Comorbidities in patients with osteoarthritis: frequency and impact on pain and physical function

Alice Abath Leite[1], Aline Jurema Gesteira Costa[1], Beatriz de Arruda Matheos de Lima[1], Adriana Valentina Lopes Padilha[2], Emidio Cavalcanti de Albuquerque[3], Claudia Diniz Lopes Marques[4]

ABSTRACT

Introduction: As the prevalence of osteoarthritis (OA) increases with age, the coexistence of other chronic diseases is common. **Objectives:** To evaluate the frequency of comorbidities in OA patients and to measure their impact on pain and physical function of those patients. **Methods:** Cross-sectional study in OA patients of a public rheumatology clinic. Pain was measured by use of the Visual Analogue Scale (VAS) and physical function by use of the Lequesne's and SACRAH indices. A screening for depression was performed, as were the following measurements: anthropometric data; blood pressure; fasting glycemia; and lipid profile. **Results:** The study assessed 91 patients (mean age 59.3 years; 91.4% female). The metabolic syndrome frequency was 54.9%. Hypertension occurred in 75.8% of the patients, dyslipidemia in 52.6%, and obesity in 57.1%. The screening for depression was positive in 61.3% of patients. When comparing the metabolic syndrome components individually, patients with hypertension had higher SACRAH scores, with statistically significant differences (P = 0.035). For the other variables, no differences among the Lequesne's, SACRAH and VAS scores were observed. **Conclusion:** This group of OA patients showed a high frequency of depression, metabolic syndrome and its components in isolation, which can impact the pain and physical function of those patients. Such results showed the need for investigating and treating those comorbidities in OA patients.

Keywords: osteoarthritis, metabolic syndrome X, depression, chronic disease.

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INTRODUCTION

Osteoarthritis (OA) is considered the most common disorder of the musculoskeletal system and the greatest cause of disability in both developed and the so-called emerging countries.[1] Since the the population is aging, the prevalence of OA has increased, and its consequences have a great socioeconomic impact. Approximately 40% of the adults over the age of 70 years have knee OA, and 80% of those with OA have any type of limitation of movement.[1] Data obtained from the Framingham study place OA at the same level of both cardiovascular diseases and chronic obstructive pulmonary disease as the major cause of chronic physical disability.[2]

Because the prevalence of OA increases with aging, coexistence with other chronic diseases is common, further increasing the impact on the quality of life of those patients. The major comorbidities of OA patients are systemic arterial hypertension (SAH), cardiovascular disease, diabetes, and dyslipidemia.[3,4] Metabolic syndrome, defined as the association of SAH, central obesity, glucose intolerance, and

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Instituto de Medicina Integral Professor Fernando Figueira – IMIP, Recife, PE, Brazil.
1. Scientific Initiation scholarship from IMIP/CNPq – Medical student of the Faculdade Pernambucana de Medicina – FPS
2. MSc candidate in Internal Medicine of the Universidade Federal de Pernambuco (UFPE); Cardiologist, Tutor at the Ambulatório de Ensino de Clínica Médica of the FPS
3. Statistician; MSc in Public Health at the Centro de Pesquisas Aggeu Magalhães – Fiocruz
4. PhD at the Centro de Pesquisas Aggeu Magalhães – Fiocruz; MCs in Internal Medicine at the UFPE; Tutor at the FPS
Correspondence to: Claudia Diniz Lopes Marques. Rua dos Coelhos, 300, Boa Vista. Recife, PE, Brazil. Zip Code: 50070-550.
E-mail: claudia_reumatologia@terra.com.br.

hypertriglyceridemia or low HDL levels (at least three of the five criteria) in the same individual,[5] also occurs at a high frequency in OA patients.[6] Despite the clear relation between OA development and the trauma resulting from excessive weight, the occurrence of OA in joints that do not bear load suggest that the chronic inflammation status existing in patients with metabolic syndrome can alter the metabolism of cartilage, regardless of excessive weight.[7] In addition, glucose intolerance can also collaborate to maintain that persistent inflammation status in obese individuals with metabolic syndrome.[8]

As OA is the major cause of pain in elderly patients, a population with a very high prevalence of depression, the coexistence of both diseases is frequent. The impact of depression on OA is significant, since it influences the two major joint symptoms: pain and physical disability. Depressed individuals are more likely to report chronic or more severe pain, and more than half of the patients with chronic pain are depressed.[9]

The presence of diabetes, heart disease or even visual alterations are not only more frequent in OA patients, but also lead to a greater impairment of physical functions and quality of life, in addition to worsening the prognosis of arthroplasties.[10,11]

Although OA is the disease that most commonly causes physical disability, the real extension of the impact of its combination with other chronic diseases on physical function has not yet been assessed among us. A study in England has concluded that the presence of comorbidities increases the frequency of physical disability in OA patients, and the influence of the combination is higher than that expected for OA alone or for each disease in isolation. The treatment of such comorbidities in OA patients would, thus, be crucial to reduce the impact on physical disability, and, consequently, enhance the quality of life of those individuals.[11]

This study aimed at assessing the frequency of the association of chronic degenerative diseases in patients diagnosed with OA, as well as the impact of such associations on the physical function of those patients, measured by use of the Lequesne's algofunctional and SACRAH indices, both validated for the Portuguese language.[12,13]

METHODS

This was a cross-sectional study including patients with OA of the hands, knees, and hips, being followed up at the outpatient clinic of rheumatology of the Fundação Professor Martiniano Fernandes, Instituto de Medicina Integral Professor Fernando Figueira (IMIP), from August 2008 to May 2009.

Patients underwent their regular consultation in the outpatient clinic of rheumatology, and, those diagnosed with OA according to the criteria of the American College of Rheumatology[14-16] were invited to participate in the study. Once accepted the invitation, the written informed consent was read and signed, and an interview followed.

The interview comprised the application of a questionnaire specifically developed for the study, with information about the disease duration, life habits (smoking), previous history of SAH, *diabetes mellitus*, obesity, dyslipidemia, and depression, in addition to site of OA and pain severity, by use of a 100-mm visual analogue scale (VAS). If the patient was being treated for SAH, *diabetes mellitus*, and dyslipidemia, those data were computed as positive in the final analysis, even if during the interview blood pressure was normal or the laboratory tests showed no alterations.

The following were also applied: the Lequesne's algofunctional index for knees and hip validated for the Portuguese language;[12] SACRAH validated for the Portuguese language;[13] and the Goldberg depression questionnaire.[17] When patients had at least three depressive symptoms of the Goldberg scale, the ICD-10[18] diagnostic criteria for major depression were applied. For analysis, the cutoff points of the Lequesne's index used were as follows: score from 8 to 10 means severe OA; from 11 to 13, very severe; and equal to or greater than 14, extremely severe. For patients with OA affecting more than one joint, the questionnaire was directed to the most painful or disabling joint. Then, physical examination was performed, and included the following measurements: blood pressure (BP) on two occasions at a 5-minute interval; abdominal circumference (AC); weight; and height. At the end of the consultation, the following complementary tests were carried out at the IMIP: fasting glycemia; and lipid profile, comprising LDL, HDL, triglycerides and total cholesterol.

Patients returned 21 days after the first interview, and BP was once again measured following the same technique of the first contact; if BP remained altered, the patients were then classified as hypertensive. After assessing the results of the laboratory tests, at the same consultation, patients were classified as either having or not having the following: *diabetes mellitus*,[19] SAH,[20] obesity,[21] dyslipidemia,[22] and metabolic syndrome.[5] Classification was based on the specific criteria used in clinical practice, even in the absence of positive previous history for each condition.

Data were stored in the Excel 2000 software and analyzed by use of the SPSS statistical program, version 13.0, with 95% significance. For comparing quantitative variables, Student's *t* test or Mann-Whitney test were used in case of

normal distribution. For categorical variables, the chi-square and Fisher's exact tests were used to identify the statistically significant associations.

The study was approved by the Committee on Ethics and Research of the IMIP, and all participants provided written informed consent.

RESULTS

The study included 93 patients as follows: 67 with knee OA; 24 with hand OA; and two with hip OA. To make the sample more homogeneous, we chose to exclude the two patients with hip OA. Thus, the final sample comprised 91 patients [83 (91.2%) of the female sex; mean age, 59.3 years (38-85 years)]. Table 1 shows the demographic data, frequency of anterior diseases, most frequent OA sites, and frequencies of SAH, *diabetes mellitus*, dyslipidemia, obesity, metabolic syndrome, and depression identified in this study.

We observed a higher frequency of SAH, dyslipidemia, and depressive symptoms than that initially reported by the patients. For example, only 25% of the patients reported a previous history of depression, and, when applying the Goldberg questionnaire, 56% screened positive for depression (P = 0.003). Regarding SAH, 63% of the patients reported a previous history, but during physical examination, SAH was identified in 75.8% of the patients (P = 0.000). Of the 52.6% patients diagnosed with dyslipidemia, only 33.9% reported the disease previously (P = 0.065). The same was not observed with *diabetes mellitus*, because all patients identified as diabetic in the study reported previous history of that disease.

The frequency of metabolic syndrome was 54.9% in that group of patients and distributed as follows: 82% in knee OA and 18% in hand OA. No statistically significant difference was observed between groups (P = 0.078). Individually, 61.2% of the patients with knee OA had metabolic syndrome.

When comparing individually the components of metabolic syndrome (SAH, dyslipidemia, obesity, increased abdominal circumference, *diabetes mellitus*), patients with SAH showed higher SACRAH scores, with a statistically significant difference (P = 0.035). Regarding the other variables, no statistically significant difference was observed among the VAS, Lequesne's, and SACRAH scores.

Statistically significant differences were observed for the pain scale (VAS) and SACRAH questionnaire in patients who screened positive for depression as compared with patients who screened negative (P = 0.006 and 0.000, respectively). The same has not occurred with the Lequesne's index, although its mean was greater in the group with depressive symptoms.

Table 1
Frequency of the variables studied in OA patients cared for at the IMIP – August 2008 to May 2009

Variables	n	%
Age (years)		
38-50	11	12.1
51-70	65	71.4
> 70	15	16.5
Sex		
Male	8	8.8
Female	83	91.2
OA site		
Knees	67	73.6
Hands	24	26.4
Personal data		
Smoking habit	15	16.5
DM	16	17.6
SAH	63	69.2
Dyslipidemia	32	35.2
Obesity	49	53.8
Depression	25	27.5
Blood pressure		
Stage 1 SAH	23	25.3
Stage 2 SAH	27	29.6
Stage 3 SAH	19	20.9
Normal	22	24.2
Comorbidities identified in the study		
DM	16	17.6
Dyslipidemia	38	41.8
Obesity	52	57.1
Metabolic syndrome	50	54.9
Positive screening for depression	56	61.5

DM: *diabetes mellitus*; SAH: systemic arterial hypertension; BMI: body mass index.

Table 2 shows the means and standard deviations of the VAS, Lequesne's and SACRAH scores in OA patients with and without each of the comorbidities studied.

DISCUSSION

Our results showed a high frequency of comorbidities, such as metabolic syndrome, SAH, dyslipidemia, obesity, diabetes, and depression, in the OA patients cared for at the outpatient clinic of rheumatology of the IMIP. With the increase in the life expectancy of the population, the coexistence of chronic and

Table 2
Mean and standard deviation of the physical function and pain scales in OA patients cared for at the IMIP – August 2008 to May 2009, according to the presence or absence of comorbidities

SAH			
	Yes (Mean)	No (Mean)	P value
VAS (cm)	7.7	7.55	0.825**
Lequesne	12.44	10.92	0.374*
SACRAH	6.24	3.95	0.035*
Diabetes mellitus			
	Yes (Mean)	No (Mean)	P value
VAS (cm)	8.19	7.55	0.325**
Lequesne	12.73	12.00	0.670*
SACRAH	6.17	5.31	0.607*
Dyslipidemia			
	Yes (Mean)	No (Mean)	P value
VAS (cm)	8.00	7.42	0.475**
Lequesne	12.74	11.76	0.520*
SACRAH	5.34	5.45	0.923*
Metabolic syndrome			
	Yes (Mean)	No (Mean)	P value
VAS (cm)	7.9 ± 2.603	7.4 ± 2.607	0.307**
Lequesne	12.0 ± 5.828	12.4 ± 4.980	0.758*
SACRAH	5.8 ± 2.340	5.2 ± 2.884	0.599*
BMI			
	Normal (Mean)	Overweight (Mean)	Obesity (Mean)	P value
VAS (cm)	6.46	7.15	8.21	0.239#
Lequesne	8.30	11.20	12.98	0.130*
SACRAH	4.89	4.86	6.75	0.224*
Positive screening for depression			
	Yes (Mean)	No (Mean)	P value
VAS (cm)	8.3 ± 1.929	6.6 ± 3.146	0.006**
Lequesne	13.1 ± 5.652	10.8 ± 4.993	0.092*
SACRAH	6.7 ± 1.752	2.6 ± 1.963	< 0.001*

BMI: body mass index. Significance: 95% ($P < 0.05$); *Student *t*; **Mann-Whitney; #Kruskal-Wally.

degenerative diseases is becoming more and more frequent, increasing the impact on the health and quality of life of the population.

Possible explications for the relation between OA and those comorbidities include shared etiology and physiopathology or the result of the aging biological process, in which different events occur more frequently (cartilage degeneration, increased insulin resistance, weight gain, dyslipidemia), and, thus, can appear simultaneously, even if not interrelated.[23] Perhaps, more important than identifying the cause leading to the simultaneity of those diseases is defining to what extent they can influence the health status of OA patients. Previous studies have shown that comorbidities, such as visual disorders, diabetes, and cardiovascular disease not only occur more frequently than expected in OA patients,[23] but also result in greater physical function impairment[10] and adverse results for patients undergoing arthroplasty.[24]

To the extent of our knowledge, in Brazil, there are no previous studies on the frequency of the comorbidities in OA patients. For the sake of comparison, we looked for studies assessing the presence of those comorbidities in individuals without OA and observed that the frequency in our sample was higher than that found in patients without the disease.[25-7]

The estimated prevalence of SAH in the Brazilian population is approximately 30%.[25] Sighn *et al*.,[4] in the United States, in a study interviewing 115.9 million people, reported a 21% frequency of OA patients, of whom 40% had SAH, whose frequency in the general North-American population is 25%. In our sample, the frequency of SAH was much higher, reaching 75.8%, for all hypertension classes. That discrepancy can be explained by the cultural differences of our population that resists adhering to treatment, in addition to the difficulties in having access to appropriate follow-up and medication, which is often not made available for free in the public health system. In addition, of the OA therapeutic options, undoubtedly non-steroidal anti-inflammatory drugs (NSAIDs) are the most commonly used. They are known to be able to cause elevations in blood pressure levels, mainly in patients treated with angiotensin-converting enzyme (ACE) inhibitors and beta-blockers.[28]

Clinical and epidemiological studies have shown the coexistence of obesity and hand and knee OA. Several clinical conditions associated with obesity and sedentary lifestyle, such as SAH and type II *diabetes mellitus*, are also frequently found in OA patients. The presence of OA is significantly increased in overweight individuals and can be associated with the trauma caused by the body mass excess on joints that bear load, such as the hips and knees.[29] However, the increased OA frequency in joints that do not bear load has suggested that a component of the overweight syndrome can alter the metabolism of cartilage and subchondral bone, regardless of the load.[7] Rojas-Rodriguez *et al*.[8] have studied the role of the pathogenesis of obesity in inducing OA. The metabolic alterations in the striated muscle induced by the interaction of insulin resistance and systemic inflammation in obese individuals with metabolic syndrome would lead to OA as a final consequence. In England, Kadam *et al*.[11] have concluded that the non-musculoskeletal

comorbidity most commonly associated with OA is obesity. In our sample, the minority of patients had adequate weight, and the association of OA and *diabetes mellitus* was also high.

In our study, the percentage of patients with dyslipidemia was 40.9%, also higher than those reported in studies performed in other countries, emphasizing the importance of assessing the components of the metabolic syndrome in patients with OA. Singh *et al*.[4] have reported a 32% prevalence of dyslipidemia in OA patients when assessing only total cholesterol. Another study in Germany has concluded that high serum levels of cholesterol are independent systemic risk factors for OA.[30]

Individuals with persistent pain have a greater tendency to have disorders such as anxiety and depression (classified according to the CID-10 criteria) than individuals without pain.[30] Kadam *et al*.[11] have reported an association between depression and OA, confirmed in our study, showing a high frequency of patients reporting being diagnosed with depression, and an even greater number of patients meeting the criteria for depressive symptoms.

Regarding the impact of the coexistence of those diseases on OA patients, we observed that SAH and the depressive symptoms lead to greater pain perception in patients with hand OA. In addition, patients screening positive for depression had a more impaired hand function, with a statistically significant difference.

Despite the lack of statistically significant difference between the other variables studied regarding the functional tests (Lequesne's and SACRAH) and VAS, a tendency towards a worse score is observed in the group with each of the diseases, as shown in Table 2.

Kadam and Croft,[11] in a study with OA patients over the age of 50 years in England, have shown that the presence of comorbidities increases the possibility of physical function impairment, and that the influence of their combination is higher than that expected for OA or comorbidities isolated.

CONCLUSION

The frequency of comorbidities in OA patients is very high, mainly SAH, *diabetes mellitus*, obesity, dyslipidemia, metabolic syndrome, and depression. The recognition of such associations by the internist and rheumatologist is extremely important. Those associations can jeopardize the result of the OA treatment due to the interaction of such comorbidities with the chronic pain symptomatology. In addition, OA therapy can cause complications and aggravation of those diseases. The routine follow-up of OA patients should include periodic measurements of BP, lipid profile, and fasting glycemia, in addition to instructions about weight control and identification of depressive symptoms, which can be easily obtained by applying the Goldberg scale. The adequate control of each of those situations and referral to a specialist can help with the OA treatment and improve the quality of life of our patients.