Body mass and osteoarthritic pain: results from a study in general practice

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Abstract

Objective

To define the relationship between body mass index (BMI) and pain due to osteoarthritis (OA) of the hand, hip, and knee in patients seen in general practice; to evaluate if overweight is related to co-morbidity and education, and influences the prescription patterns of GPs.

Methods

2,764 Italian GPs recruited 10 consecutive patients with symptomatic OA, diagnosed according to the ACR criteria. Pain intensity on a visual analogue scale, BMI, years of formal education, comorbidities, pharmacological and non-pharmacological interventions, and referral to specialists were recorded.

Results

The most painful joints were the knee in 12,827 patients (53.6%), the hip in 5,645 (23.6%), and the hand in 5,467 (22.8%). A BMI indicative of overweight or obesity was found in 74.8% of men and in 68.3% of women. Mean BMI was higher in knee OA (27.9±3.9), in generalised OA (27.5±4.2), and hip OA (27±3.7) than in hand OA (25.5±3.4). The prevalence of obesity for hip and knee OA was higher than that reported for the general Italian population. Obesity was an important risk factor for pain in all OA localisations. Co-morbidities and lower education were associated with obesity and more intense pain ($p<0.0001$). Obesity and overweight were less frequent in institutionalised patients.

Conclusion

Our study confirms that more than two thirds of Italian patients with symptomatic OA seen by GPs are overweight or obese. Obesity is clearly associated with OA pain, a finding which is probably underestimated by GPs who are not used to modulate treatment and specialist referral according to patients' BMI.

Key words

osteoarthritis, obesity, BMI, Italy, general practitioner

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Introduction

One of the best studied, and potentially modifiable, risk factors for osteoarthritis (OA) is obesity. Population-based studies have consistently shown that excess weight is a major risk factor for knee OA (1). In addition, obese patients have a particularly high risk of bilateral knee OA, more so in women than in men. This association is not attenuated by data adjustment for other obesity-related factors such as hyperlipidaemia, hyperuricaemia, and diabetes. The association between overweight and hip OA in radiographic studies is less clear. In a recent systematic review, positive association with obesity was reported as moderate in monolateral hip OA and limited in bilateral hip OA (2). In another study, height but not weight, was associated with hip OA (3). Interestingly, overweight could also be a risk factor for hand OA (4).

The mechanisms relating overweight to OA are of several types (5). First, the joints support an increased dynamic stress that promotes cartilage disruption. A recent study showing that only knee OA, but not hip and hand OA, were associated with excessive weight is in keeping with this hypothesis (6). Second, obese patients have a higher bone mass, which may increase stiffness in the subchondral bone and facilitate cartilage breakdown. Finally, systemic factors, such as insulin-like growth factor, leptin, adiponectin, and resistin could be at work both in overweight and in OA (7). In addition, obesity is a pro-inflammatory state and cytokines, mainly IL-1, have been demonstrated to contribute to OA (8). Co-morbidities frequently associated with obesity, such as atherosclerosis and diabetes mellitus, could accelerate OA by inducing microvascular changes of the subchondral bone and increased cartilage stiffness. Local factors associated with OA, such as malalignment of the joint, could also contribute to making the joint more vulnerable to the effect of obesity. This mechanism has been recently demonstrated for the varus knee (9).

The relationship between obesity and pain intensity in OA is not sufficiently clear. In the general elderly population, obesity is associated with higher levels of pain, even after adjustment for the presence of OA, neuropathy, and NSAID use (10). Ideally, more advanced OA should be associated with more pain, but lack of correlation between anatomical damage seen on radiographs and patient's symptoms contradicts this statement. In one study, obese patients more frequently complained of diffuse than localised or regional knee pain (11). Several cross-sectional (12-14) and prospective (15, 16) studies suggested that obesity could increase knee pain in OA patients, a finding that is supported by the moderate decrease in knee pain induced by weight reduction (17). However, a recent study looking at the type of pain in knee OA (concordant or non concordant at two time points) could not find an association of persisting (and thus more severe) pain with the body mass index BMI (18). In addition, in most of these studies pain was evaluated as a dichotomous variable and no effort was made to measure its severity. Obesity is also a major determinant of functional impairment in symptomatic knee OA (19). Disability scores for all the tasks of the WOMAC disability scale were higher with increasing BMI (19). However, in contrast to the high number of studies on the relationship between obesity and risk of OA, studies on the relationship between obesity, overweight and severity of pain in OA are scant, especially for hip and hand OA.

To define the relationship between BMI, OA in different locations, and pain severity, we studied a large cohort of Italian patients visited by their attending general practitioners (GPs) because of symptomatic OA of the hand, hip and knee. The association of BMI with several clinical variables and the prescription pattern of GPs in patients with and without overweight were also analysed.

Patients and methods

The AMICA study (*Approccio Multidisciplinare Italiano alla Cura e diagnosi dell'Artrosi,* Italian Multidisciplinary Approach to the Diagnosis and Treatment of Osteoarthritis) is a study involving rheumatologists, orthopedic surgeons, physical medicine specialists, and general practitioners (GPs)

throughout Italy. The general framework of the study and previous descriptive results it has produced have been described (20). Briefly, 2,764 GPs participated in the AMICA study. Each of them was asked to enrol 10 consecutive patients with OA of the hand, hip and knee diagnosed according to the ACR clinical criteria (21-23). In a series of previous local meetings, GPs were trained to apply ACR clinical criteria by musculoskeletal system specialists in order to standardise the diagnosis. GPs were also periodically visited by trained monitors who reinforced the information given in the seminars. After clinical examination of the patient, each GP administered a questionnaire evaluating demographic data, clinical characteristics of OA, and information on previous diagnostic and therapeutic interventions. They also measured height and weight of the patients on a manual scale in kilograms and using a wall-mounted ruler in centimetres, with shoes removed, respectively. The body mass index (BMI) was calculated by dividing weight (kg) by height^2 (m^2). Patients were classified as underweight if their BMI was less than 18.5 kg/m^2, normal weight (BMI 18.5 to 24.9 kg/m^2), overweight (BMI 25 to 29.9 kg/m^2), or obese (BMI greater than 30 kg/m^2) (24). Patients with secondary OA, defined as OA resulting from trauma, previous inflammatory arthritis, or joint misalignement, were excluded. In the absence of a generally agreed consensus of the concept of generalised OA (GOA), patients with 2 or 3 symptomatic sites were classified as GOA (25-27). Pain intensity was assessed by asking the patient to indicate the degree of pain experienced in the last week on a 10 cm visual analogue scale (VAS). In our study, intense pain was defined as visual analogue scale score higher than 60 mm, which value represented the median overall pain reported by the patients. If the patient had pain in different joints, he was asked to indicate the most painful one. As a result, some of the results refer to the OA localisation with more intense pain even when multiple joints were involved; some other results refer to specific localisations or combinations thereof. The intensity of overall pain was recorded also by GPs on a 5-point Likert scale from 0=no pain to 5=very intense pain. The patient was also requested to subjectively score his/her quality of life (0=unchanged, 1=worsened, 2=highly worsened) and joint function (0=good, 1=decreased, 2=highly decreased). GPs indicated which pharmacological (no intervention, pure analgesics, NSAIDs, coxibs, steroids, or so-called "DMOADs" – disease-modifying osteoarthritis drugs) or non-pharmacological (no treatment, active and passive exercise, manipulation, physical therapy, spa therapy, surgery) interventions were suggested to the patient during the visit. GPs also noted to which specialist (rheumatologist, orthopaedic surgeon, or physioterapist) they eventually referred the patient.

Statistical analysis. Data were expressed as means ± standard deviation or as medians and range, if their distribution was not normal. The student's *t*-test, one way ANOVA or the chi square test was used for comparisons. Age and sex adjusted odds ratios and 95% confidence intervals were calculated when appropriate. The Pearson's Correlation Coefficient was used for correlations. Multiple regression analysis was used to evaluate the relative influence of the different risk factors for intense pain.

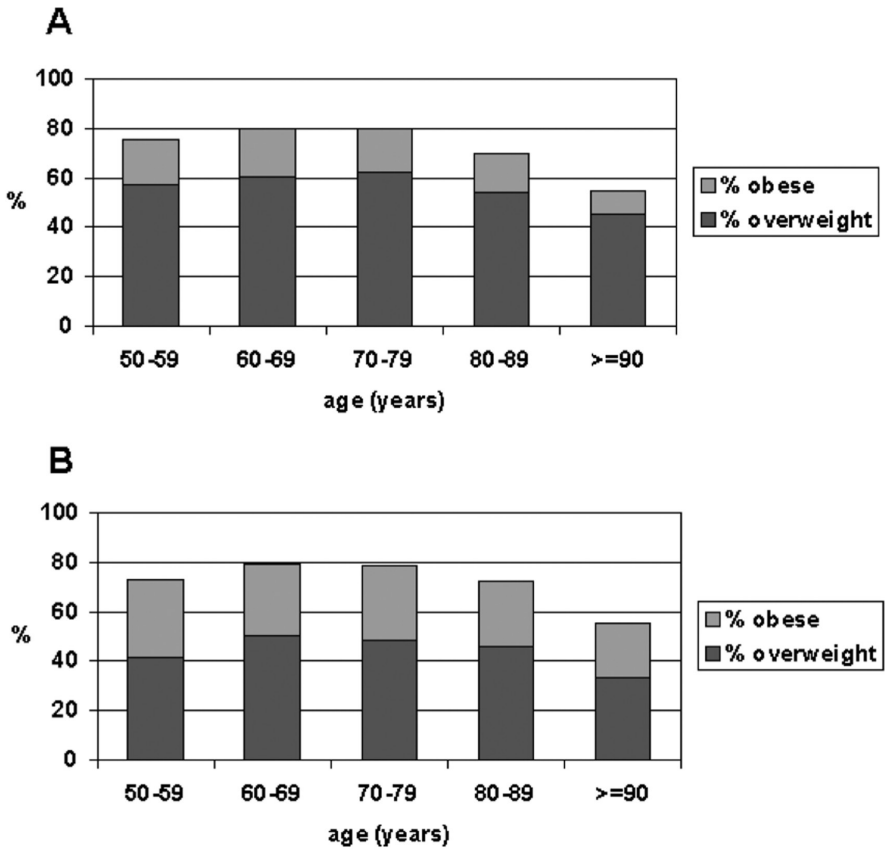

Fig. 1. Prevalence of overweight and obesity in our population of OA patients according to the different age classes. **A**: men; **B**: women.

Results

A total of 26,896 patients were enrolled. Of them, 1,451 (5.4%) were not included because (a) they failed to fulfil the ACR criteria (n=667, 2.5%), or (b) their gender was not recorded in the questionnaire (n=220, 0.8%), (c) or weight and height were missing (n=564, 2.1%). Of the remaining 25,445 patients, 17,567 (69%) were women and 7,878 (31%) men. In addition, in 1,650 patients the most painful joint was not indicated; these patients could be not included in some of the statistics on pain and overweight. A single OA site (hand, hip or knee, mono- or bilateral) was reported in 19,777 (77.7%) patients; two sites were reported in 4,861 (19.1%), and all three sites in 807 (3.2%). The most

painful joints were the knee, which was affected in 12,827 patients (53.6%), the hip in 5,645 (23.6%) and the hand in 5,467 (22.8%). The combination of hand plus knee involvement was seen in 2,157 patients, hand plus hip in 491 patients, and hip plus knee in 2,213 patients. Median age was 70 years (range 50-104 years) in the total patient population, with no difference between sexes. Mean disease duration was 8.3±7.1 years and median age at symptoms onset was 60 years (range 20–95 years).

A BMI indicative of overweight or obesity was found in 74.8% of men and in 68.3% of women. Men were more frequently overweight, whereas women were more frequently obese. The distribution of patients with symptomatic OA at different localisations, according to their BMI, is shown in Figure 1. Mean BMI was higher in knee OA (27.9±3.9), in GOA (27.5±4.2), and hip OA (27±3.7) than in hand OA (25.5±3.4) (p<0.0001 by ANOVA). Women with knee OA had higher BMI than men (28.2±4.3 *vs*. 27.4±3.3; p<0.0001). Conversely, men with hand OA had higher BMI than women (26.2±3 *vs*. 25.4±3.5; p<0.0001). No gender-related difference of BMI was seen for hip OA and GOA. The prevalence of obesity, defined as above, is reported in Table I. For comparison, data from the Italian general population indicate that the prevalence of obesity is 13% in men and 12% in women (28), values which are similar to those observed for hand OA but definitely less than those observed for hip and knee OA.

The prevalence of overweight and obesity was similar in all age groups (Fig. 2), except for a decline in the age group over 90 years. OA patients with comorbidities were more frequently obese with a dose-effect relationship as shown in Figure 3 for women with knee OA (p<0.0001). The same significant pattern was seen in both sexes and for all OA locations. When the mean BMI of patients without comorbidities (26.2±3.6 kg/m^2) was compared with that of patients with the comorbidities more frequently associated with overweight and obesity, *i.e*. diabetes (28.4±4.2), hypertension (27.9±4.1), and myocardial infarction (27.4±3.8), there was a striking difference (p<0.0001). This difference persisted after stratification for sex and disease localisation.

A total of 2,327 subjects (9.3%) declared that their joint function was good, 17,102 (67.2%) that it was decreased, and 6,007 (23.6%) that it was highly decreased. 3,363 patients (13.2%) stated that their quality of life had not been changed by OA, 17,164 (67.4%) stated that their quality of life had worsened, and 4,916 (19.3%) that it had highly worsened. The percentage of patients with very poor joint function and considerably worsened quality of life increased with increasing BMI (p<0.0001).

In OA patients, there was an inverse relationship between years of formal education and prevalence of obesity (Fig. 4), which was present in both sexes and in all OA locations (p<0.0001). Of our patients, 78.6% lived in the family, 20.4% lived alone at home, and 1% were institutionalised. Obesity and overweight were less frequent in institutionalised patients in comparison with patients living in the family (56.9% *vs*. 68.7%; p=0.0001) and with those living alone (56.9% *vs*. 67.4%; p=0.0006).

The risk factors for intense pain were obesity, female sex, age over 70 years, duration of OA longer than 7 years, presence of comorbidities, low educa-

Table I. Prevalence (%) of obesity (BMI ≥30) according to sex and OA localisation (GOA = generalised OA).

Sex	Hand OA	Hip OA	Knee OA	GOA
Men	9.3	15.9	18.6	18.3
Women	9.4	21.3	29.8	24.9

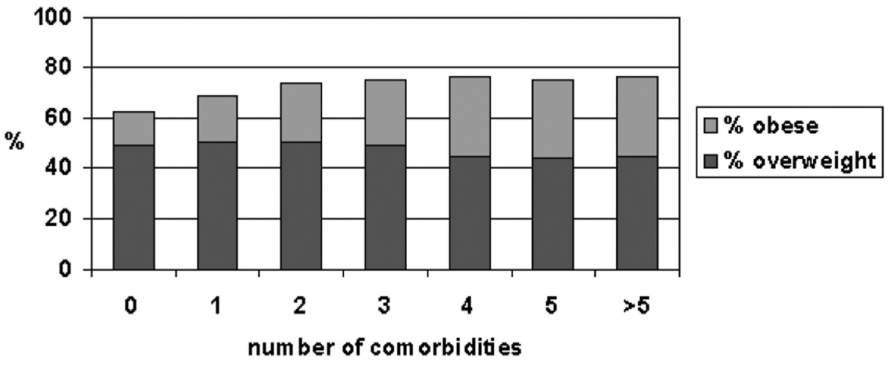

Fig. 2. Percentage of female patients with knee OA who are overweight or obese according to the number of co-morbidities. The correlation between number of co-morbidities and frequence of obesity is significant (p=0.0001).

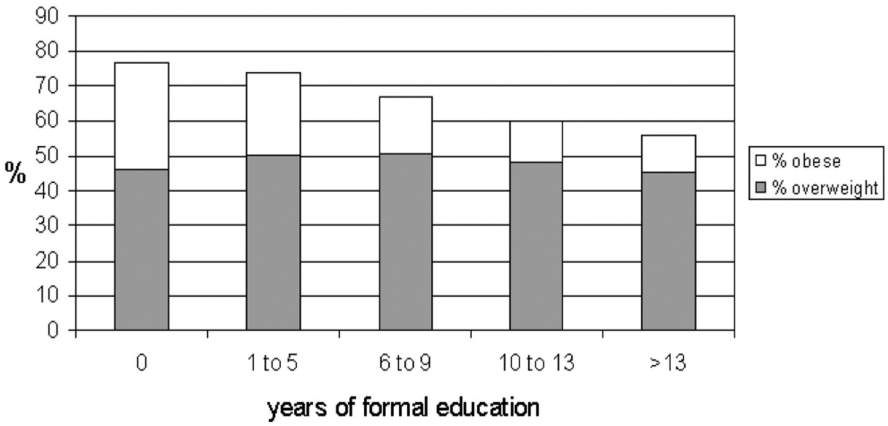

Fig. 3. Prevalence of overweight and obesity in our population of OA patients according to the number of years of formal education (r=-0.16; p<0.0001).

Table II. Distribution of patients with symptomatic OA at different localisations according to their BMI.

BMI		<18.5	18.5-24.9	25-29.9	≥30
Hip OA	Men	2 (0.1)	481 (27.5)	991 (56.7)	275 (15.7)
	Women	3 (0.1)	1017 (32.3)	1474 (46.9)	651 (20.7)
Knee OA	Men	2 (0)	984 (21.8)	2701 (59.9)	819 (18.2)
	Women	9 (0.1)	1720 (22.6)	3627 (47.7)	2243 (29.5)
Hand OA	Men	2 (0.2)	337 (36.2)	507 (54.4)	86 (9.2)
	Women	13 (0.3)	2017 (50.7)	1581 (39.8)	364 (9.2)
Generalised OA	Men	1 (0.1)	342 (25.5)	756 (56.5)	240 (17.9)
	Women	9 (0.2)	1198 (28.7)	1964 (47)	1010 (24.2)
Total	Men	7 (0.1)	2144 (25.2)	4955 (58.1)	1420 (16.7)
	Women	34 (0.2)	5952 (31.5)	8646 (45.8)	4268 (22.6)

tional level, and GOA. The odds ratio of experiencing intense OA pain was 1.68 (95% CI 1.56–1.80) for obese patients, in comparison with patients with BMI less than 25 kg/m^2. The same odds ratio was 1.77 (CI 1.51–2.06) for obese patients with GOA, 1.57 (CI 1.40–1.75) for those with knee OA, 1.48 (CI 1.19–1.85) for those with hand OA, and 1.35 (CI 1.12–1.61) for those with hip OA. Among patients who were overweight, a significantly increased risk of experiencing intense pain was seen in those with GOA (OR 1.21, CI 1.06–1.37) and knee OA (OR 1.18, CI 1.06–1.30). Multiple regression analysis of the odds ratios for the different risk factors showed that all of them significantly contributed to intense pain levels with multiple joint involvement (OR 2.05, CI 1.91–2.19), comorbidities (OR 1.61, CI 1.50–1.73), OA duration (OR 1.60, CI 1.52–1.68), BMI (OR 1.52, CI 1.42–1.61), age (OR 1.46, CI 1.39–1.54), low educational level (OR 1.44, CI 1.36–1.51), and female gender (OR 1.38, CI 1.32–1.48) resulting most significant (p<0.0001). Only generalised OA, presence of comorbidities, and duration of OA longer than 7 years were more closely associated with OA pain than BMI.

The GPs evaluated the patients' pain as absent in 173 (0.7%) patients, mild in 4842 (19.2%), moderate in 12 330 (48.8%), intense in 7241 (28.7%), and very intense in 667 (2.6%). 11.4% of the patients received no pharmacological treatment, 4.3% were treated with steroids, 9.6% with DMOADs, 18% with analgesics, 33.9% with NSAIDs and 56% with Coxibs. Non-pharmacological treatment was prescribed to 56.6% of patients with surgery accounting for 4.1%. Pharmacological and non pharmacological prescriptions of GPs for patients with normal weight, overweight or obesity did not differ. Accordingly, also referral of patients to specialist consultation was not influenced by BMI (data not shown).

Discussion

Most epidemiological studies have considered the association between excess weight and radiological OA and only few studies have investigated the impact of overweight and obesity on OA-associated pain. Joint pain and the associated causative factors have been studied in postmenopausal women (29). BMI was a significantly and strong predictor of joint pain at any location, although the strength of the association varied by OA localisation. Pain in the knee, ankle and shoulder were significantly associated with BMI whereas the association of hip pain was weaker. However, in this study the identification of painful joints was based on the response to a questionnaire, whereas in our accepted clinical criteria for OA were used. Therefore, we feel that our results are particularly relevant for clinical OA.

In another study of patients with knee OA, the variables predicting the severity of pain were determined using three different scales, the WOMAC, the McGill pain questionnaire, and a 0-100 VAS (30). BMI was significantly related to all three. Using the WOMAC, BMI was only associated with pain on walking, climbing stairs, or standing, a finding suggesting a mechanical role in pain production. Our study has considered only the VAS to measure pain because more practical in such a large setting, although we recognise that a number of other instruments could be useful in this type of study (31). We considered not only knee OA, but also hip and hand OA, two conditions in which the role of obesity as determinant of pain severity has been only rarely studied. Our large sample of patients is representative of those seeking medical care because of OA. Although not representative of the general population, this subgroup certainly carries the highest economic impact, at least in terms of direct costs.

Our results confirm that OA patients seeking medical attention for OA are frequently obese. This does not necessarily imply that obesity was a risk factor for OA pain since it could also have been the consequence of a sedentary lifestyle induced by pain itself. Longitudinal studies suggest, however, that increased weight antedates the presentation of knee and hand OA. Manninen *et al*. showed that BMI was directly and strongly correlated with the risk of developing disabling knee OA over a period of 10 years (32). Similar results were obtained for hand OA (33). In our study, there was no association between BMI and OA duration possibly suggesting that patients with OA were overweight also in the early phases of OA, thus confirming the possible causative role of obesity. However, we are aware that this relation should be studied in a prospective follow-up study and not in a cross-sectional design. On the other hand, obesity was clearly an important risk factor for more severe pain in both sexes and for all locations of OA, including the hand.

Overweight and obesity were common in patients with OA at any location, except for the hand. They were more common for knee OA and GOA. Women were more frequently obese whereas men were more frequently overweight. This pattern is commonly observed in the general population. The presence of co-morbidities was associated with obesity with a dose-effect relationship. In particular, OA patients with type-II

diabetes, hypertension, and myocardial infarction had a significantly higher BMI than those without co-morbidities. This fact is not surprising since obesity and overweight are associated with increased incidence of many co-morbidities including type-II diabetes, different types of cancer, cardiovascular diseases, asthma, gallbladder disease, OA, and low back pain (34). Years of formal education were inversely correlated with the frequency of obesity. This finding is common in the general population of all industrialised countries, whereas the opposite is seen in developing countries (35). An interesting finding was that institutionalised patients were less frequently obese or overweight than patients living alone or in the family. This observation can be related to a more healthy diet used in institutions or, alternatively, to the fact that institutionalised patients may suffer from undernutrition because of poorer health conditions and older age. Therapy prescribed by GPs did not differ according to the weight of OA patients. Also the referral pattern was not different in patients with normal or increased weight. This observation may suggest that the peculiar characteristics of obese OA patients, such as the increased amount of pain and the frequently associated comorbidities, are not fully weighted by Italian GPs when therapy is chosen. The difficulties associated with pharmacological treatment of OA patients on the basis only of their pain has been recently discussed (36). The observation of a very high prescription of Coxibs is most probably related to the fact that this class of drugs had been marketed in Italy shortly before this study.

This study suffers from the typical weaknesses of the large multicenter trials. In particular, data were collected by 2,764 GPs, a number that makes standardisation difficult. To reduce variability, however, small seminars were hold by rheumatologists, orthopaedic surgeons, and physical medicine specialists before the beginning of the study to show the correct application of the ACR criteria and to explain and discuss the questionnaire. During the study, the GPs were periodically visited by trained monitors who reinforced the information given in the seminars. We feel that this approach and the very large sample may have diluted the effect of non-differential misclassification.

The clinical definition of OA includes pain, which is also a focus of our research; however, our attention was paid to pain intensity rather than to the presence of pain as dichotomous variable as in other studies (15). Therefore we do not think that a selection bias could have influenced our results.

By including consecutive patients with pain, we might have overestimated its prevalence in OA.

Since OA pain has been demonstrated to be fluctuating (18), the cross-sectional design of the study, common to the major part of those on this topic, may have contributed to misclassify patients with regard on their pain status. Fluctuating OA pain is more likely to occur in milder OA, a fact that would not alter the direction of the relationship, however.

Another possible problem is that performance of the ACR criteria for OA is not well known, especially in epidemiological studies. The risk of misdiagnosing patients with extraarticular painful conditions is always lingering without a gold standard and in consideration of the scarce relationship between clinical and radiological data. This problem is inherent in the criteria and probably less important in a clinical than in a population setting. In addition, lack of a control group and of information on some potential confounding factors, such as history of smoking, physical exercise and trauma, precluded control of these variables in the analysis. Finally, we admit that statistical significance of the differences found in our study should be taken cautiously. In studies involving such a large number of patients, almost every comparison can be significant. We feel, however, that the data presented here are biologically relevant because of the absolute differences and of the dose-effect relationship observed for several risk factors.

In conclusion, our study confirms that more than two thirds of Italian patients with symptomatic OA seen by GPs are overweight or obese. These results could be relevant also for other populations in view of the epidemic of obesity, which is affecting the developed world (37). Obesity is an important risk factor for OA pain, not only for knee OA but in all OA localisations. This finding is probably underestimated by GPs who are not used to modulate treatment and specialist referral according to patients' BMI.

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