Clinical Comorbidity in Osteoarthritis: Associations with Physical Function in Older Patients in Family Practice

UMESH T. KADAM and PETER R. CROFT

ABSTRACT. ***Objective.*** To determine the influence of comorbidity on physical function in osteoarthritis (OA) consulters aged 50 years and over in family practice.

Methods. The study design linked morbidity consultations during an 18-month period to self-reported physical function status measured at the end of the period. Clinical comorbidity was compared between consulters with (n = 1026) and without (n = 8160) OA. Comorbidity was defined by morbidity counts (1–2 low, 3–4 medium, ≥ 5 high) and by a measure of severity of individual morbidities based on chronicity. Associations between comorbidity and physical function were assessed using unconditional logistic regression, adjusting for age, sex, and socioeconomic deprivation.

Results. Of the 1026 OA consulters, 38 (3.7%) had an OA consultation only, 260 (25.3%) had low, 288 (28.1%) medium, and 440 (42.9%) high morbidity counts. Higher OA comorbid counts were associated with poorer physical function, after adjusting for age, sex, and socioeconomic deprivation. Associations between OA comorbidity severity and poor physical function showed estimates that were in excess of simply multiplying the individual effects of OA and comorbidity severity separately. Comorbidity, however, did not explain all of the association between OA and poor physical function.

Conclusion. Comorbidity increases the likelihood of poor physical function in patients with OA in population-based family practice. The combined influence is greater than would be expected from the influence of either OA or the comorbid conditions alone. Treating comorbidity in patients with OA is likely to be crucial in preventing or reducing the related physical decline. (First Release July 15 2007; J Rheumatol 2007;34:1899–904)

Key Indexing Terms:
OSTEOARTHRITIS COMORBIDITY QUALITY OF LIFE
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Osteoarthritis (OA) is a common condition in older people, a frequent reason for family practice consultation, and a major cause of physical disability, and results in high healthcare use and related costs[1-3]. In an aging population, the importance of OA is likely to increase, and it commonly coexists with other chronic conditions[4,5]. Possible explanations for these comorbid links include shared pathogenesis and shared etiology, or the biological aging process in which different events increase in frequency with age and therefore are more likely to co-occur by chance with age even though they are otherwise unrelated to each other[6,7].

Distinct from the question of why OA comorbidity might occur is the separate question of how it influences the health status of the patient with OA. Studies have shown that comorbidity, such as visual disorders, diabetes, and heart disease, not only co-occurs more frequently than expected with OA[7], but results in adverse physical function[8,9] and adverse outcomes in joint replacement[10]. Two studies also raised the possibility of a synergistic process, i.e., the combination of OA and another chronic condition results in much worse health status than expected[11,12]. However, much of the current comorbidity research has been limited to pairs of chronic diseases and to selected comorbid chronic conditions.

Implicit in the definition of comorbidity is that there are combinations of 2 or more morbidities, and the key question that this raises is how the combinations of different numbers and types of morbidities influence the health status of individuals and populations. Despite OA being one of the most physically disabling conditions, the full extent to which OA combines with other nonchronic conditions to influence the physical status of such patients is unknown. The importance of this issue lies in the possibility that demonstrating the larger combined effects of comorbidity and OA may point to alternative clinical management pathways and the fact that in aging populations the numbers of people with OA and associated comorbidity are likely to increase.

From the Primary Care Sciences Research Centre, Keele University, Staffordshire, England.

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U.T. Kadam, MB, ChB, MSc, MPhil, PhD, GP Epidemiologist; P.R. Croft, BA, MB, ChB, MSc, MD, Professor of Primary Care Epidemiology, Primary Care Sciences Research Centre, Keele University.

Address reprint requests to Dr. U.T. Kadam, Primary Care Sciences Research Centre, Keele University, Staffordshire, England ST5 5BG. E-mail: u.kadam@cphc.keele.ac.uk

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We have already shown that musculoskeletal and nonmusculoskeletal comorbidity in OA consulters in population-based family practice is extensive[13]. We have now investigated the relationship between comorbidity and subsequent physical function in a cohort of consulters in primary care with and without OA, using measures of morbidity severity that can be used to define comorbidity based on family practice consultations[14]. Two hypotheses were tested, as follows. First, that the combined effect of OA and concurrent comorbidity on physical function is equal to multiplication of the separate effects of OA and comorbidity, and second, that the influence of OA on physical function is explained by the presence of comorbidity.

MATERIALS AND METHODS

Design. Our study linked individual patient morbidity data from consultations during an 18-month period to their self-reported health status at the end of the period. The research was carried out with the approval of the local research ethics committee.

Setting. North Staffordshire General Practice Research Network (NSGPRN) is a collection of practices, in which all family practitioners (FP) record morbidities using the Read system of codes in actual patient consultations. The Read thesaurus has 2 main elements: morbidity data (e.g., symptoms and diseases) and process data related to administrative and clinical processes (e.g., tests and administration)[15]. There are 19 main Read chapters that incorporate 4 numbered hierarchical levels, each providing progressively finer diagnostic detail. Since there are several thousand morbidity codes available, we collated all consultations at the third hierarchical level. The FP actively participated in training and feedback to ensure that the highest quality clinical data are recorded in their practice[16].

Study family practices. In 2001, 6 practices with 34 FP in NSGPRN had participated in health surveys of their registered populations aged 50 years and over[17,18]. Self-reported physical function status was measured using the 6 items contained in the Short-Form-12 instrument, a validated generic measure, to form a summary Physical Component Score[19,20]. The SF Health Outcomes Scoring Software was also used to impute any missing data to obtain the most complete set of summary scores[21]. Consultation data from family practice records for the 18-month period prior to the surveys was then linked to the physical function status score. These linked data were available for 10,974 patients.

Postal (residential) codes from the survey were used to allocate socioeconomic deprivation status to individual participants. The socioeconomic deprivation score is based on United Kingdom national census data 2001, and uses data on housing quality, car ownership, and number of people in the household to produce a composite (Townsend) score of relative deprivation linked to postal code[22].

OA and non-OA groups. The definition of OA was based on consultations coded to any diagnosis under the third hierarchy of the musculoskeletal and connective tissue disease Read thesaurus, namely N05, "osteoarthritis and allied disorders"[15]. All patients who had consulted for OA at least once during the 18-month study period formed the index group, and the non-OA group consisted of all consulters who had no record of OA during the same period.

Of the 10,974 patients aged 50 years and over with linked survey and consultation data, 9439 had consulted for at least one morbidity in the 18-month period, of whom 1026 had consulted at least once for "osteoarthritis" (OA group) and 8160 had no such consultation for OA (non-OA group). We excluded 253 patients who did not have a morbidity code for OA but the term "OA" or "osteoarthritis" was mentioned by the FP in the free text record of the patient.

Clinical comorbidity definition. Comorbidity was defined by Feinstein as the study of an index condition (OA in this case) in the presence of other clinical conditions (hence our term "clinical comorbidity")[23]. For the non-OA group, we used the separate and distinct term "multimorbidity" to describe the presence of any 2 or more problems in this reference group. Across both groups, patients had consulted for conditions in a total of 876 different morbidity (all causes) categories, other than OA, in the 18-month period. Each category relates to at least one consultation in the study time period; repeat consultation within the same category was not included in the definitions or categorization of comorbidity or multimorbidity.

Two separate definitions were applied. First, total morbidity counts were calculated for each individual during the 18-month period. These counts relate to the number of different morbidity categories and they were then grouped into: single morbidity, 2 or 3 (low count), 4 or 5 (medium count), and 6 or more morbidities (high count). The reference group within the OA cases were patients who had consulted for OA only, and within the non-OA controls were patients who had consulted for a single morbidity only.

Second, individuals in the OA and non-OA groups were classified by consensus-developed measures for classifying morbidity by severity[14] and which have been validated in 2 countries[24]. In this classification, 133 morbidities had been classified on the ordinal chronicity scale as follows: acute, acute-on-chronic, and chronic; OA itself had been classified as a chronic morbidity. A selection of the commonly prevalent classified morbidities is given in Table 1. We excluded consulters with 2 or more unclassified morbidities from the severity analyses, leaving a final sample of 7265 non-OA and 853 OA patients for assessment by the chronicity measure. Comorbidity or multimorbidity was defined on the chronicity dimension by combinations of morbidities classified as acute, acute-on-chronic, and chronic categories. The reference group within the OA cases comprised patients who had consulted for OA only, i.e., no comorbidity. The reference group within the non-OA controls comprised patients who had consulted for a single unclassified morbidity. Individual patients within the OA and non-OA groups may have also consulted for other morbidities not in the chronicity classification.

Statistical analysis. The SF-12 scores were dichotomized into "poor" and "good" physical function categories using the mean for the study population to provide an outcome measure for estimating odds of poor outcome at different levels of comorbidity in OA. Associations between the defined comorbid or multimorbid groups and poor physical function were estimated using unconditional logistic regression to estimate odds ratio (OR) with 95% confidence intervals (CI), adjusting for age, sex, and socioeconomic deprivation. First, we estimated the overall association of OA with poor physical function (OA vs non-OA group). Second, the associations of comorbidity with poor physical function were assessed separately within OA and non-OA groups, stratified by morbidity counts and chronicity. Third, we estimated the associations of OA with poor physical function (relative to non-OA), but this time adjusting for each of the stratified count and chronicity groups.

"Effects" of any 2 concurrent individual factors can be combined in 2 ways: adding or multiplying them. The concept is illustrated as follows. First, assume that the overall "effect" of OA on poor physical function was 3 times that of non-OA. Second, assume in the non-OA group that the overall "effect" of multimorbidity on poor physical function was 3 times that of single morbidity consulters. Then the expected effect of OA and comorbidity together can be modelled either by adding ($3 + 3 = 6$) or multiplying ($3 \times 3 = 9$) the individual effects. On a multiplicative scale, patients consulting with OA and comorbid conditions have a 9-fold likelihood of worse physical function compared with single non-OA morbidity consulters. We chose to test our comorbidity hypotheses on the more stringent multiplicative scale. Any departure from this multiplicative scale was defined either as "antagonistic" (where the combined effects are less than multiplicative) or "synergistic" (where the combined effects are more than multiplicative)[25]. To assess the combined effect of OA and comorbidity, we first estimated the observed OR using logistic regression analyses, for the associations between the OA and physical function stratified by counts and chronicity. We then calculated the joint effects we might have "expected" by multiplying the individual effect of OA alone (relative to single morbidity in the consulters without OA) with the comorbidity effect from the corresponding groups without OA. Any differences between observed and "expected" estimates indicate antagonistic or synergistic effects. This descriptive but classical approach to evaluating the

Table 1. Commonest prevalent examples of the classification.

Read Code	Read Grouping	Period Prevalence per 10,000*	Classification
H06	Acute bronchitis and bronchiolitis	1197	Acute
N24	Soft tissue disorders	1143	Acute
H05	Acute upper respiratory infections	1060	Acute
F50	Disorders of external ear	903.6	Acute
K19	Urethral and urinary tract disorders	637.6	Acute
F4C	Disorders of conjunctiva	388.2	Acute
K15	Cystitis	276.4	Acute
H01	Acute sinusitis	250.5	Acute
AB0	Dermatophytosis tinea/ringworm	241.2	Acute
M18	Pruritus and related conditions	228.8	Acute
H02	Acute pharyngitis	222.5	Acute
M03	Cellulitis and abscess	197.7	Acute
E20	Neurotic disorders	555.8	Acute-on-chronic
H33	Asthma	552.7	Acute-on-chronic
J10	Diseases of esophagus	235	Acute-on-chronic
J51	Diverticula of intestine	169.8	Acute-on-chronic
G20	Essential hypertension	2102	Chronic
N05	Osteoarthritis and allied disorders	1088	Chronic
C10	Diabetes mellitus	631.4	Chronic
C32	Disorders of lipoid metabolism	415.1	Chronic
C04	Hypothyroidism	242.2	Chronic
G83	Varicose veins of the legs	235	Chronic
G57	Cardiac arrhythmias	195.6	Chronic
F59	Hearing loss	194.6	Chronic
F4F	Lacrimal system disorders	150.1	Chronic
F46	Cataract	141.8	Chronic

* Consulting period prevalence based on 18-month record review of consulters.

joint effects was done in preference to statistical tests of interaction because such tests have low power to detect differences[25,26]. All analyses were performed using SPSS version 11.0 for Windows.

RESULTS

Overall, after adjusting for age, sex, and socioeconomic deprivation, consulters with OA had significantly poorer physical function compared with non-OA consulters (OR 3.3, 95% CI 2.8–3.8). Of the 1026 OA consulters in the 18-month study period, 38 (3.7%) had an OA consultation only and 260 (25.3%) had low, 288 (28.1%) medium, and 440 (42.9%) high morbidity counts.

The 2 definitions showed that comorbidity within the OA group and multimorbidity within the non-OA group were associated with poor physical function when compared to their respective single morbidity reference groups.

Within the OA group, when comorbidity categories defined by counts were compared to the OA-only category, the OR for the associations with poor physical function adjusted for age, sex, and socioeconomic deprivation were as follows: low count 2.0 (95% CI 1.0–4.2), medium count 2.8 (1.4–5.6), and high count comorbidity 3.7 (1.8–7.4) (Table 2).

Within the OA group, increasing severity of comorbidity as defined by chronicity compared to the OA-only group showed increasing strength of associations with poor physical function, adjusting for age, sex, and socioeconomic deprivation. The associations ranged from acute comorbidity (OR 2.2, 95% CI 1.1–4.5) to acute and acute-on-chronic and chronic comorbidity (OR 8.2, 95% CI 2.9–22.8). Further details are given in Table 3.

The observed effect of comorbidity in OA consulters was greater than expected from the multiplicative model for low and medium morbidity counts, and less than expected for high morbidity counts (Table 2). For the chronicity dimension, the expected estimates were higher than multiplicative for all combinations within this dimension, and the highest difference was for the most severe level of comorbidity (a combination of acute, acute-on-chronic, and chronic morbidity; Table 3).

The analyses in Table 4 show the comparison of physical function in the OA group compared to the non-OA group that have been adjusted by the multimorbidity categories. In the direct comparisons of the OA groups with the corresponding non-OA groups, for all 3 measures, OA was associated with poor physical function, independently of comorbidity of any type or degree. The estimates were similar in strength across all comorbid categories.

DISCUSSION

Our study results show that poor physical function was significantly associated overall with OA consultation, and this was

Table 2. Associations between morbidity counts and physical function within OA and non-OA groups.

Group	Morbidity Counts	n	Physical Function		Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Multiplicative Model	
			Good	Poor			Observed OR†	"Expected" OR††
Non-OA	Single	1721	1149 (66.8)	572 (33.2)	1.0	1.0	1.0	1.0
	2 or 3	3103	1780 (57.4)	1323 (42.6)	1.5 (1.3–1.7)	1.4 (1.3–1.6)	—	—
	4 or 5	1743	759 (43.5)	984 (56.5)	2.6 (2.3–3.0)	2.5 (2.1–2.8)	—	—
	≥ 6	1593	494 (31.0)	1099 (69.0)	4.5 (3.9–5.2)	4.1 (3.5–4.8)	—	—
OA	Single	38	17 (44.7)	21 (55.3)	1.0	1.0	2.1	2.1*1.0 = 2.1
	2 or 3	260	80 (30.8)	180 (69.2)	1.8 (0.9–3.6)	2.0 (1.0–4.2)	4.5	2.1*1.4 = 2.9
	4 or 5	288	69 (24.0)	219 (76.0)	2.6 (1.3–5.1)	2.8 (1.4–5.6)	5.8	2.1*2.5 = 5.3
	≥ 6	440	78 (17.7)	362 (82.3)	3.8 (1.9–7.5)	3.7 (1.8–7.4)	7.7	2.1*4.1 = 8.6

* Adjusted for age, sex, and socioeconomic deprivation. † Estimates from logistic regression. †† Expected estimates calculated using OA-only "effect" multiplied by OR for the respective non-OA category.

Table 3. Associations between morbidity severity as measured by chronicity and physical function within OA and non-OA groups.

Group	Morbidity Classified by Chronicity	n	Physical Function		Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Multiplicative Model	
			Good	Poor			Observed OR†	"Expected" OR††
Non-OA	Single	873	587	286	1.0	1.0	1.0	1.0
	Acute (A) only	2301	1301	1000	1.6 (1.3–1.9)	1.5 (1.2–1.8)	—	—
	A-on-CH (AC) only	351	196	155	1.6 (1.3–2.1)	1.6 (1.3–2.0)	—	—
	Chronic (CH) only	1219	600	619	2.1 (1.8–2.5)	1.7 (1.4–2.0)	—	—
	A & AC	562	245	317	2.7 (2.1–3.3)	2.6 (2.0–3.2)	—	—
	A & CH	210	79	131	3.4 (2.5–4.7)	2.9 (2.1–3.9)	—	—
	AC & CH	1345	556	789	2.9 (2.5–3.5)	2.3 (1.9–2.8)	—	—
	A & AC & CH	406	116	290	5.2 (4.0–6.7)	4.0 (3.1–5.3)	—	—
OA	OA only	38	17	21	1.0	1.0	2.0	2.0*1.0 = 2.0
	Acute (A) only	263	74	189	2.1 (1.0–4.2)	2.2 (1.1–4.5)	4.5	2.0*1.5 = 3.0
	A-on-CH (AC) only	40	7	33	3.8 (1.4–10.8)	4.4 (1.5–12.8)	9.0	2.0*1.6 = 3.2
	Chronic (CH) only	116	29	87	2.4 (1.1–5.2)	2.3 (1.0–5.0)	4.3	2.0*1.7 = 3.4
	A & AC	94	20	74	3.0 (1.3–6.7)	3.4 (1.5–7.7)	7.1	2.0*2.6 = 5.2
	A & CH	27	5	22	3.6 (1.1–11.4)	3.2 (0.96–10.4)	5.9	2.0*2.9 = 5.8
	AC & CH	202	36	166	3.7 (1.8–7.8)	3.7 (1.7–7.8)	7.3	2.0*2.3 = 4.6
	A & AC & CH	73	7	66	7.6 (2.8–20.9)	8.2 (2.9–22.8)	17.3	2.0*4.0 = 8.0

* Adjusted for age, sex, and socioeconomic deprivation. † Estimates from logistic regression. †† Expected estimates calculated using OA-only "effect" multiplied by OR for the respective non-OA category.

Table 4. Associations of OA with poor physical function compared to non-OA, adjusting for comorbidity.

Classification	Subgroups	OA Physical Function Good:Poor	Non-OA Physical Function† Good:Poor	OA "Effect" Adjusted OR* (95% CI)
Counts	Single	17:21	1149:572	2.1 (1.0–4.1)
	2 or 3	80:180	1780:1323	3.1 (2.3–4.1)
	4 or 5	69:219	759:984	2.4 (1.8–3.2)
	6 or more	78:362	494:1099	1.8 (1.4–2.4)
Chronicity	Single	17:21	587:286	1.9 (0.9–3.8)
	Acute (A) only	74:189	1301:1000	3.0 (2.2–3.9)
	A-on-CH (AC) only	7:33	196:155	5.4 (2.3–13.0)
	Chronic (CH) only	29:87	600:619	2.6 (1.7–4.1)
	A & AC	20:74	245:317	2.8 (1.6–4.8)
	A & CH	5:22	79:131	2.5 (0.9–7.1)
	AC & CH	36:166	556:789	3.1 (2.1–4.5)
	A & AC & CH	7:66	116:290	3.8 (1.7–8.7)

† Individual non-OA groups are reference category for the corresponding OA category. * Adjusted for age, sex, and socioeconomic deprivation.

independent of age, sex, and socioeconomic deprivation. However, poor physical function in OA is associated with comorbidities and their severity. The specific study hypotheses were refuted. First, when comorbidity was defined by severity based on chronicity, there was evidence that the combined effect of OA and comorbid severity on physical function was greater than expected on the basis of their separate effects. However, this effect was not found when comorbidity was measured by morbidity counts. Second, in contrast to previous evidence suggesting that individual conditions contributing to comorbidity do not have independent effects[12], our study shows that the influence of OA on poor physical function is independent after adjusting for comorbidity, and consistent across categories of comorbidity severity.

Previous research has shown that for specific chronic disease pairs with arthritis, there may be a synergistic effect on poor overall health status and impairment of specific tasks[11,12]. For example, the combination of arthritis and hypertension was associated with overall disability, but that of arthritis and vision impairment was specifically associated with mobility impairment. A more recent study using simple counts, however, did not find such combined effects[27]. Our study is novel in providing the wider picture of multimorbidity and comorbidity as seen in population-based family practice, where most patients with OA are seen.

Our results also showed that the influence of OA comorbidity on poor physical function is comparable to that of multimorbidity on poor function. Further, adjusting for multimorbidity showed that OA still plays an independent role in the adverse effect on physical function in these patients. Additional adjustment for age, sex, and deprivation is likely to have taken account of other associated psychosocial factors. Other research indicates that OA and musculoskeletal conditions have the greatest adverse impact on overall health status of any of comparable chronic diseases[28,29]. This research may also explain why in OA consulters the combined comorbid effects were only synergistic at the most severe comorbidity level. It is plausible that an OA diagnosis in family practice represents the more severe end of the spectrum and low levels of comorbidity (count or severity) do not add substantially to the effect of the OA itself on physical function[30].

The 2 approaches to defining comorbidity allowed us to test the consistency of the results. We used all-cause morbidity counts as a simple measure, but it does not, for example, distinguish between major disease and minor symptom morbidity. We also used morbidity severity as measured by shared clinical characteristics (extrapolation of the concept of "chronic" disease but not focusing on a disease category). The strength of this approach is that it does distinguish between grades of different morbidities and allowed the grouping of a larger number of morbidities from the "morbidity pool." An alternative definition of comorbidity could have focused on specific disease pairs, i.e., OA and another morbidity. Such attempts in literature have been problematic in that the combined prevalence of even 2 common morbidities tends to be low. So our classification that focuses on the "morbidity or disease attribute" of chronicity offers one way of meeting the challenges of defining comorbidity, which is often limited by small sample sizes. However, individual patient experience of morbidity severity may be different; for example, individual patients have a different severity of OA, and the severity classification was used to place "osteoarthritis" on a severity scale relating to the spectrum of morbidities seen in family practice. The severity classification may also need to be adapted for actual practice, as treatments will be specific for individual morbidity and the severity of patient symptoms will dictate clinical management. In estimating the joint effects of OA and comorbidity on physical function, there may also be other factors (e.g., body mass index) that influence this relationship, but we did adjust for the major confounders of age, sex, and socioeconomic deprivation.

Although the list of morbidities classified by severity was extensive, from symptoms to psychological disorders to disease pathology, it does not relate to all morbidities that could be classified or are seen in routine family practice. Our study used consultation-based measures (diagnosis and classification) for examining and defining comorbidity. Such computer-recorded consultations are based on what patients choose to present and the prinicipal diagnostic management pathway of the FP at that point. Nevertheless, it is worth emphasizing that in the British context, family practice offers an insight into the experience of population-level morbidity over time — almost all of the population are registered with a family practice. The study time period allowed for consultation data to identify a chronic disease, as part of routine chronic disease clinics in English family practices, and it also allowed for the assessment of short-term morbidity that might adversely influence poor physical function over time. Although previous studies have clearly established the validity and quality of clinical data in the family practice setting[16,31], FP still have to contend with the range of symptoms and morbidity presented by patients, which may represent different stages of the disease process. Our definition excluded multiple morbidities within a single consultation and the frequency with which the same morbidity was presented in the time period. Such inclusions to the comorbidity definition might have added to the categorization of comorbidity, but would have resulted in complexity that might have overwhelmed the dataset with a measure of general health surveillance rather than comorbidity.

Our study in older consulters with OA in family practice shows the adverse influence of clinical comorbidity on poor physical function, which is over and above the influence of OA on its own. The clinical implications are that (1) improving the physical health of patients with OA will also require the associated comorbidity to be addressed if there is to be any overall health benefit, and (2) the separate influence of OA may require targeted and arguably conventional chronic disease-type management. Our measures were based on routine

consultations, in the setting where most patients with OA are seen, and provide a practical means by which such patients might be identified and specific interventions planned. Further clinical and research work in the field of OA is still required to study the causes of clinical comorbidity and the use of clinical comorbidity as a prognostic factor for progression of OA, and in defining comorbidity for the design of new interventions.

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