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Research Article

Chronic Musculoskeletal Pain in Metabolic Syndrome: Most Common Anatomic Sites and Diseases

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Abstract

Purpose: Musculoskeletal diseases can lead to deterioration of metabolic syndrome (MetS) as patients develop sedentary behaviors; these behaviors can result in loss of muscle mass, which is linked to increased damage of musculoskeletal structures. To better understand the relationship between musculoskeletal diseases and MetS, we aimed to study chronic musculoskeletal pain in patients with MetS by comparing clinical and laboratory features between groups with and without MetS.

Materials and Methods: This case-control study included the following two groups of patients with similar age and sex distribution: 64 and 42 adults with and without MetS, respectively. Blood samples were collected to determine the erythrocyte sedimentation rate, C-reactive protein (CRP) and uric acid (UA) levels. Patients with chronic musculoskeletal pain underwent clinical evaluation of the musculoskeletal system to determine the location and the specific diagnosis, which were compared between the two study groups. For significant or marginally significant variables in the univariate analysis, we determined the odds ratio and 95% confidence interval by logistic regression before and after inclusion of body mass index, categorized as < 25 kg/m^2 and ≥ 25 kg/m^2 (overweigh/obesity) for each variable.

Results: Patients with MetS had a significantly higher rate of chronic musculoskeletal pain (73.44 vs. 52.38%, p = 0.044) as well as knee pain (35.93% vs. 4.76%, p = 0.0001), hip pain (10.94% vs. 0%, p = 0.04), and ankle and feet pain (32.81% vs. 7.14%, p = 0.002). They also had a higher frequency of knee osteoarthritis (KOA) (23.44% vs. 2.38%, p = 0.003), plantar fasciitis (PF) (17.19% vs. 2.38%, p = 0.026), and fibromyalgia (20.31% vs. 4.76%, p = 0.043). After adjustment for overweight/obesity, the association between MetS and low back pain was significant (OR = 6.17, 95%CI = 1.41 - 31.85, p = 0.016). Also, there was an attenuation of the relationship between MetS and KOA (OR = 12.31, 95%CI = 1.03 - 147.7, p = p-0.048); meanwhile, the link between MetS, PF, and fibromyalgia was not significant. CRP (OR = 1.53, 95%CI = 1.12 - 2.09) and UA (OR = 1.94, 95%CI = 1.25 - 3.01) were also significantly associated with MetS after adjusting for overweight/obesity; however, they were not associated with any musculoskeletal chronic pain site or other diseases described in this study.

Conclusion: There was a higher rate of chronic musculoskeletal pain in MetS, particularly in the weight-bearing sites, including LBP and KOA, which could impair walking; consequently, physical activity is reduced and further contributes to deterioration of MetS and musculoskeletal health.

Keywords: Metabolic Syndrome; Overweight; Obesity; Chronic Pain; Musculoskeletal Diseases

Abbreviations

MetS: Metabolic Syndrome; CRP: C Reactive Protein; UA: Uric Acid; OR: Odds Ratio; CI: Confidence Interval; BMI: Body Mass Index; LBP: Low Back Pain; KOA: Knee Osteoarthritis; WC: Waist Circumference; HDL-C: High Density Lipoprotein Cholesterol; ACR: American College Rheumatology; PF: Plantar Fasciitis; ESR: Erythrocyte Sedimentation Rate; OA: Osteoarthritis; MRI: Magnetic Resonance Imaging

Introduction

Metabolic syndrome (MetS) is associated with multiple risk factors for type 2 diabetes and cardiovascular diseases [1]. Also, the metabolic complications of obesity can increase the risk for musculoskeletal diseases [2]. The key components of the pathogenesis of MetS include visceral adiposity due to high caloric intake, lack of physical activity, and insulin resistance [3]. A link has been proposed between MetS and musculoskeletal tissue damage, namely that low-grade inflammation and vasoconstriction due to hypertension and endothelial dysfunction are associated with altered lipid and glucose metabolism [4]. Moreover, patients with musculoskeletal diseases may experience a deterioration of MetS as they develop sedentary behavior, leading to loss of muscle mass and intramuscular lipid deposits; consequently, this can cause damage to musculoskeletal structures [4,5]. Additionally, the prevalence of MetS is increasing worldwide [6] and the prevalence of musculoskeletal diseases, such as osteoarthritis (OA), is also expected to increase as the population ages [7]. Therefore, to better understand the implications of musculoskeletal damage in MetS, we aimed to study chronic musculoskeletal pain in patients with MetS and compare the clinical and laboratory features between patients with and without MetS.

Materials and Methods

This was a case-control study comparing two groups of participants with and without MetS with similar age and sex distribution. The ethics committee of Grande Dourados University (UFGD) approved the study (CAAE57333816.5.0000.5160), and all participants signed an informed consent form before participating in the study. The inclusion criteria for both groups were people aged 18 years or over who had undergone a health checkup in the last six months. The exclusion criteria, also for both groups, were participants who had infectious diseases or had undergone a surgical procedure within one month preceding the interview. Equally important, people with a previous diagnosis of chikungunya virus infection were also excluded. Lastly, sixty-four patients who fulfilled the 2009 Joint Consensus definition for MetS [1] and 42 subjects without MetS were included in this study.

Patients with MetS were recruited between June 2018 and September 2019 from different outpatient clinics (except rheumatology and orthopedics) of the hospital of UFGD, while the participants without MetS included were employees of the hospital and relatives of the patients. A structured questionnaire, applied by the researchers during a face-to-face interview, was used to collect demographic and clinical data, including details on medications and comorbidities. The following measurements were obtained from their health checkups,: blood pressure on at least two separate occasions, fasting glucose, triglycerides, and high-density lipoprotein cholesterol (HDL-C). Waist circumference (WC) was measured to the nearest 0.1 cm at full expiration at the narrowest point between the lower rib margin and iliac crest. Height was measured to the nearest 0.1m and weight to the nearest 0.1 kg with a calibrated scale. Body mass index (BMI) was calculated as the ratio of weight to the square of height (kg/m^2). Subjects were considered underweight, normal weight, overweight, or obese if their BMI was < 18.5, between 18.5 and 24.99, between 25 and 29.99, and ≥ 30, respectively [8].

Seven participants did not have measurements of high-density lipoprotein cholesterol (HDL-C) and triglycerides; however, it was possible to determine whether they had MetS. Indeed, the participants were classified as having MetS if they fulfilled three or more of the following five criteria: 1) elevated WC; 2) triglycerides ≥ 150 mg/dL or drug treatment for elevated triglycerides; 3) HDL-C < 40 mg/dL in men and < 50 mg/dL in women or drug treatment for reduced HDL-C; 4) elevated blood pressure (systolic ≥ 130 and/or diastolic ≥ 85 mmHg or drug treatment for hypertension); 5) fasting glucose ≥ 100 mg /deciliter (mg/dL) or drug treatment for elevated glucose. For WC, we used the following cut-off points, which are associated with an increased risk for cardiovascular disease: ≥ 94 cm in men and ≥ 80 cm in women [1,9].

The questionnaire included a question about musculoskeletal pain, namely pain lasting more than 12 weeks without previous trauma in the following nine specific joint regions: neck, upper back, lower back, shoulders, elbows, wrist and hand, hips, knees, and ankles and feet [10]. If the patient experienced pain, they were scheduled for a visit to the rheumatology clinic, within seven days after the first interview, where a clinical evaluation of the musculoskeletal system was performed to verify if the patient had tenderness to palpation, painful or impaired range of motion, and any

inflammatory sign, crepitus, or bone enlargement at each anatomical site.

Then, sera were collected for C-reactive protein (CRP) and uric acid (UA) assays using routine kits for the COBAS 6000 autoanalyzer (Roche, Rotkreuz, Switzerland). The Westergren method was used to determine the erythrocyte sedimentation rate (ESR).

Besides, a rheumatologist identified two patients who required further laboratory and image investigation to excluded rheumatoid arthritis and ankylosing spondylitis. Nevertheless, image examinations could not be performed for the majority of the participants with chronic musculoskeletal pain due to logistic issues.

Four patients in the MetS group did not have CRP or UA tests, while six and five subjects in the group without MetS did not have CRP and UA measurements, respectively. ESR was not performed in four and eight patients with and without MetS, respectively.

For this study, we focused on the identification of the most frequent chronic pain anatomic sites and specific musculoskeletal diseases. Upper limb and neck disorders were classified based on the Southampton examination schedule [11]. The criteria for low back pain (LBP) included pain between the twelfth rib and the gluteal folds and/or sciatic pain [12]. Hip pain included pain in the groin associated with painful hip range of motion [13] and trochanteric bursitis was considered as lateral hip pain and tenderness to palpation of the bursa overlying the great trochanter [14]. Additionally, the participants were classified as having knee OA (KOA) and fibromyalgia if they met the clinical criteria of the American College of Rheumatology (ACR) for KOA [15] and the ACR 2010 fibromyalgia criteria [16], respectively. Plantar fasciitis (PF) was clinically diagnosed based on the following findings: pain in the medium plantar region of the heel, particularly after taking the first steps following a period of inactivity, and tenderness to palpation of the posterior insertion of the plantar fascia on the medial process of the calcaneal tuberosity [17].

Data were reported as mean (standard deviation) or median (interquartile range) for continuous variables, and frequencies and percentages for categorical variables. The two-sample Student's t-test or Mann-Whitney U test was used to compare continuous variables. Chi-square or Fisher's exact test was used to evaluate categorical data. We performed univariate logistic regression to calculate the odds ratio (OR) and 95% confidence intervals (CI) for the clinical variables that revealed significant, or marginally significant, results, excluding seven patients taking lipid-lowering drugs. Further analysis was performed for each significant variable, including BMI categorized as < 25 kg/m^2 (normal) and ≥ 25 kg/m^2 (overweight/obesity) in the logistic regression. Laboratory parameters with significant results were also analyzed by logistic regression, including BMI. For uric acid, we also performed a logistic regression analysis adjusted to include patients being treated with diuretics.

Data were analyzed using the SPSP 22 (IBM, Chicago, IL, USA), and p <0,05 (two-tailed) was considered statistically significant.

Results

As expected, patients with MetS revealed a statistically significant association with the following factors: elevated blood pressure or previous diagnosis of hypertension (46/64, 71.87% vs. 3/42, 7.14%, p < 0.0001); fasting glucose ≥ 100 mg/dl or drug treatment for elevated glucose (58/64, 90.62% vs. 7/42, 16.67%, p < 0.0001); high triglycerides (41/58, 70.70% vs. 5/41, 12.19%, p < 0.0001); low HDL-C (34/58, 58.62% vs. 7/41, 17.10%, p < 0.0001); and WC associated with an increased risk for cardiovascular disease (60/64, 93.75% vs.9/42, 21.43%, p < 0.0001). Mean BMI was significantly higher in the MetS group than in the group without MetS: 35.24 (6.61) and 24.63 (3.24) kg/m^2, respectively, p < 0.0001. BMI ≥ 25 kg/m^2 (overweight/obesity) was observed in 62 of 64 (96.87%) patients with MetS and in 17 of 42 (40.48%) patients without MetS, p < 0.0001. No participant was underweight.

The mean age of patients with and without MetS was 50.72 (9.87) and 48.90 (8.65) years, respectively, p = 0.33. No differences were seen in the percentage of women between groups: 31 of 64 (48.44%) in the MetS group and 21 of 42 (50%) in the group without MetS, p = 1.00. There was a significantly higher rate of chronic musculoskeletal pain at any anatomic site in the MetS group (47of 64 ([73.44%]) than in the group without MetS (22 of 42 [52.28%], p = 0.044).

Table 1 shows the results of the comparison between individuals with and without MetS in the rate of chronic musculoskeletal pain at different anatomic sites. The lower back was the most common site of pain in both groups, with a higher rate observed in the MetS group than in the group without MetS. Neck, shoulders, elbow, wrist, and hand pain were similar in both groups. A significantly higher rate of pain was observed in the hips and thighs, knees, and ankles and feet in the Mets group than in the group without MetS.

History and physical examination suggested the presence of trochanteric bursitis and OA in six patients with hip pain. Due to

	With MetS (64)	Without MetS (42)	P
Neck n*(%)	12 (18.75)	5 (11.90)	0.42
Shoulders n*(%)	9 (14.06)	4 (9.52)	0.56
Elbows n*(%)	6 (9.37)	3 (7.14)	1.00
Wrists/hands n*(%)	6 (9.37)	2 (4.76)	0.47
Lower back n*(%)	26 (40.62)	9 (21.43)	0.065
Hips/thighs n*(%)	7 (10.94)	0	0.040
Knees n*(%)	23 (35.93)	2 (4.76)	0.0001
Ankles/feet n*(%)	21 (32.81)	3 (7.14)	0.002

Table 1: Musculoskeletal pain at specific anatomical sites in patients with and without metabolic syndrome.

*n = Number; upper back pain was observed in only one patient with MetS and in another patient without MetS.

	Univariate analysis			Analysis adjusted BMI ≥ 25 Kg/m^2		
	OR*	95%CI**	P	OR**	95%CI**	P
Chronic MSK$^{\$}$ pain at any site	2.38	1.05 - 5.40	0.038	2.14	0.76 - 6.01	0.14
Low back pain	2.48	1.00 - 6.15	0.050	6.71	1.41 - 31.85	0.016
Knee Osteoarthritis	13.35	1.68 - 106.15	0.014	12.31	1.03 - 147.70	0.048
Plantar fasciitis	8.72	1.07 - 71.09	0.043	3.56	0.42 - 30.02	0.24
Fibromyalgia	5.33	1.12 - 25.29	0.035	3.56	0.57 - 22.14	0.17

Table 2: Odds ratio for musculoskeletal diseases in patients with metabolic syndrome#.

#: Seven patients with metabolic syndrome under statin or fibrate treatment were excluded from this analysis, $^{\$}$: Musculoskeletal, *: Odds ratio; **: 95% confidence interval.

the small sample size, we did not include hip pain in the logistic regression analysis.

Fifteen of 64 (23.44%) patients in the MetS group met the classification criteria for symptomatic KOA compared to 1 of 42 (2.38%) subjects in the group without MetS, p = 0.0014. The most frequent cause of ankle and foot pain was PF, which was observed in 11 of 64 (17.19%) patients with MetS and in only one (2.38%) subject in the group without MetS (p = 0.041). Fibromyalgia was also higher in the MetS group (20.31% vs. 4.76%, p = 0.041) than in the group without MetS.

Table 2 shows the OR and 95% CI for significant variables in the previous analysis after exclusion of patients taking statins or fibrates. Further inclusion of overweight/obesity in the logistic regression showed that the association with MetS was significant for LBP; meanwhile, it was reduced but significant for KOA and was no longer significant for chronic pain at any anatomic site, for PF or fibromyalgia. No differences were observed in age between the MetS group and the group without MetS after exclusion of patients taking statins or fibrates (50.52 ± 9.97 and 48.90 ± 8.65. years, p = 0.40) or based on sex distribution (42.86% and 50% of women in the MetS group and group without MetS, respectively, p = 0.62).

Figure 1 shows that 59 patients with MetS had higher levels of UA when compared to 34 controls (mean 6,03 ± 1.80 mg/dL vs. 4,64 ± 2.00 mg/dL, respectively, p < 0,0001). They also had a significantly higher level of CRP, median 3.8 (2 - 8.35) and 1.25 (0.62 - 2.17), p < 0,0001. ESR was similar between the groups, with a median of 10 (5 - 24) mm in the MetS group and 10 (5 - 15) mm in the first hour in the group without MetS, p = 0.22.

Figure 1: C-reactive protein and uric acid levels in subjects with and without metabolic syndrome.

*: Miligrams/liter, **: Miligrams/deciliter, #: Metabolic Syndrome.

Logistic regression showed an association of UA (OR = 1.98, 95%CI = 1.36 - 2.98, p = 0.0004) with MetS. When adjusted for treatment with diuretics (13 patients), the association remained significant (OR = 2.01, 95% CI = 1.36 - 2.97, p = 0.0005). Analysis

adjusted for overweight/obesity and including both UA and CRP levels also showed a significant association between UA (OR = 1.94, 95%CI = 1.25 - 3.01, p = 0.0029), CRP (OR = 1.53, 95%CI = 1.12 - 2.09, p = 0.007) and MetS.

We did not observe a link between UA, CRP, or ESR and any chronic musculoskeletal pain site or diseases described in this study (data not shown). None of the participants had clinical features of gout, ankylosis spondylitis, rheumatoid arthritis, or other autoimmune rheumatic disease.

Discussion

We observed an increased rate of chronic musculoskeletal pain at any anatomic site in patients with MetS compared with individuals without MetS, particularly in weight-bearing sites, such as the lower back, hips, knees, ankles and feet. The factors that were adjusted for overweight/obesity showed significant associations between MetS, LBP and KOA; however, the association between chronic MSK-related pain at any site, PF and fibromyalgia was no longer significant. Furthermore, no association was observed between any laboratory parameters and MSK disease. Nevertheless, a positive correlation was observed between UA, CRP levels, and MetS before and after adjustment for overweigh/obesity.

Goodson., *et al*. (2013) [18] reported an association between chronic pain and MetS (OR = 1.42, 95%CI = 1.24 - 1.62), adjusted for age and sex, and multivariate analysis identified age, sex, smoking, dyslipidemia, obesity, and waist-hip ratio as independently associated with chronic pain. In our study, the association between MetS and chronic musculoskeletal pain became non-significant after adjustment for overweight/obesity. In this regard, studies have demonstrated that obesity has implications in several MSK diseases, such as soft tissue conditions, OA and inflammatory arthritis [19]. After adjustment for age, sex, educational and physical activity levels and depressive symptoms, a Brazilian study showed that obesity and abdominal obesity were associated with musculoskeletal pain at any anatomic site and multisite musculoskeletal pain, with a dose-response relationship observed with increased levels of obesity [20]. Moreover, there is evidence of a higher prevalence of chronic musculoskeletal diseases affecting the lower limb at one or more locations in overweight (OR = 1.6, 95%CI = 1.3 - 1.9) and obese (OR = 2.5, 95%CI = 1.9 - 3.2) individuals [21].

Obesity has also been associated with tendinopathy, particularly Achilles tendinopathy and PF, in which increased weight is associated with increased load on these tendons during standing and walking [22,23]. One study showed that plantar fascia and Achilles tendon thickness were significantly increased on ultrasound in patients with diabetes compared with individuals with normal glycemic levels and normal weight. They also found a correlation between BMI and plantar fascia thickness (r = 0.749, p < 0.0001) [24]. These observations support our findings in relation to PF, since we showed that the significance of the association between PF and MetS disappeared after adjustment for overweight/obesity.

One study described an OR of 5.56 (95%CI = 1.25 - 24.74) for women with fibromyalgia [26] who met the 1990 ACR criteria [25] for MetS compared with healthy controls with a similar BMI. They also described a statistically significant association between all factors associated with MetS in patients with fibromyalgia when compared with controls [26]. On the other hand, our study showed a higher rate of fibromyalgia in patients with MetS; however, the association was not significant when values for overweight/obese subjects were included in the logistic regression. Indeed, it has been shown that fibromyalgia is associated with obesity and low-level physical activity in women [27] as well as high levels of leptin, with a positive correlation with BMI [28].

Regarding hip pain, a recent study on 119 patients with MetS and 235 controls demonstrated that hip OA defined by magnetic resonance imaging (MRI) was not associated with MetS [29]. Also, a systematic review concluded that the influence of obesity on the development of hip OA is moderate, and the association is stronger in studies in which the diagnosis is based on both clinical symptoms and radiological criteria than in those based only on X-ray results [30]. Additionally, chronic, work-related, restricted hip pain is associated with obesity in men (OR = 3.15, 95%CI = 2.07 - 4.83) and women (OR = 3.25, 95%CI = 2.42 - 4.38) compared to the general population [31]. In our study, hip pain was more frequent in patients with MetS; however, due to the small sample size, it was not possible to adjust the analysis for BMI. Interestingly, in a study with subjects with mean BMI = 51 (8.0) kg/m^2 before bariatric surgery, significant symptomatic improvement of chronic pain after surgery and weight loss was not observed for hip pain; however, it was observed for knee, ankle, and foot pain, as well as for fibromyalgia [11].

There are multiple reports on the association between increased BMI and incidence and progression of KOA defined by imaging criteria with or without clinical symptoms [19]. It was reported that mechanical overloading causes collagen network damage and proteoglycan loss of the articular cartilage. The cartilage

matrix breakdown products lead to inflammation and transcription of nuclear factor-κB and mitogen-activated protein kinases [32]. Nevertheless, obesity-related metabolic factors, particularly levels of adipokines, such as leptin, adiponectin and resistin, are recognized to be more important factors than mechanical overload in the development of KOA. These adipokines could influence OA by direct local joint degradation or through control of the local inflammatory process [33]. Leptin has been associated with the degree of cartilage degeneration and a synergic relationship with proinflammatory cytokines [34].

A case-control study described a significantly higher prevalence of KOA in 60 individuals with MetS (83.3%) than in controls, with a statistically similar BMI (73.3%), p = 0.034 [35]. In our study, we were not able to balance the groups in terms of BMI; however, the adjustment for overweight/obesity reduced, but did not eliminate, the significance of the association between KOA and MetS. A study using MRI demonstrated an association between medial knee compartment cartilage volume loss and MetS, and low HDL-C after adjustment for central obesity and BMI [36]. However, the Framingham OA study with 991 individuals reported that after adjustment for BMI, the association between KOA and all factors associated with MetS, except hypertension, became non-significant [37]. On the other hand, a study using a cohort of 16,362 participants aged ≥ 55 years without diabetes at baseline and controlled for confounders reported that the presence of hip/knee OA was a significant independent predictor of diabetes incidence [38].

The association between obesity and LBP is controversial and there is a lack of a clear dose relationship between LBP and BMI [19,39]; however, obesity is associated with the transition from acute to chronic occupational back pain [40]. One study with 1395 individuals demonstrated a higher prevalence of LBP in women with MetS than in controls (OR = 1.5, 95%CI = 1.0 - 2.5), but not in men [41]. Also, it has been reported that MetS is associated with disability due to LBP among care workers after adjustment for age, sex, job demands, intensity and duration of pain, social support, and fear of movement [42]. In a Brazilian study, LBP was associated with overweight (OR = 1.18, 95%CI = 1.02 - 1.36) and obesity (OR = 1.26, 95%CI = 1.05 - 1.53), as well as hypertension (OR = 1.42, 95% CI = 1.23 - 1.65) and high cholesterol (OR = 1.6, 95%CI = 1.34 - 1.920) when adjusted for age and education [43]. Our results showed a significant statistical relationship between LBP and MetS only after adjustment for overweight/obesity, suggesting an interaction between MetS and overweight/obesity.

Associations between UA and MetS have been consistently described in the literature [44]. A case-control study demonstrated higher levels of UA in individuals with MetS than in controls (5.70 ± 1.62 vs. 4.97 ± 1,30 mg/dL, respectively, p = 0.001), and after adjustment for age, sex, and BMI, the association of UA and MetS was still significant (OR = 2.11 [95%CI = 1.30 - 3.41, p = 0.002) [45]. The increased renal absorption of UA at the proximal renal tubules secondary to hyperinsulinemia is reportedly associated with high UA levels in MetS [46]. It has also been shown that individuals with hyperuricemia (UA > 7 mg/dL) have an increased risk of developing insulin resistance [hazard ratio (HR) = 1.36, 95%CI = 1.23 - 1.51] and prediabetes (HR = 1.25, 95%CI = 1.04 - 1.52) [47]. However, we did not find an association between UA and MSK pain, or any other specific disease included in our study. Afzal., *et al.* (2003) [48] compared two groups of 36 patients each, with and without chronic, nonspecific musculoskeletal pain, and reported that the experimental group had higher levels of UA compared with controls (p = 0.05), and female patients had a significantly lower UA excretion (p < 0.001). One study described the association of UA and KOA in women [49] and another study found an association between higher UA levels with the presence of synovitis on MRI (OR = 1.017, 95%CI = 1.007 - 1.028) and soft tissue swelling (OR = 1.008, 95%CI = 1.00 - 1.016) in individuals with KOA [50]. There is also an interesting report on the correlation between UA levels and joint space narrowing in non-gout patients with KOA, suggesting that UA could be a biomarker for OA progression [51].

The association of CRP and MetS has been demonstrated after adjustment for BMI [52] and this association is cumulative by increasing the number of factors linked with MetS [53]. Some researchers have described a relationship between radiographic OA and increased CRP; however, higher levels were observed in obese patients with OA, as well as obese patients without OA, than in non-obese patients. They concluded that the high correlation with obesity limited the use of CRP as a marker for OA [54]. Few studies have addressed the link between CRP and non-specific LBP, and none showed an association between CRP and chronic LBP, only with acute pain [55].

The cross-sectional design and the small sample size of this study limited our ability to detect causal relationships between chronic musculoskeletal pain and MetS. These limitations also contributed to our inability to control other possible confounding factors, such as occupational physical demands. Another limitation is the fact that the study was conducted in a single institution, therefore generalized conclusions cannot be drown from our results.

Conclusion

In conclusion, this study adds to the growing body of evidence that MetS is linked to musculoskeletal complications and higher levels of CRP and UA. Differently from the majority of the studies that observed associations of MetS with individual musculoskeletal disease, we considered the relative frequency of musculoskeletal pain at different anatomic sites in patients with MetS. Thus, this paper described that patients with MetS have more chronic pain localized in the lower limb joints. Also, the factors that were adjusted for overweight/obesity showed significant associations between MetS, LBP, and KOA supporting that both mechanical overload and systemic factors contribute to these associations. Although the cross-sectional design and the small sample size of this study limited our ability to detect causal relationships between chronic musculoskeletal pain and MetS, the pain in these joints could impair walking, leading to a reduction in physical activity and exercise, and contribute to a cycle of weight gain and deterioration of MetS condition and musculoskeletal health [7]. Nevertheless, further prospective studies are needed to elucidate if CRP and/or UA could be associated with the progression of musculoskeletal conditions, other than gout, associated with MetS, which may provide insights into management options that addresses both, musculoskeletal diseases and MetS.

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Conflict of Interest

All the authors declare that they have no conflict of interest for this manuscript.

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