METABOLIC SYNDROME AND ITS COMPONENTS IN PRIMARY KNEE OSTEOARTHRITIS

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SUMMARY

Objectives: To determine the prevalence of metabolic syndrome in patients with primary knee osteoarthritis and the associations of its components with grades of osteoarthritis. Subjects and methods: 582 patients with primary knee osteoarthritis according to the criteria of American College of Rheumatology 1991 were included. Metabolic syndrome was defined by using the International Diabetic Federation 2005 criteria. This is a cross-sectional study. Results: A total of 582 patients (86.6% women), mean age was 56.7 ± 8.2 years, prevalence of metabolic syndrome was 51.7%. The Kellgren-Lawrence grades 1, 2, 3, 4 were 34.7%, 55.4%, 63.5%, 72.7%, respectively. In late stage, prevalence of metabolic syndrome, high waist circumference, hypertension, high triglycerides, high fasting glucose were 64.2%, 83.1%, 75.0%, 64.9%, 51.4%, and significantly higher than in early knee osteoarthritis 47.5%, 67.3%, 60.6%, 53.7%, and 41.0%, respectively. Conclusions: Prevalence of metabolic syndrome among knee osteoarthritis was 51.7%, and increased with Kellgren-Lawrence grades. Therefore, management of metabolic syndrome should be empathized in patients with knee osteoarthritis to reduce their risk of cardiovascular diseases.

** Keywords: Knee osteoarthritis; Metabolic syndrome; Kellgren-Lawrence grades.*

INTRODUCTION

Knee osteoarthritis is the most common chronic disease, affects synovium, ligaments, tendons, muscle, and subchondral bone... Recently, studies revealed that metabolic factors might contribute substantially to knee osteoarthritis (KOA) pathogenesis [1].

Metabolic syndrome (MetS) is characterized by insulin resistance, visceral obesity, atherogenic dyslipidemia, and hypertension. Of these components, insulin resistance and visceral obesity seem to be absolute requirements for its definition [2]. Previous studies had shown that the prevalence of MetS and its components are higher among OA patients than in normal individuals [1]. There are no studies on the prevalence of MetS and its components in patients with KOA in Vietnam. The aim of this study was: *To determine the prevalence of metabolic syndrome in patients with primary KOA and its association with grades of KOA.*

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SUBJECTS AND METHODS

1. Subjects.

This study was carried out on Outpatient Department in the Bachmai Hospital between 01 - 2014 and 04 - 2017. This is a cross-sectional, descriptive hospital-based study on consecutive adults satisfying the ACR 1991 clinical criteria for KOA. Patients with inflammatory arthritis, previous knee surgery, congenital abnormalities of the knee and hip, post-traumatic injury to the knee… and those who declined to take part in the study were excluded. The hospital ethical committee approved the study; written informed consent was obtained from patients. The sample size was estimated based on previous community prevalence of KOA of p = 0.5 [3], d = 0.05, $\propto$ = 0.05, z = 1.96 using the formula $n = z^2pq/d^2 = 384$, we selected 582 patients.

2. Methods.

** Clinical assessment:*

Data was collected using a medical history, clinical examination, laboratory findings, and radiographic findings. The IDF 2005 criteria were used to identify patients with MetS [2]. Patients were with central obesity defined as waist circumference (WC) ≥ 90 cm in male and ≥ 80 cm in female plus two of the following: triglyceride ≥ 1.7 mmol/L, high density lipoprotein cholesterol (HDL-C) < 1.03 mmol/L in men and < 1.29 mmol/L in women, blood pressure (BP) ≥ 130/85 mmHg, or fasting glucose ≥ 5.6 mmol/L. Anteroposterior and lateral radiographs of the knees were taken, classification by using the Kellgren-Lawrence (KL) criteria from grade 1 to 4. Defined KL grade 1 and 2 as early stage, KL 3 and 4 as late stage.

** Statistical analysis:*

Data was analyzed using SPSS version 20.0 software. Normality of continuous variable was assessed using the Kolmogorov - Smirnov test. Normally distributed variables were expressed as $\overline{X}$ ± SD. The average values were compared between the two groups by t-test and the ratios were compared by χ^2 test. Value of p < 0.05 was considered statistically significant.

RESULTS

1. Demographic characters.

Table 1: Demographic data in KOA patients (n = 582).

Variables	n (%) or $\overline{X}$ ± SD
Age (years)	56.7 ± 8.2
Sex (female)	504 (86.6)
BMI (kg/m^2)	24.0 ± 3.0
BMI 23 - 24.9 (kg/m^2) (overweight)	157 (27.0)
BMI ≥ 25 (kg/m^2) (obesity)	201 (34.5)

Mean age was 56.7 ± 8.2 years. Prevalence of female (86.6%) was higher than male. Prevalence of overweight and obesity (61.5%) was higher than the other group (BMI < 23 kg/m^2).

2. Prevalence of MetS and its components in KOA.

Table 2: Prevalence of MetS and its components in stages.

Items	Total (n = 582)	Late (n = 148)	Early (n = 434)	p OR (95%CI)
	n (%)	n (%)	n (%)	
MetS*	301/582 (51.7%) Female 279/504 (55.4%)	95 64.2	206 47.5	< 0.001 2.0 (1.4 - 2.9)
High WC*	415 71.3	123 83.1	292 67.3	< 0.001 2.4 (1.5 - 3.9)
Hypertension*	374 64.3	111 75.0	263 60.6	< 0.05 2.0 (1.3 - 3.0)
High fasting glucose*	254 43.6	76 51.4	178 41.0	< 0.05 1.5 (1.04 - 2.2)
High triglycerides*	329 56.5	96 64.9	233 53.7	< 0.05 1.6 (1.1 - 2.3)
Low HDL-C	314 54.0	83 56.1	231 53.2	> 0.05 1.1 (0.8 - 1.6)

Prevalence of MetS was 51.7% and MetS was seen 55.4% in female group, higher than men (44.6%). Prevalence of MetS, high WC, hypertension, high fasting glucose, high triglyceride in late stage were significantly higher than early with ORs were 2.0, 2.4, 2.0, 1.5, and 1.6, respectively.

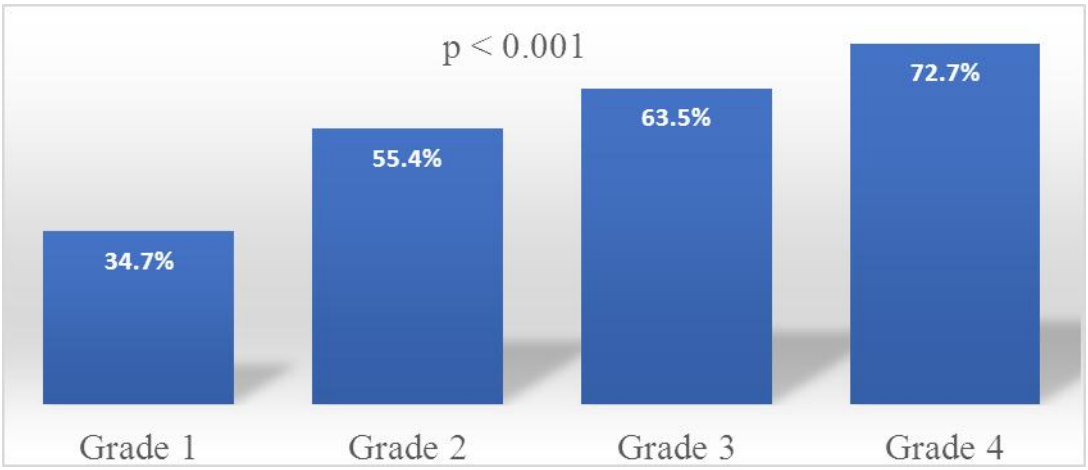

Figure 1: Prevalence of MetS in KL grades (n = 582).

Prevalence of MetS in KL grades 1, 2, 3, 4 were 34.7%, 55.4%, 63.5%, 72.7%, respectively. Prevalence of MetS increased with KL grades increased.

DISCUSSION

Well established risk factors for KOA include aging, obesity, and female gender. Due to the strong correlation of age and KOA, KOA has commonly been viewed as a part of "normal aging". However, the onset of KOA can begin by age forty and the incidence of disease levels off in older age groups. KOA is not an inevitable consequence of aging but instead, age related changes may make the joint more vulnerable to joint damage [4]. The mean age of 582 KOA patients in our study was 56.7 ± 8.2 years, the same as Hussein N.A (54.64 ± 7.7) [5]. Sex is one of unchangeable risk factors for KOA. There were 504 female (86.6%) (*table 1*), similar to Hussein's result (85.7%) [5]. The rate of female KOA was higher than male, especially in post-menopause, possibly due to estrogen deficiency and imbalance bone turnover associated with leptin.

Obesity is a widely acknowledged and changeable risk factor for KOA. The relationship between obesity and KOA has conventionally been thought to operate through a mechanism of increased mechanical loading across the joint. However, not all obese individuals have KOA nor are all persons with KOA obese. This combined with observed associations between obesity and OA in non-weight bearing joints have prompted new hypotheses about the role of adipose tissue in joint damage related underlying inflammatory component in both obesity and OA. Adipocytes secrete adipokines (leptin, adiponectin…) which lead to synovial inflammations, cartilage deformations and remodeling of the bone matrix which may be an incentive or predictor for the development and severity of OA. Our patients (61.5%) had BMI ≥ 23 kg/m^2 with a mean BMI was 24.0 ± 3.0 kg/m^2 (normal range: 18.5 - 23.0 kg/m^2) (*table 1*).

MetS was seen in 51.7% of our patients using the IDF criteria, 55.4% of the female higher than 28.2% of the male (OR was 3.2 and 95%CI from 1.9 - 5.3 ($p < 0.001$) (*table 2*). Studies have shown that MetS in OA ranges from 20 to 59% [2, 3, 6] and frequency higher in patients with OA than in populations without OA [1]. This wide range in frequency may be attributed to the differences in terms of the criteria used in classifying patients with MetS and KOA.

Central obesity is a key factor in MetS. The study by Vasilic-Brasnjevic [7] showed that obesity and abdominal obesity were strongly related to KL grades. In our study, 83.1% high WC was seen in late stage, higher than early (67.3%).

Regarding the components of MetS, 64.3% of our patients were hypertensive. Lanas reported a similar frequency of 57.6% after evaluating a large cohort study of OA patients [8]. They showed that OA and hypertension coexist by sharing common risk factors such as aging, obesity, and sedentary lifestyle. Hypertension associates with OA through subchondral ischemia, which can compromise nutrient exchange into articular cartilage, trigger bone remodeling.

Diabetes mellitus had been considered to a risk factor for KOA. In a meta-analysis involving 645,089 OA patients, prevalence of diabetes mellitus was 14.4 ± 0.1% [9]. Rate of high fasting glucose in our patients was 43.6%. Hyperglycemia and OA interact at both local and systemic levels, local effects of oxidative stress and advanced glycation end-products are

implicated in cartilage damage, whereas low-grade systemic inflammation accumulation and contributes to a toxic internal environment that can exacerbate OA.

The lipid profile of our patients was remarkable, with 56.5% having serum triglyceride above 1.7 mmol/L, low HDL-C (54.0%), our results were the same as Bui's (52.4%). Ectopic lipid deposition in chondrocytes induced by dyslipidemia might initiate OA development, exacerbated by deregulated cellular lipid metabolism in joint tissues [10]. Prevalence of MetS in KL grade 1, 2, 3, 4 was 34.7%, 55.4%, 63.5%, 72.7%, respectively. We found that prevalence of MetS increased with KL grades increased (*figure 1*). Prevalence of MetS in late KOA group was higher than that of mild with the OR was 2.0 and 95%CI from 1.4 to 2.9 ($p < 0.001$) (*table 2*). Our result was coincidence with Vasilic-Brasnjevic S's research [6]. This means that when the OA is progressive, the patients have more comorbid conditions such as hypertension, hyperglycemia, dyslipidemia.

CONCLUSION

The cross-sectional design of the study has limitations in terms of establishing any causal relationship between MetS and KOA. This study shows that prevalence of MetS among KOA patients was 51.7%, increased with KL grades. Prevalence of MetS in female was higher than KOA male group; prevalence of MetS, high WC, hypertension, high triglycerides, high fasting glucose in late KOA group were higher significant than early. Therefore, management of MetS should be empathized in patients with KOA to reduce their risk of cardiovascular diseases.

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