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# Association between Knee Osteoarthritis and Metabolic Syndrome in Non-Institutionalized Elderly Patients*

## *Associação entre osteoartrite de joelho e síndrome metabólica em pacientes idosos não institucionalizados*

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## Abstract

**Objective** This study aimed to analyze the association between knee osteoarthritis (OA) and metabolic syndrome (MS) in non-institutionalized elderly patients.

**Methods** A cross-sectional, randomized study, drawn from a probabilistic cluster study conducted with 416 elderly people from a Family Health Unit (USF, in the Portuguese acronym) of our municipality. Metabolic syndrome was defined according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III), and OA according to the Kellgren-Lawrence (KL) scale ($\geq 2$).

**Results** For the statistical analysis, we performed an exploratory data analysis, Mann-Whitney or Chi-Squared tests and univariate and multivariate logistic regressions, with significance level of $p < 0.05$; the concordance between the evaluators was verified through the Kappa coefficient. There was an association between OA and body mass index (BMI) ($p = 0.0021$) and between OA and waist circumference (WC) ($p < 0.001$; odds ratio [OR] = 3.524). There was no significant association between OA and the number of metabolic components nor with SM itself.

**Conclusion** We conclude that knee OA is associated with WC, regardless of weight, and that the increase in its measure reflects a greater chance of MS in non-institutionalized elderly patients.

**Keywords**
- osteoarthritis
- metabolic syndrome
- obesity
- aging
- health promotion

## Resumo

**Objetivo** Este estudo teve o objetivo de analisar a associação entre a osteoartrite (OA) de joelho e a síndrome metabólica (SM) em pacientes idosos não institucionalizados.

**Métodos** Pesquisa transversal, aleatorizada, extraída de um estudo probabilístico por conglomerado realizado com 416 idosos de uma Unidade de Saúde da Família do nosso município. A SM foi definida de acordo com o *National Cholesterol Education Program*

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*Adult Treatment Panel III* (NCEP-ATP III), e a OA de acordo com a escala Kellgren-Lawrence (KL) ($\geq 2$).

**Resultados** Para a análise estatística, foi realizada uma análise exploratória de dados, testes de Mann-Whitney ou Qui-quadrado e regressões logísticas uni e multivariadas, com nível de significância de $p < 0,05$; a concordância entre os avaliadores foi verificada através do coeficiente de Kappa. Verificou-se associação entre OA e índice de massa corpórea (IMC) ($p = 0,0021$) e entre OA e circunferência de cintura (CC) ($p < 0,001$; razão de chances [RC] = 3,524). Não foi encontrada associação significativa entre a OA e o número de componentes metabólicos nem com a SM em si.

**Conclusão** Conclui-se que a OA de joelho associa-se à CC, independente do peso, e que o aumento em sua medida reflete em uma maior chance de SM em idosos não institucionalizados.

**Palavras-chave**
- osteoartrite
- síndrome metabólica
- obesidade
- envelhecimento
- promoção da saúde

## Introduction

The increase in fat intake and sedentarism is evident in the modern world.[1] Both have a direct influence on the increasing prevalence of obesity, dyslipidemia, hypercholesterolemia and a clinical condition currently known as insulin resistance syndrome or "metabolic syndrome" (MS).[2]

The study of MS has been hampered by the absence of a consensus in its definition and in the cutoff points of its components. The World Health Organization (WHO)[3] suggested a definition based on clinical and laboratory data with starting point in the evaluation of insulin resistance or glucose metabolism disorder. In 2001, the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III)[4] proposed a number of similar criteria that are simple to assess, which include: glucose fasting, systolic blood pressure (SBP), waist circumference (WC), triglycerides and high-density lipoprotein (HDL), facilitating clinical use. Other definitions have also emerged, such as those of the American Association of Clinical Endocrinologists (AACE)[5] and the European Group for the Study of Insulin Resistance (EGIR),[6] but the WHO and the NCEP are the most used.

metabolic syndrome is a complex disorder represented by a set of cardiovascular risk factors, usually related to central fat deposition and insulin resistance, and its importance should be highlighted from an epidemiological point of view, since it is responsible for increased cardiovascular mortality estimated at 2.5 times.[7] In addition, recent research has pointed out that these metabolic alterations may also influence the increase in the incidence and progression of OA.[2,8,9]

In this sense, the literature highlights that the possible pathogenic mechanisms in common between osteoarticular and metabolic diseases are low-grade inflammation related to the tissue and oxidative stress.[10–13] Some researchers point out that these mechanisms seem to have direct systemic effects on the joint and could damage cartilage, bone, and synovial tissue, regardless of the excess weight.[14–16]

Such damages, arising from OA, affect millions of people and present as main characteristics pain, joint stiffness, and decline in functionality, such as impairment in performance of daily living activities (DLA).[17] The research also highlights that its incidence increases with the advancement of age, particularly in individuals above 60 years old.[9,14–17]

Considering the changes in body composition during the aging process and the importance of OA as a factor of functional impairment and of MS as a risk factor for cardiovascular disease, the present study aimed to analyze the association between knee OA and MS in non-institutionalized elderly patients. And, considering the scarcity of studies of this nature, especially with this population, this research is necessary even to direct future public health policies for the elderly.

## Methodology

This is a randomized, cross-sectional research, extracted from a probabilistic study by conglomerate, entitled "Comparative Analysis of the Epidemiological Profile of Elderly in a Community: a Cohort Study".

The sample was randomly drawn through a sample size calculation of 416 individuals between the 820 registered in the Family Health Unit (USF, in the Portuguese acronym) of Jardim Camanducaia /Amparo, SP. Subjects born up to the year 1948, residents of Amparo, registered in the corresponding USF and who signed the informed consent form were included. Elderly individuals with severe physical and/or cognitive impairments (described in the medical records) and those who did not complete the stages of the study were excluded; 56.25% of the subjects did not complete all the steps, so the final sample comprised 182 elderly patients.

First, we applied a questionnaire on sociodemographic information, anthropometric data, and health conditions. Subsequently, an X-ray of anteroposterior incidence was performed on both knees, and, finally, blood samples were collected for laboratory analysis of fasting glycemia and lipid profile—all individuals were instructed to fast for 12 hours before collection.

The diagnosis for OA considered the Kellgren-Lawrence ($KL \geq 2$)[18] scale, and the diagnosis of MS adopted the NCEP criteria,[4] which determines the presence of at least 3 of the 5 factors (or use of medication): abdominal obesity (waist circumference [WC] > 102 cm and 88 cm for men and women

**Table 1** Classification of the elderly according to gender, age, and body mass index

| Variables | N[a] | % | Mean ± SD[b] |
|---|---|---|---|
| Gender | | | |
| Female | 104 | 57.1 | |
| Male | 78 | 42.9 | |
| Total | 182 | 100.0 | |
| Age | 182 | | 73.0 ± 5.6 |
| BMI (kg/cm$^2$) | 182 | | 27.9 ± 4.8 |

Abbreviations: BMI, body mass index; SD, standard deviation.
[a]number of subjects.
[b]standard deviation.

respectively ) or central (body mass index [BMI] > 30kg/m2), hypertriglyceridemia (> 150 mg/dL), low levels of HDL cholesterol (< 35 mg/dl and 45 mg/dl for men and women respectively), systemic arterial hypertension (> 130 × 85 mmHg), and blood glucose fasting (> 100 mg/DL.).

Fieldwork was carried out between the years 2013 and 2014, by 3 researchers trained by a main researcher. The radiographic examination was performed in a city clinic, the blood samples were collected at the USF and analyzed by the municipal laboratory.

An exploratory data analysis was performed by means of summary measures (mean, standard deviation, minimum, median, maximum, frequency, and percentage). The concordance between the evaluators was verified through the Kappa coefficient. The comparison between the groups with and without OA was performed using the Mann-Whitney or Chi-squared test, and the influence of the MS components in OA was evaluated by logistic regression; in the multiple model, the criterion of variables used was stepwise. The significance level adopted was 5%.

The research protocol was approved by the research ethics committee of our institution under the number no. 387,026.

## Results

►**Table 1** shows a higher proportion of female elderly subjects(57.1%), with a mean age of 73.0 ± 5.6 years old and mean BMI of 27.9 ± 4.8 kg/m$^2$.

►**Figure 1** shows the proportion of elderly patients diagnosed or not with MS and ►**Figure 2** presents the proportion of the elderly in relation to the number of metabolic components accumulated in the presence or absence of OA. There was no significant association between OA and the accumulation of components ($p = 0.6320$), but most subjects with OA presented 2 to 4 components.

►**Table 2** shows the association of OA with age, gender and the components of MS, and the agreement between evaluators for OA diagnosis was substantial for both knees (right Kappa coefficient = 0.7459 and left = 0.7527). A relationship between OA and WC ($p$-value < 0.0001) was found.

►**Table 3** shows the association between presence or absence of MS with the presence or absence of OA. There was no significant association ($p > 0.05$).

►**Table 4** shows the influence of MS on OA. There was a significant association between WC and OA ($p < 0.0001$). And, through multiple analysis, it was evidenced that the increase of 1 centimeter in WC increases by 3.5 times the chance of OA (OR = 3.524; 95%CI = 1.794–6.921).

## Discussion

The present study evaluated the association between knee OA and MS in the elderly patients of the community, and the main results show radiographic association between OA knee with increase of WC. The subjects with OA also had the highest ages, higher BMI levels, higher WC measurements, higher values of systemic arterial hypertension (SAH) and higher triglyceride levels.

The first major study responsible for investigating this association (OA x MS) was performed in 2007, by Schett et al.[16] The researchers followed 927 men and women aged

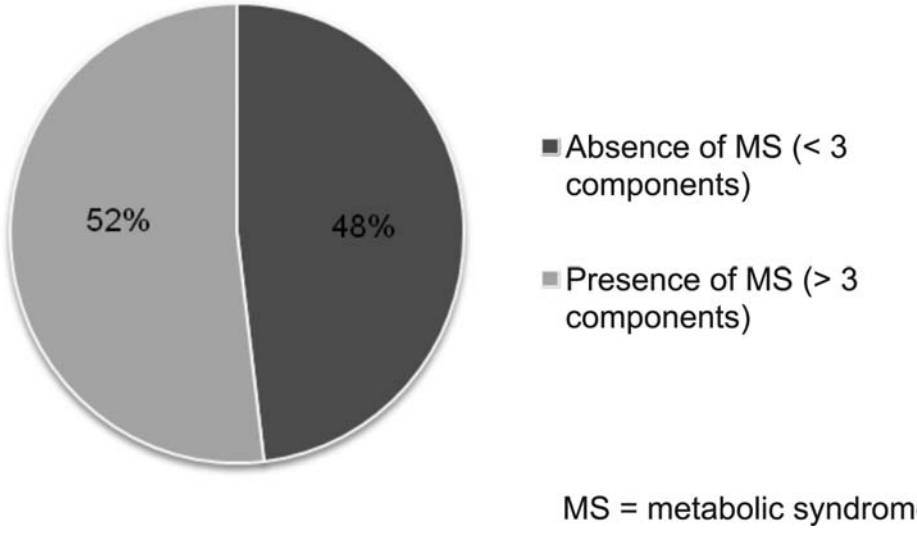


**Fig. 1** Proportion of elderly diagnosed or not with metabolic syndrome according to the National Cholesterol Education Program Adult Treatment Panel III.

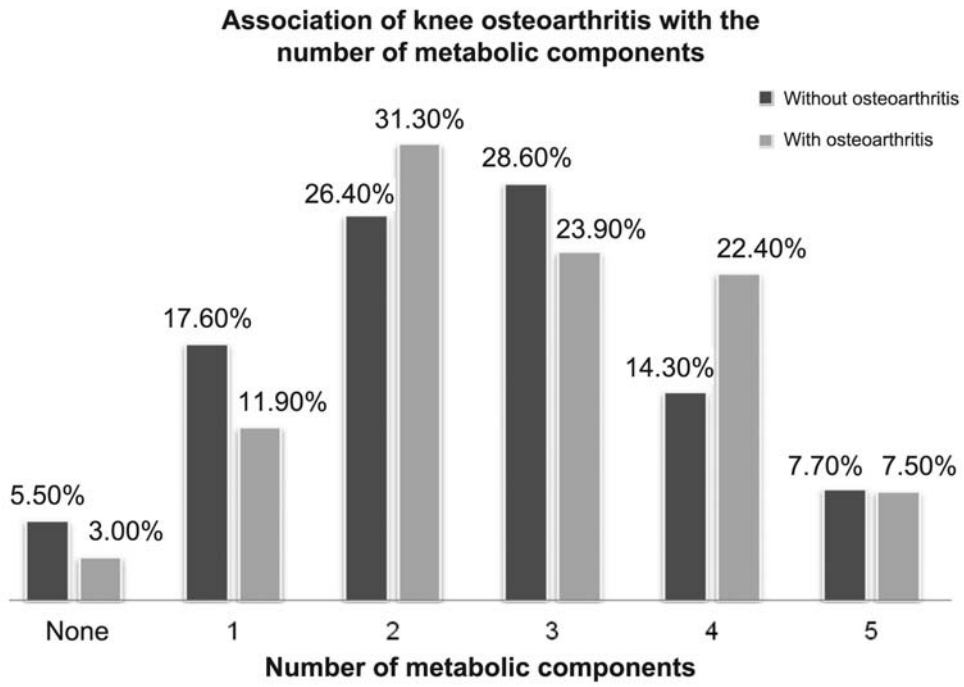


**Fig. 2** Association of knee osteoarthritis with the number of metabolic components in the elderly.

between 40 and 80 years for more than 20 years. The results showed knee or hip arthroplasty rates resulting from OA two times higher in patients with type 2 diabetes mellitus (DM), a correlation between the risk of arthroplasty and the duration of diabetes and higher levels of synovial inflammation and pain in diabetics. These data reinforced the hypothesis of the influence of metabolic components on the pathogenesis of OA.

Following the same path, Dahaghin et al[19] found a two-fold higher rate of hand OA in diabetic patients compared to non-diabetic patients, evidencing that the pathogenesis of OA is independent of weight and overload.

Although DM and OA have not shown a statistically significant association in the present study, other authors observed that DM was a predictor of reduction of articular space in men with established OA knee[20] and greater joint degradation in diabetic subjects.[21] In addition, an experimental model[22] demonstrated that diabetic rats had a higher blood glucose level, decreased collagen fibers and proteoglycans in the ligaments and articular cartilage, and increased collagen in the synovial tissue compared with control rats, evidencing the influence of DM on structural remodeling.

Under normal conditions, the human synovial fluid contains low cholesterol concentrations compared to plasmatic levels;[23] however, in the presence of inflammation these values show high levels. Animal models[24] have shown associations between fat-rich diets with increased production of proinflammatory cytokines in the synovial fluid, formation of osteophytes and degradation of articular cartilage, regardless of body weight; and that the decrease in cholesterol levels could minimize these effects.

However, although some authors report a positive link between hypercholesterolaemia[25–27] and OA, the present study, as well as that of Eymard et al,[20] showed a non-significant correlation.

In relation to SAH, recent researches[13,25–27] indicate high levels of SAH in subjects with OA, such as the study conducted by Jungmann et al.[21] In this study, the authors found, in a sample of 1,000 patients with hip OA, a prevalence rate of SAH and/or cardiovascular disease (CVD) of 55%.

This relationship between SAH and joint wear can be explained by the fact that cartilage is an avascular tissue. Therefore, the impairment in blood flow interferes negatively in the exchanges between nutrients and oxygen causing greater cartilage degeneration.[11]

For Redon et al,[12] the prevalence rate of SAH was significantly higher in patients with MS. The author also found that in hypertensive subjects the risk of developing MS was higher when compared with the population without blood pressure elevation. In another study with almost 1,400 hypertensive patients,[13] 50% of them presented impaired glucose metabolism and associated MS, in addition to significantly higher cardiovascular risk.

The present study found similar prevalence results to the literature, since in the OA group, 86.8% of the elderly presented SAH. Although this association has already been reported by some authors,[21,28] SAH and OA were not significantly associated in this study. Yasuda et al,[25] in turn, found an association between SAH and the symptomatology of OA, but not with its severity and radiological progression.

The literature also emphasizes the association of WC with OA. Maddah et al[26] evaluated the association between OA and MS and found a significant association between WC and OA risk. For Eymard et al[20] and Shin,[29] this connection represented an increase in the severity of symptoms, and, for Jungmann et al,[21] Han et al,[27] and Niu et al,[28] it translated

**Table 2** Association of knee osteoarthritis with age, gender, and the metabolic components in elderly

| | Knee Osteoarthritis | | | |
|---|---|---|---|---|
| **Variable** | **No OA** | **With OA** | **Total** | ***P*-value** |
| Age (mean ± SD)<br>Total | 72.3 ± 5.6<br>106 | 73.9 ± 5.5<br>76 | 73.0 ± 5.6<br>182 | 0.0571[a] |
| Gender | | | | 0.6332[b] |
| Female | 59 (55.7%) | 45 (59.2%) | 104 (57.1%) | |
| Male | 47 (44.3%) | 31 (40.8%) | 78 (42.9%) | |
| Total | 106 | 76 | 182 | |
| **Waist circumference** | | | | **< 0.0001**[b] |
| **Within the boundary** | **61 (58.0%)** | **21 (27.0%)** | **82 (45.0%)** | |
| **Out of bounds** | **45 (42.0%)** | **55 (73.0%)** | **100 (55.0%)** | |
| **Total** | **106** | **76** | **182** | |
| Blood pressure | | | | 0.4808[b] |
| Within the boundary | 18 (17.0%) | 10 (13.2%) | 28 (15.4%) | |
| Out of bounds | 88 (83.0%) | 66 (86.8%) | 154 (84.6%) | |
| Total | 106 | 76 | 182 | |
| Triglycerides | | | | 0.8274[b] |
| Within the boundary | 51 (49.0%) | 39 (50.7%) | 90 (49.4%) | |
| Out of bounds | 55 (51.0%) | 37 (49.3%) | 92 (50.6%) | |
| Total | 106 | 76 | 182 | |
| HDL—cholesterol | | | | 0.8881[b] |
| Within the boundary | 71 (67.7%) | 51 (66.7%) | 122 (67.0%) | |
| Out of bounds | 35 (32.3%) | 25 (33.3%) | 60 (33.0%) | |
| Total | 106 | 76 | 182 | |
| Fasting glycemia | | | | 0.0937[b] |
| Within the boundary | 61 (57.5%) | 53 (69.7%) | 114 (62.6%) | |
| Out of bounds | 45 (42.5%) | 23 (30.3%) | 68 (37.4%) | |
| Total | 106 | 76 | 182 | |

Abbreviations: HDL, high-density lipoproteins; N, number of subjects; OA, osteoarthritis; SD, standard deviation.
[a]Mann-Whitney test.
[b]Chi-square test.

**Table 3** Association between knee osteoarthritis and metabolic syndrome in elderly

| Knee osteoarthritis | | | |
|---|---|---|---|
| **Metabolic syndrome** | **No OA** | **With OA** | ***P*-value** |
| Absence MS<br>(< 3 components) | 49.5% | 46.3% | 0.6924[a] |
| Presence MS<br>(3 components) | 50.5% | 53.7% | |

Abbreviation: MS, Metabolic syndrome; OA, osteoarthritis.
[a]Chi-square test.

an increase in the incidence of radiographic OA. similarly to the aforementioned literature, this research found an association between increased WC and increased chance of OA.

For Niu[28] and Shin,[29] the accumulation of metabolic components represented a higher incidence of OA, but, contradicting these findings, the present study did not find a significant association between them.

In this research, interestingly, among the elderly with OA, only 7.5% had all the 5 components of MS. This low prevalence of subjects with higher metabolic impairment can be explained by the association between age, multimorbidity and functional impairment.[30,31] These associated factors elevate the symptomatology of OA and in this case, they seem to have made the participants' way to the exam collection site more difficult.[25,29]

And, although the involvement of metabolic factors in the etiology of OA is supported by both epidemiological studies as for experimental data, some authors did not find a significant association between OA and MS,[20,25] such as in the present research. In contrast, Jungmann et al[21] reported that OA increased the probability of MS in women and Han et al[27] and Shin[29] observed that MS increased the probability of OA. However, this correlation has not remained

**Table 4** Odds ratio of the influence of metabolic components on knee osteoarthritis in the elderly

| Simple analysis (univariate) | | | |
|---|---|---|---|
| **Factor** | **OR** | **95%CI (OR)** | ***P*-value** |
| **Waist circumference** | **3.729** | **1.949 7.133** | **< 0.0001** |
| Blood pressure | 1.350 | 0.585 3.116 | 0.4819 |
| Triglycerides | 0.935 | 0.510 1.714 | 0.8275 |
| HDL— cholesterol | 1.048 | 0.543 2.025 | 0.8880 |
| Fasting glycemia | 0.588 | 0.316 1.097 | 0.0950 |
| **Multiple analysis (multivariate)** | | | |
| **Factor** | **OR** | **IC95% (OR)** | ***P*-value** |
| Waist circumference | 3.524 | 1.794 6.921 | 0.0003 |

Abbreviations: CI, confidence interval; HDL, high-density lipoproteins; OR, odds ratio.

significant in most studies after adjustments of confounding factors,[27–29] such as weight and BMI.

The discrepancies in the results may result from the sample differences—different ethnicities and mean age, and lack of standardization of diagnostic criteria for OA and MS.

Among the limitations of the study, we highlight: sample comprised of individuals from a single region of a municipality, which does not imply population generalizations; non-consideration of sociodemographic data; non-consideration of the actual values of each component of MS—being detached only if the component was or was not altered; displacement of subjects—may have excluded subjects with greater impairments; and transversality of the study—prevents the evaluation of direct causal relationships between the variables the studied.

Although no relationship was found between MS and knee OA, similar researches are required, mainly longitudinal, in other Brazilian municipalities, both with the elderly in the community as well as with institutionalized elderly, so that there could be a follow-up beyond the evolution of diseases, the level of functionality of the elderly, and the implications of these variables in the health of the elderly. Investigations on the actions and influences of the metabolic pathways in the pathogenesis of OA could also open up a new therapeutic avenue and assist in the health promotion of this population.

## Conclusion

It is concluded that although MS does not significantly associate with knee OA, the measurement of WC above the limits established by WHO is associated with a higher chance of knee OA and increases the chance of MS in non-institutionalized elderly patients.

### Conflict of Interests

The authors have no conflict of interests to declare.

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