Magna Scientia Advanced Research and Reviews

eISSN: 2582-9394

Cross Ref DOI: 10.30574/msarr

Journal homepage: https://magnascientiapub.com/journals/msarr/

(RESEARCH ARTICLE)

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# The association of osteoarthritis with metabolic disorders

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Magna Scientia Advanced Research and Reviews, 2024, 12(01), 110–121

Publication history: Received on 26 August 2024; revised on 02 October 2024; accepted on 05 October 2024

Article DOI: https://doi.org/10.30574/msarr.2024.12.1.0158

## Abstract

Osteoarthritis (OA) is the most common form of synovial joint arthritis that causes chronic pain and disability to a large number of people worldwide. Most often, osteoarthritis affects the joints of the knees, hips, spine and hands. The Global Burden of Disease (GBD, 2021) estimates that osteoarthritis will be the fourth leading cause of disability by 2030, with enormous healthcare costs for treatment, as well as significant indirect costs due to loss of productivity and premature retirement.

The aim of our research is to determine in what way prevalent metabolic syndrome is among participants with osteoarthritis of one of the synovial joints (knees, hips, hands), and whether metabolic disorders are a risk factor for the development and worsening of osteoarthritis.

A prospective clinical study was conducted at the Public Health Institution Health Center Živinice, from July 2022 to May 2024, on a random sample of 200 participants with a confirmed clinical diagnosis of osteoarthritis (OA), who were divided into a group with metabolic syndrome and a group without metabolic syndrome based on the NCEP ATP III panel criteria for metabolic syndrome.

The prevalence of knee osteoarthritis is significantly higher compared to the prevalence of hip and hand osteoarthritis, and it is greater among participants with a higher BMI (in participants with the highest BMI, knee osteoarthritis occurs with a 100% probability) and with the presence of metabolic syndrome, especially in more severe forms, specifically radiologically confirmed osteoarthritis, regardless of age and gender. Unlike OA knees the prevalence of OA hips and hands shows no correlation with BMI and metabolic syndrome. Multiple comparative analysis of differences in the average severity of osteoarthritis of the knee of subjects with normal glycemia / prediabetes / diabetes type *2* it showed a statistically significant difference in the average severity of knee osteoarthritis in subjects with regular blood sugar compared to subjects with prediabetes/diabetes mellitus type 2 regardless of age and gender. This means that with an increase in blood sugar levels, the degree of severity of osteoarthritis of the knee increases, since each subsequent Group has a higher average value of this indicator ($p<0.05$; CI 95%).

**Keywords:** Osteoarthritis; Metabolic syndrome; Body mass index; Diabetes mellitus type 2

## 1. Introduction

Osteoarthritis (OA) is the most common form of synovial joint arthritis that affects all structures of the joint and causes suffering and pain, and disability to a large number of people around the world. Most often, osteoarthritis affects the

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knee joint, followed by the hips, hands and spine. Osteoarthritis usually begins in the late 40s or mid 50s. In 2021, over 22% of adults over 40 years old had knee osteoarthritis, which is estimated to be over 500 million individuals worldwide affected by osteoarthritis. A continued global rise in the prevalence of osteoarthritis is expected with the aging population and the increasing rates of obesity and injuries. The Global Burden of Disease (GBD, 2021) estimates that osteoarthritis will be the fourth leading cause of disability by 2030, with enormous healthcare costs for treatment, as well as significant indirect costs due to loss of productivity and premature retirement.[1]. In the United States, it is projected that by 2030 there will be 67 million adults diagnosed with osteoarthritis, compared to 52.5 million in 2010-2012. The severity of pain and disability associated with osteoarthritis are significant predictors of the risk of death from any cause (even when controlled for potential confounders such as obesity-related conditions).

Today, it is known that the cause of the disease is not only aging and wear and tear of the joint, but it is a multifactorial disease that results from the action of local and systemic factors in each other. The biggest risk factors for the development of OA are age, overweight and obesity, then injuries, repeated use of joints, muscle weakness and joint relaxation. Pathophysiological OA is a disease of synovial joints characterized by synovitis and proinflammatory/catabolic condition of chondrocytes, resulting in degradation of articular cartilage and narrowing of joint space, thickening of synovium with periarticular bone response in the form of sclerosis (thickening) of bone and formation of bone growths, osteophytes [3]. Clinical symptoms include joint pain and stiffness, resulting in impaired mobility of the affected joint. Numerous studies have shown that systemic metabolic disorders by various mechanisms, such as chronic low-grade inflammation and oxidative stress, can cause local effects on the joints. One of the main risk factors for OA is obesity. Obesity not only increases mechanical stress on the articular cartilage but also leads to a higher prevalence of osteoarthritis (OA) in non-weight-bearing joints, such as the joints of the hand. Adipose tissue functions as an endocrine organ, meaning it produces various humoral factors that alter the metabolism of articular cartilage. Adipose tissue is also infiltrated by inflammatory cells (macrophages, T and B lymphocytes, mast cells, neutrophils) that, together with adipocytes, secrete various pro-inflammatory mediators (cytokines, adipokines, free fatty acids, reactive oxygen species, etc.), resulting in systemic low-grade inflammation that negatively affects joint tissues. Leptin, one of the major pro-inflammatory adipokines, can be produced by both osteoblast and chondrocyte cells, and local production of this substance may be of great importance given its catabolic effect on joint tissues. Leptin levels in synovial fluid positively correlate with cartilage destruction, weight, and pain in the OA of the hip and knee. Also, leptin levels in plasma and synovial fluid correlate positively with body fat percentage and BMI. [4]. Obesity itself is associated with disturbed lipid metabolism, leading to a reduction in high-density lipoproteins (HDLs) and an increase in free fatty acids (FFAs), triglycerides, and oxidized low-density lipoproteins (LDLs), resulting in atherogenic dyslipidemia [5]. Obesity and type 2 diabetes have become a pandemic and the most common health risks of modern society worldwide. Obesity and diabetes are associated with the occurrence and increase of numerous diseases such as hypertension, coronary heart disease, stroke, ischemic heart disease, osteoarthritis, breast cancer [6]. Recent studies have shown the positive effect of metformin on reducing the progression of osteoarthritis in participants with diabetes. Along with these studies demonstrating the positive effects of metformin on structural damage and the progression of osteoarthritis, this indicates that dietary intake/composition is likely an important factor that lowers the threshold for the development of OA [7]. This is promising for future strategies for osteoarthritis prevention since diet can be modified, and the gastrointestinal microbiome is sensitive to intervention therapy [8].

## 2. Participants and methods

A prospective clinical study was conducted at the Public Health Institution Health Center Živinice from July 2022 to May 2024, on a random sample of 200 participants with a confirmed clinical diagnosis of osteoarthritis (OA). The participants were divided into two groups: those with metabolic syndrome (Group A) and those without metabolic syndrome (Group B), based on the NCEP ATP III panel criteria for metabolic syndrome. Statistical data analysis was performed using techniques and methods of inferential and descriptive statistics, presented through appropriate tabular summaries and graphical representations. Correlation analysis (Pearson's linear correlation coefficient) and descriptive statistical analysis were used to test the association between individual parameters. A one-factor analysis of the variance of different groups was used to determine the differences in the average severity of knee osteoarthritis versus the presence of prediabetes/diabetes mellitus. A prospective clinical study was conducted at the Public Health Institution Health Center Živinice on a sample of 200 participants over the age of $\geq$40, who were clinically diagnosed by a physiatrist with knee, hip, or small joint hand osteoarthritis, according to the classification by The American College of Rheumatology (Table 1).

**Table 1** The ACR diagnostic criteria for osteoarthritis of the knee, hand, and hip (Altman et al., 1986)

| **OA** | **Clinical criterion** | |
|---|---|---|
| ACR diagnostic criteria for knee | Knee pain plus ( + ) the presence of three or more of the following signs | Age > 50 years |
| | | morning joint stiffness less than 30 minutes |
| | | and crepitations in the joint for the active movements |
| | | Joint sensitivity |
| | | Enlargement of the wrist |
| | | Absence of heat in the joint |
| ACR diagnostic criteria for hand | Pain or stiffness of the hand plus the presence of three or more of the following signs | Increase in hard tissue in ≥ 2 out of 10 * selected joints |
| | | Increase in hard tissue in ≥ 2 distal interphalangeal of joints |
| | | < 3 swollen metacarpophalangeal of the joint |
| | | Deformities ≥ 1 out of 10 selected joints |
| | | The 10 selected joints are the proximal and distal interphalangeal joints of the second and third fingers and the first carpometacarpal joint on both hands |
| ACR diagnostic criteria for hip | Hip pain + ≥ 2 signs | Erythrocyte sedimentation rate < 20 mm / h |
| | | Eadiologically visible osteophytes of the femur or acetabulum |
| | | Radiologically visible narrowing of the joint space |

Radiological confirmation and grading of osteoarthritis severity in the examined joints were performed in the Radiology Department of the Public Health Institution Health Center Živinice using a Siemens Polydoros LX50 machine. Anteroposterior (AP) radiography in a standing position was conducted for the knee and hip joints, while standard AP radiography of both hands was performed for the hand joints. In order to grade the severity of changes, we used the Kellgren-Lawrence (KL) radiological scale to assess osteoarthritis severity in the knee joints in the standing AP position (grades I-IV), based on parameters such as joint space narrowing, presence of osteophytes, subchondral sclerosis, and bone deformity.

Radiological diagnosis of osteoarthritis of the knee was made on the basis of KL score ≥2, and severe OA in KL score ≥3 (Table 2.).

**Table 2** Kellgren-Lawrence grading sistem for osteoarthritis of the knee (Kellgren and Lawrence, 1957)

| **Grade** | **Radiologic finding** |
|---|---|
| 0 | No radiographic findings of osteoarthritis. |
| I | Doubtful narrowing of joint space and possible osteophytic lipping |
| II | Definite osteophytes and possible narrowing of the joint space |
| III | Moderate multiple osteophytes, definite narrowing of joint space, small pseudocystic areas with sclerotic walls, and possible bone deformity of bone contour |
| IV | Large osteophytes, marced narrowing of the joint space, severe sclerosis and definite bone deformity of bone contour |

Both clinical and biochemical analysis were performed for the presence of metabolic syndrome (MetS). After anthropometric measurements of participants (body mass, body height, waist circumference in centimeters) BMI was calculated according to the valid formula TM/TV2. Then, while seated and after a ten-minute rest, blood pressure (BP) was measured using a manual mercury sphygmomanometer (Bosch) in mmHg on the brachial artery of both the left and right arms, and the average value was recorded, Additionally, any prior instances of elevated blood pressure or the

use of antihypertensive medications were noted. In the Laboratory Diagnostics Department of the Health Center Živinice, biochemical parameters in serum were measured using the Beckman Coulter DxC 700 AU; fasting glucose, total cholesterol (TC), cholesterol fractions (high-density lipoprotein cholesterol - HDL-C and low-density lipoprotein cholesterol - LDL-C), triglycerides, and any previous diagnosis of type 2 diabetes, atherogenic dyslipidemia, or the use of antidiabetic and hypolipidemic medications in treatment were also recorded.

The presence of metabolic syndrome in patients was determined based on the updated NCEP ATP III panel diagnostic criteria (2004) for the confirmation of metabolic syndrome, where the presence of three or more clinical criteria is required for the confirmation of MetS (Table 3).

**Table 3** Criteria for clinical diagnosis of metabolic syndrome (NCEP ATP III, AHA, NHLBI)

| **Components of metabolic syndrome (MetS)** | **Clinical criteria** |
|---|---|
| Central (abdominal)obesity | Waist circumference ≥ 102 cm for men and women. ≥ 88 for women. |
| Insulin resistance | Fasting glucose ≥ 5.6 mmol / l (100.8 mg / dl) or pharmacological treatment of hyperglycmaia |
| Atherogenic dyslipidemia | Triglycerides ≥1.7 mmol / l (150 mg / dl) or pharmacological treatment of elevated triglycerides<br>HDLc < 1.03 mmol / l (40 mg / dl) for men, and <1.29 mmol/l(50 mg/dl) for women or pharmacological treatment (both HDLc and triglycerides are considered individual criteria) |
| High blood pressure | SDP ≥135mmHg, DBP≥85 mmHg or pharmacological treatment art.hypertension |

## 3. Results

In the random sample of patients with a clinical diagnosis of osteoarthritis (OA), women dominated, with 131 female participants, accounting for 65.50%, while there were a total of 69 male participants, or 34.50%.

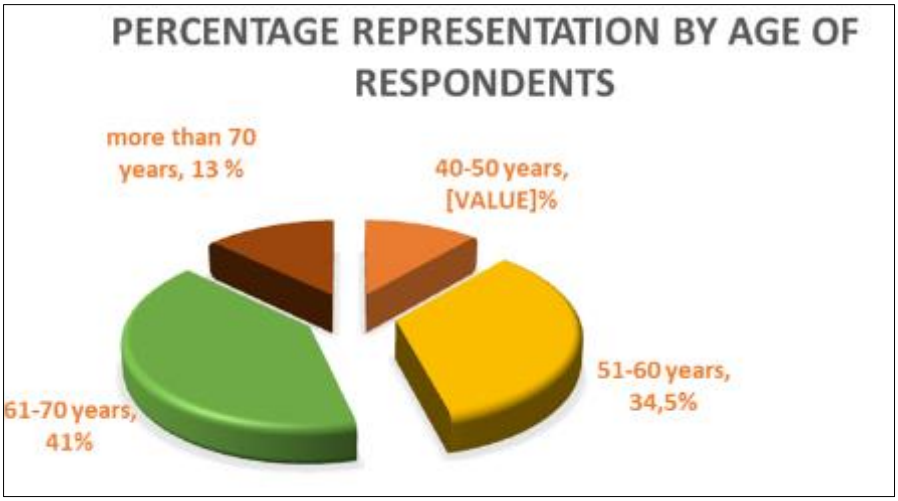


**Figure 1** The age structure of participants

The research sample included participants of different age categories, 40 years of age and older (Figure 1.). Most of them, 41% are between the ages of 61 and 70. Between the ages of 51 and 60, there are 34.50% of participants in the sample, 13% are older than 70 years, while the remaining 11.50% are patients aged between 40 and 50 years. The average age of the participants covered by the survey sample is 61.01 years of age.

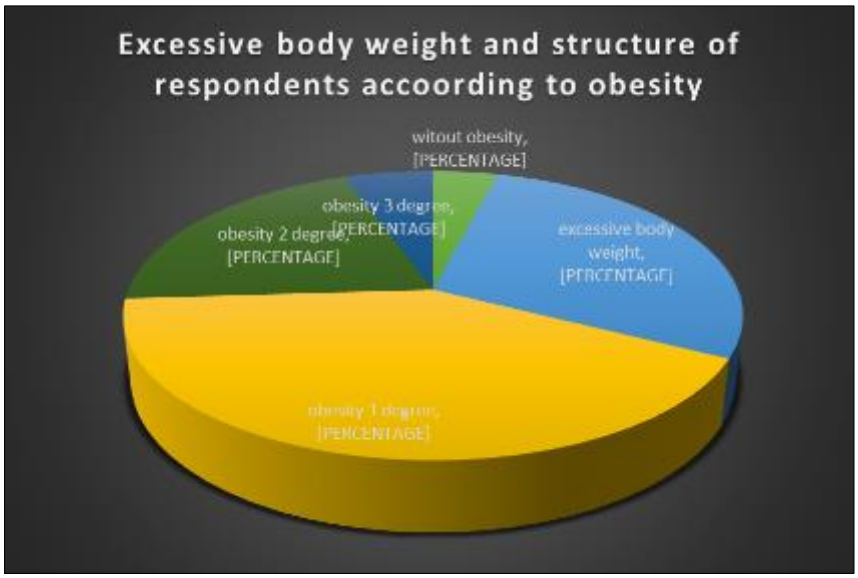


**Figure 2** Structure of participants according to body mass index

The structure of the participants according to the body mass index is presented in Figure 2. In 41.5% of participants, first-degree obesity is evident, 28.5% of participants are overweight, while 20.5% of participants have second-degree obesity. In the category of obesity of the third degree (obesity 3) there are 5.5% of the participants, while only 4% of the participants have a normal body mass.

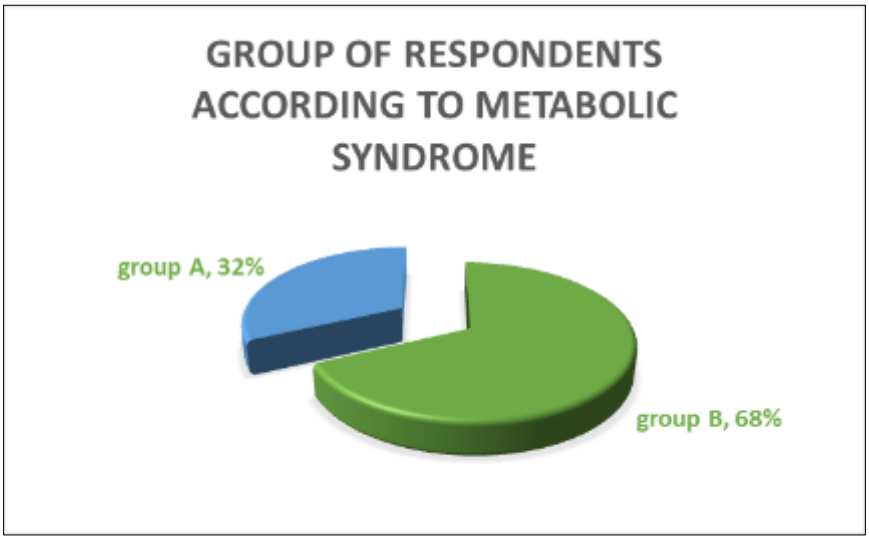


**Figure 3** Structure of participants according to the presence of metabolic syndrome

On the basis of the NCEP ATP III panel diagnostic criteria for metabolic syndrome, participants were categorized into two groups according to the presence or absence of metabolic syndrome: Group A (without metabolic syndrome) and Group B (with metabolic syndrome). Figure 3. presents a significantly higher proportion of participants in the sample that have the presence of metabolic syndrome (68%), while 32% of participants did not meet the criteria for metabolic syndrome.

The results are presented in Table 3.4. and as the dominant is presented the diagnosis of osteoarthritis of the knee since it was confirmed in 78.5% of the participants. With significantly lower prevalence, hip and hand osteoarthritis are present, therefore a hip osteoarthritis diagnosed in 11.5% and hand osteoarthritis in 10% of participants in the sample (Table 4).

**Table 4** Distribution of participants by type of osteoarthritis

| | number of respondents | % of respondents |
|---|---|---|
| OA of hips | 23 | 11.50 |
| OA of knees | 157 | 78.50 |
| OA of hands | 20 | 10.00 |
| total | 200 | 100.00 |

The results of the analysis of the prevalence of osteoarthritis by groups A and B (relative to the presence of MetS) and by the gender of the participants are presented in Table 5.

**Table 5** Prevalence of osteoarthritis versus gender of participants

| sample / group | categories | OA of hips | | OA of knees | | OA of hands | | total | |
|---|---|---|---|---|---|---|---|---|---|
| | | number | % | number | % | number | % | number | % |
| full sample | male | 18 | 26.09 | 51 | 73.91 | 0 | 0.00 | 69 | 100.00 |
| | female | 5 | 3.82 | 106 | 80.92 | 20 | 15.27 | 131 | 100.00 |
| Group A | male | 7 | 22.58 | 24 | 77.42 | 0 | 0.00 | 31 | 100.00 |
| | female | 3 | 9.09 | 22 | 66.67 | 8 | 24.24 | 33 | 100.00 |
| Group B | male | 11 | 28.95 | 27 | 71.05 | 0 | 0.00 | 38 | 100.00 |
| | female | 2 | 2.04 | 84 | 85.71 | 12 | 12.24 | 98 | 100.00 |

F (2.87) = 15.543; $p<0.001$; $\chi^2=0.26$ (male participants); F (2.87) = 25.003; $p<0.001$; $\chi^2= 0.36$ (female participants)

The results present that in both genders the most commonly diagnosed is knee osteoarthritis. Osteoarthritis of the hip is more common in men, while the prevalence of osteoarthritis of the hands is higher in women. When observed by groups formed based on the presence of metabolic syndrome, it is possible to note a higher prevalence of hip osteoarthritis and a slightly lower prevalence of knee osteoarthritis in male participants with metabolic syndrome compared to the group without metabolic syndrome. In contrast, in female participants of this group, a lower prevalence of hip and hand osteoarthritis and a higher prevalence of knee osteoarthritis can be observed.

The results show a significantly higher prevalence of knee osteoarthritis compared to other joints, across all age groups, with the highest prevalence in the younger age group (40-50 years of age), regardless of the presence of metabolic syndrome. In the older groups, an increase in the prevalence of knee OA in patients with metabolic syndrome has been reported relative to the MetS-free group. In patients over the age of 70, a decrease in the prevalence of knee osteoarthritis was observed compared to other joints in the group without metabolic syndrome, whereas this was not the case in the group with metabolic syndrome. In the case of hip osteoarthritis, it is other way around —there is an increase in the prevalence of hip osteoarthritis in patients over the age of 70 (accounting for 30% of all osteoarthritis cases, and as high as 50% in participants without metabolic syndrome), while no cases were recorded in the 40-50 age group. When it comes to hand osteoarthritis, the highest prevalence is observed in female patients aged 51 to 60 years. If we observe based on the presence of metabolic syndrome, the highest prevalence is in the 51-60 and 61-70 age groups, while in the group without metabolic syndrome, the highest prevalence is in the 51-60 years of age group.

**Table 6** Prevalence of osteoarthritis over age of participants

| sample / group | categories | OA of hips | | OA of knees | | OA of hands | | total | |
|---|---|---|---|---|---|---|---|---|---|
| | | number | % | number | % | number | % | number | % |
| full sample | 40-50 years of age | 0 | 0.00 | 21 | 91.30 | 2 | 8.70 | 23 | 100.00 |
| | 51-60 years of age | 7 | 10.14 | 53 | 76.81 | 9 | 13.04 | 69 | 100.00 |
| | 61-70 years of age | 8 | 9.76 | 66 | 80.49 | 8 | 9.76 | 82 | 100.00 |
| | more than 70 years of age | 8 | 30.77 | 17 | 65.38 | 1 | 3.85 | 26 | 100.00 |
| Group A | 40-50 years of age | 0 | 0.00 | 12 | 92.31 | 1 | 7.69 | 13 | 100.00 |
| | 51-60 years of age | 2 | 6.90 | 22 | 75.86 | 5 | 17.24 | 29 | 100.00 |
| | 61-70 years of age | 4 | 28.57 | 9 | 64.29 | 1 | 7.14 | 14 | 100.00 |
| | more than 70 years of age | 4 | 50.00 | 3 | 37.50 | 1 | 12.50 | 8 | 100.00 |
| Group B | 40-50 years of age | 0 | 0.00 | 9 | 90.00 | 1 | 10.00 | 10 | 100.00 |
| | 51-60 years of age | 5 | 12.50 | 31 | 77.50 | 4 | 10.00 | 40 | 100.00 |
| | 61-70 years of age | 4 | 5.88 | 57 | 83.82 | 7 | 10.29 | 68 | 100.00 |
| | more than 70 years of age | 4 | 22.22 | 14 | 77.78 | 0 | 0.00 | 18 | 100.00 |

($\chi^2$=30.869; df=9; p<0.001)

The Kruskall-Wallis test presented that the differences between the groups were also statistically significant ($\chi^2$=30.869; df=3; p=0.001), and the highest intermediate rank has Group B, as presented in Table 6.

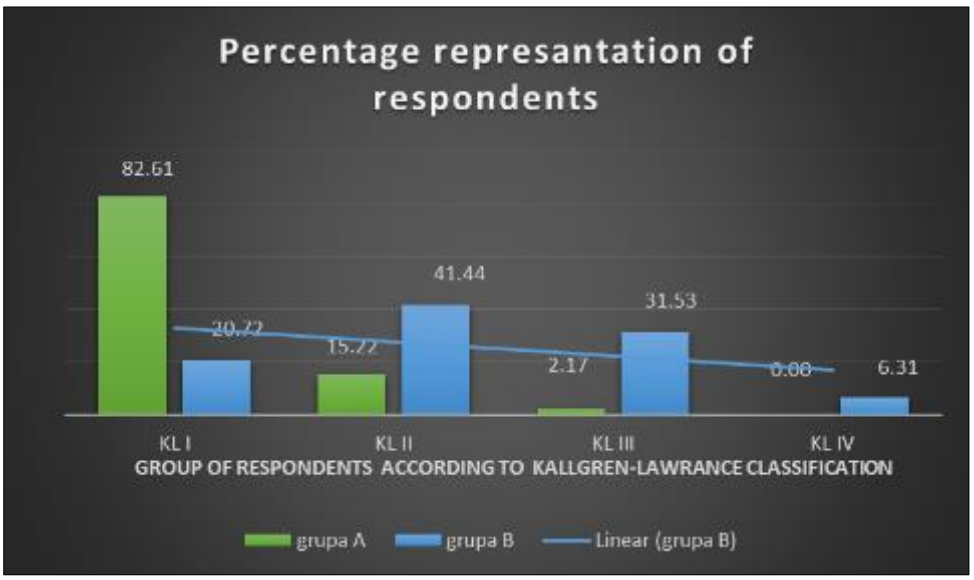


**Figure 4** Prevalence of osteoarthritis of the knee according to the presence of metabolic syndrome

The severity of osteoarthritis was assessed on the basis of radiological changes in the knee joint, using a four-stage Kellgren-Lawrence. These parameters were calculated separately for participants with and without the presence of metabolic syndrome (Figure 5).

As we can see from the presented results, among participants in whom metabolic syndrome is not present, the dominant participation of subjects with first-degree osteoarthritis of the knee (radiologically initial changes suspected of OA), while osteoarthritis of the knee of second, third and fourth degree severity (radiologically confirmed OA) is more prevalent in participants with metabolic syndrome present. Descriptive statistical indicators of the severity of knee osteoarthritis were calculated for participants in both groups, and the obtained results are presented in Table 7. These

results presented that the standard deviations, as well as the variability in the degree of knee osteoarthritis severity, are almost twice as high in participants diagnosed with metabolic syndrome.

**Table 7** Descriptive statistical indicators of the severity of osteoarthritis of the knee against the presence of metabolic syndrome

| | **N** | **min.** | **max.** | **average** | **st. deviation** |
|---|---|---|---|---|---|
| Group A | 46 | 1 | 3 | 1.20 | 0.453 |
| Group B | 111 | 1 | 4 | 2.23 | 0.852 |

ANOVA: F (3, 156) = 7.864; p<0.001

The results of the obtained averages present a higher degree of severity of knee osteoarthritis in participants with a present metabolic syndrome. More precisely, while the average severity level recorded in participants from this group was 2.23, the average severity of osteoarthritis in participants without metabolic syndrome included in the study was 1.20. Further analysis of the prevalence of specific forms of osteoarthritis and the severity of knee osteoarthritis was conducted based on fasting blood glucose levels (Group 1—normal values, Group 2—prediabetes, Group 3—type 2 diabetes), as presented in Table 8.

**Table 8** Distribution of participants according to type of osteoarthritis / severity of knee osteoarthritis and blood sugar level/presence of prediabetes, i.e. diabetes mellitus type 2

| **type of osteoarthritis** | **degree of osteoarthritis of the knee** | **Group 1** | | **Group 2** | | **Group 3** | |
|---|---|---|---|---|---|---|---|
| | | **number of respondents** | **% of respondents** | **number of respondents** | **% of respondents** | **number of respondents** | **% of respondents** |
| osteoarthritis of the knee | KL I | 27 | 51.92 | 19 | 29.69 | 15 | 17.86 |
| | KL II | 8 | 15.38 | 21 | 32.81 | 24 | 28.57 |
| | KL III | 3 | 5.77 | 11 | 17.19 | 22 | 26.19 |
| | KL IV | 1 | 1.92 | 2 | 3.13 | 4 | 4.76 |
| osteoarthritis of the hip or hand | | 13 | 25.00 | 11 | 17.19 | 19 | 22.62 |
| total | | 52 | 100.00 | 64 | 100.00 | 84.00 | 100.00 |

($\chi^2$=0.775;df=4;p=0.94)

Table 9. presents that the prevalence of knee OA is highest in the prediabetes group (82.8%), followed by the group of participants with type 2 diabetes (77.4%), while the lowest prevalence is observed in the group with normal fasting blood glucose levels (75%). OA of the hip and hand were the most common in the normal blood sugar group (25%), followed by DM type 2 (22.6%), and the least common in the prediabertes group (17.19%).

**Table 9** Multiple comparative analysis testing of the differences in the average severity of knee osteoarthritis in relation to blood sugar levels/presence of prediabetes/type 2 diabetes mellitus

| (I) level of sugar in blood/presence of diabetes mellitus | (J) level of sugar in blood/presence of diabetes mellitus | mean difference (I-J) | st. error | sig. | 95% confidence interval | |
|---|---|---|---|---|---|---|
| | | | | | lower limit | upper limit |
| Level of blood sugar to 5.6 mmol / L-regular value | Level of sugar in blood in the interval between 5.6 and 6.9 mmol / L-prediabetes | -0,489* | 0.177 | 0.018 | -0.91 | -0.07 |
| | Level of sugar in blood ≥7 mmol / L (diabetes mellitus) | -0,795* | 0.170 | 0.000 | -1.20 | -0.39 |
| Level of sugar in blood in the interval between 5.6 and 6.9 mmol / L-prediabetes | Level of sugar in blood to 5.6 mmol / L-regular value | 0,489* | 0.177 | 0.018 | 0.07 | 0.91 |
| | Level of sugar in blood ≥7 mmol / L (diabetes mellitus) | -0.306 | 0.156 | 0.124 | -0.67 | 0.06 |
| Level of sugar in blood ≥7 mmol / L (diabetes mellitus) | Level of sugar in blood to 5.6 mmol / L-regular value | 0,795* | 0.170 | 0.000 | 0.39 | 1.20 |
| | Level of sugar in blood in the interval between 5.6 and 6.9 mmol / L-prediabetes | 0.306 | 0.156 | 0.124 | -0.06 | 0.67 |

*. The difference is significant at 0.001.

There is a statistically significant correlation between diabetes and osteoarthritis ($\chi^2$=33.545; df=12; p=0.001).

## 4. Discussion

Numerous epidemiological studies have confirmed that osteoarthritis is the most common joint disease and one of the leading morbidities of the locomotor system. The presence of OA affects the quality of life and exacerbates existing morbidities, due to chronic pain and difficulty in moving patients. Due to rising life expectancy and increasing global prevalence, OA represents one of the major public health problems worldwide associated with extremely high economic burden [9].

This research determined the prevalence of metabolic syndrome in patients with osteoarthritis of one of the synovial joints (knees, hips, hands) and whether metabolic disorders are a risk factor for the development and worsening of osteoarthritis.

Our research presented almost twice the prevalence of osteoarthritis symptoms in women (65.5%) compared to men (34.5%). Other epidemiological studies have also shown a higher prevalence of OA in women compared to men, with some studies reporting nearly double the rates【10】.

In both gender, knee osteoarthritis is observed as the most common joint disorder during clinical examination, which is consistent with findings from other authors. If we compare the prevalence of OA on the examined joints individually, we will see that the highest prevalence of OA of the knee is slightly higher in women than in men. OA of hips and hands are much less represented compared to OA knees. The OA of the hip is more prevalent in the older male population, while the OA of the hands is more prevalent in women. Honours and Hunter also showed a higher prevalence of knee and hand osteoarthritis in women, while hip osteoarthritis was more common in men. Analyzing the age structure of the participants, it is observed that the largest number of individuals with osteoarthritis symptoms was in the age group of 61-70 years of age, with the highest percentage related to knee osteoarthritis. In the population older than 70 years of age, there is a significantly lower prevalence of osteoarthritis, primarily concerning hip osteoarthritis in men. In contrast, among individuals under 60 years of age, there is a diverse prevalence of all forms of osteoarthritis, but hip osteoarthritis is the least common.

Given the expected increased incidence and prevalence of OA in younger patients, this can be explained by the presence of other risk factors in the younger population, such as metabolic disorders, which can cause an inflammatory reaction with more severe OA symptoms, increased physical activity and joint trauma at a younger age, as well as the appearance of a decrease in painful stimuli with more severe OA degrees. "central sensitization" in later decades of life [12].

According to new research (Long et al.,2022) in the pathogenesis of OA of the knee and hip a significant role is played by excessive load and additional injuries to the joint, due to which obese people who do heavy physical work with a lot of repetitive joint movements are most exposed. They are usually people of low socioeconomic status whose diet is high in carbohydrates, which is more accessible and cheaper, with often poorer health care and untreated metabolic disorders. A Meta-analysis conducted by Scanzello provided limited evidence that work activities requiring repeated and/or prolonged workload may increase the risk for developing osteoarthritis. The causes of OA remain unknown, despite modern advances in analysis and diagnosis, but are related to the loss of cartilage elasticity [13]. Numerous studies have shown that mechanical load (increased body mass) and aging lead to accelerated damage to articular cartilage. In a study by O'neill et al., it was observed that the average age of patients requiring hip joint replacement is 10 years lower in obese individuals, while for patients needing knee joint replacement, it is 13 years lower in obese individuals compared to those of normal weight.

The nutritional status of the studied population, indicated by BMI, presents that only 4% of our participants had a normal body weight, while nearly two-thirds of the participants suffered from obesity of the first, second, or third category. Additionally, 28.5% had excess body weight. This indicates that the study group (belonging to the adult Balkan population) is overweight in 96% of cases. If we also consider the increased average waist circumference in all groups, along with fasting glucose, cholesterol, triglyceride levels, and blood pressure values, we can observe that a significant percentage, specifically 68%, of our participants exhibit three or more metabolic disorders, indicating the presence of metabolic syndrome. The reasons for such a high number of participants with metabolic syndrome have a multifactorial etiology, primarily based on poor dietary habits, low physical activity, lower socioeconomic and educational status, and other related factors. Many epidemiological studies have found that obesity in adulthood is a risk factor for knee OA[15]. Analyzing the prevalence of osteoarthritis in relation to BMI, it has been observed that obesity is often linked to the occurrence of knee osteoarthritis, while the association is weaker for hip and hand OA, which is also confirmed by our research. Thus, in patients with the highest degree of BMI, osteoarthritis of the knee occurs with a 100% probability, while OA of the hip and hand have a lower trend of occurrence. A cohort study involving 2,597 participants in the United Kingdom demonstrated a strong positive correlation between body mass index (BMI) and knee osteoarthritis in both men and women (Martin et al., 2013). Similar results were found in the American population (both among whites and African Americans). (16)Honvo et al. demonstrated that a higher BMI is moderately associated with the progression of osteoarthritis. Participants with excess weight and a larger waist circumference experienced more frequent occurrences of osteoarthritis (17)

In our study, among female participants without metabolic syndrome, osteoarthritis of the knee at grade I on the KL scale dominates at around 80% (radiological changes suggestive of OA), while there are fewer participants with grade II OA, i.e., radiologically confirmed OA. Only 2% of respondents had OA 3. degree. Participants who have metabolic syndrome are dominated by osteoarthritis of severe degrees, i.e. radiologically proven OA had about 80% of subjects (second and third degrees over 70% of subjects), and only 20% had OA 1. the KL scale. OA 4. the grade was in a small percentage, which could be explained by small differences in radiological assessment and earlier therapeutic interventions in terms of Arthroplasty (which was not a criterion of inclusion in the study). Thus, we can conclude that a more severe degree of osteoarthritis was present as part of the various metabolic disorders that together constitute metabolic syndrome.

Analysis of all parameters of metabolic syndrome has shown that each of them, individually and collectively (through their interactions), creates an unfavorable metabolic environment that contributes to the increased prevalence of osteoarthritis in all forms, both in men and women, as well as to the progression of the severity of OA. The overall prevalence of knee osteoarthritis in both gender, hip osteoarthritis in men, and hand osteoarthritis in women was higher in the group with metabolic syndrome. The independent risk factor for knee osteoarthritis was BMI, while waist circumference can be viewed as a risk factor within the context of metabolic syndrome (as its association with other metabolic disorders has been established). This supports previous research on the pro-inflammatory effects of leptin and other pro-inflammatory factors in the initiation and progression of osteoarthritic changes in the joints. Studying the occurrence of osteoarthritis in the global population, Driban et el.[18] predicted that by 2050, the prevalence of osteoarthritis will be double. This is associated with sedentary lifestyle and diet, which leads to the occurrence of metabolic syndrome. The Melbourne Collaborative Cohort study of 2,430 participants with metabolic syndrome confirmed that central obesity and high blood pressure were associated with more severe forms of knee OA,

independent of BMI. This study also confirmed that management of metabolic syndrome can reduce the risk of knee OA [19].

## 5. Conclusion

Our study presented a high percentage (about 70%) of the presence of overweight/obese and metabolic syndrome in participants with osteoarthritis. Increased BMI has been shown to be an independent risk factor for the occurrence and exacerbation of OA. The Association of metabolic disorders, especially insulin resistance and central obesity, has been reported. The study confirmed that the prevalence of all OA forms studied, especially knee OA, as well as the degree of OA severity (measured at the knee joint), were higher in the metabolic syndrome group, regardless of age and gender of the participants. There was also a statistically significant difference ($p<0.05$) in the average severity of knee osteoarthritis in participants with regular blood sugar compared to participants with prediabetes/diabetes mellitus type 2.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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