HAQ and HAD scores were not available at entry for comparisons with outcomes, as some

of the differences in the groups at 8 years could simply reflect different levels of severity at ascertainment.

In spite of relatively small numbers, the greater utilization of hip rather than knee surgery is a cause for concern, as it does not appear to relate to disease severity or impact. This tends to support the conclusions of Tennant et al.,[20] and of the US PORT (patient outcomes research team) study on knee OA,[21] both of which suggest that knee surgery is an under-utilized intervention for knee OA. We are currently examining possible reasons for this.[22] The trend for less use of NSAIDs in patients for OA reflects national trends over the last few years[23] but may be higher than expected in part due to the attempts of some local consultants (including PAD) to reduce NSAID usage in this patient group.[24]

We have acknowledged here and previously that this study has many limitations including both the potential for our group to be unrepresentative, and the uncontrolled observational nature of our data. Nevertheless, we believe that many of the conclusions reached are likely to be generalizable, and that the data adds to our understanding of the natural history of OA and its very high impact of the disorder on many people's lives. The data supports the case of those who argue that osteoarthritis is an important disease because of its continuing burden of pain, disability and healthcare utilization over a period of many years, and it confirms that fact that people with advanced osteoarthritis at any of the major joint sites are likely to acquire disease at other sites with time, often leading to the need for surgical intervention. However, these data and our previous prospective reports also re-emphasize the heterogeneity of the clinical outcomes of OA, and suggest that it is dependent on complex psychosocial factors as well as biological ones. When considering the outcome of a chronic disease of older people a biopsychosocial model may be more appropriate than a simple biological one.

Acknowledgments

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