Factors Affecting Radiographic Progression of Knee Osteoarthritis

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ABSTRACT

Aim: to determine factors affecting radiographic progression of knee OA.

Methods: a cross sectional study comprise of patients with OA of knee joints. Kellgren and Lawrence (K-L) grading scale was used to evaluate the radiographic progression of knee OA. All of the patient were noted the demographic data including age, gender, duration of illness, body mass index and bone mass density. Lunar DEXA was used to measure total body-BMD (T-BMD), total bone mineral content (T-BMC) and legs-BMD (L-BMD).

Results: about 91 patients was enrolled in this study There were significant differences of body mass index (BMI) (p=0.01) between subgroup of knee OA grading. OR between grade 2 and grade 4 for BMI score highest tertile and BMI score lowest tertile were 5.26 (95%CI 0.59-47.20). There were no significant differences for age, sex, and duration of illness, T-BMD, L-BMD and T-BMC between subgroup of knee OA grading. There were a tendency of correlation on increased of age (OR 2.17, 95% CI 0.56-8.41), log-duration of illness, percentage of T-BMD (4 % between grade 2 and 4) with increased of knee OA grading. There was a tendency decrease of percentage of L-BMD (of 7%) between grade 3 and 4.

Conclusion: in this cross sectional model, BMI was significantly associated with increased of knee OA grading or it could be said that BMI was risk factors for radiographic progression of OA. Subjects who already have knee OA and also have high BMI must be careful about the progressivity of their knee OA.

Key words: knee osteoarthritis, radiographic progression, risk factors, BMI

INTRODUCTION

Knee osteoarthritis (OA) is one of the major causes of pain and physical disability in elderly 1. A recent World Health Organization report on the global burden of disease indicates that knee OA is likely to become the fourth most important cause of disability in women, and the eighth most important cause in men2.

Several investigations of risk factors for knee OA have been reported previously. Most of them were a cross-sectional studies on disease prevalent, using radiographic criteria to define cases with OA. Some studies have attempted to differentiate between incidence from progression of OA. They have shown that important risk factors for incidence of knee OA could be divided in to systemic and local mechanical injury. The systemic risk factors include etnic3, age4, gender4, obesity4,5, genetics factors6,7, nutrition8, hormon replacement therapy9, and bone density10. The local mechanical factors include previous knee injury11, selected physical activities12, sports13, joint alignment14, joint laxity15 and proprioseptic16. As a consequence, much of the emphasis in the development of possible preventive strategies has been on protecting the knee joint from mechanical injury and stress.

The risk factors for progression of knee OA include obesity17, joint effusion18, joint alignment19, knee injury20, and low bone density21,22. Several strands of indirect evidence suggest that the incidence and progression of radiographic knee OA may involve different processes.

The knowledge of risk factors for progression of knee OA make possibility to build a more effective public health strategy that preventing progression to severe joint damage than attempting to prevent the initiation of disease.

The objective of this study is to explore several factors affecting radiographic progression of knee OA.
METHODS

This study is a cross sectional study on a group of patients with OA of knee joints. OA of knee joints was diagnosed on the basis of clinical symptoms, physical examination and radiological findings according to the American College of Rheumatology (ACR) Criteria for Classification of OA of the knee. We used Kellgren and Lawrence (K-L) grading scale to evaluate radiographic progression of knee OA\(^1\). Each joint was classified according to a 5-point scale (0 = normal, 1 = doubtful OA, 2 = minimal OA, 3 = moderate OA, 4 = severe OA) based on the degree osteophyte formation, joint space narrowing, sclerosis, and joint deformity. The patients who had grade 0 and 1 were excluded. Informed consent was obtained from all participants. The procedures followed were in accordance with the principles of the Declaration of Helsinki in 1975, as revised in 1983.

Data Collection

All of the patient were noted the demographic data including age, gender, duration of illness, body mass index which was calculated as the ratio of weight (kg) and the square of height (m), and bone mass density.

Bone Mass Density

Bone mass density (BMD) was measured by Dual Energy X-ray Absorptiometry (Lunar DEXA, Lunar Corp, Madison, WI) for total body-BMD (T-BMD), total bone mineral content (T-BMC), legs-BMD (L-BMD).

Variables

The independent variable was the grading scale of radiographic progression of knee OA (K-L grading) of the most severely diseased knee. The dependent variable was the all of the variables noted on demographic data, for the bone mass density included T-BMD, T-BMC, and L-BMD.

Statistical Analysis

Distribution analysis showed duration of illness were not normally distributed and thus were log transformed to obtain normal distribution before statistical analyses. A comparison of variables between subgroups of OA knee grading was performed by using Analysis of variance (ANOVA), p values <0.05 were considered significant.

RESULTS

There were 91-study subject satisfied the inclusion criteria of this study. The majority of the patients were female (69.2 %) and the mean of the age were 59.68 ± 8.03 year. There were 47 patients of knee OA grade 2, 33 patients on grade 3 and 11 patients on grade 4. The mean of duration of illness was 44.11 ± 57.99 months. Most of the patient had high body mass index (overweight and obese). The mean value T-BMD was 1.079 ± 0.1022 g/cm\(^2\), L-BMD was 1.0380 ± 0.1215 g/cm\(^2\), and T-BMC was 8120.59 ± 163.63 g. (Table 1)

From the ANOVA test, there were significant differences of body mass index (BMI) between subgroup of knee OA grading (p= 0.01), further explore from this test revealed the significance was between grade 2 to 4 and grade 3 to 4. This differences was not significant for age, log duration of illness, T-BMD, L-BMD and T-BMC between subgroup of knee OA grading (Table 2). From Chi-square test, there was also no significant difference of gender between subgroup of knee OA grading (Tabel 3).

If the patient was devided into 2 group according to their age with the cutt off point of 60 years , where the patient with the age < 60 years as one group and ≥ 60 years as the another group, calculation of the odds ratio (OR) between grade 2 versus grade 3 (equal with increased 1 grade) revealed 1.68 (95% CI 0.68-4.13), and grade 2 versus grade 4 ( equal with increased 2 grade) was 2.17 (95% CI 0.56-8.41). Although the differences between those subgroup was not significant, there was a tendency increased of OR (Tabel 4).

Odds ratio for gender between subgroup of knee OA revealed for grade 2 versus grade 3 was 1.77 (95% CI:0.65-4.13) and for grade 2 versus grade 4 was 1.55 (95% CI 0.35-3.47). There was no tendency increased of OR between those subgroup (Tabel 5).

If the patient was divided into 3 group of BMI as follows : BMI < 22.7 kg/m\(^2\) as lowest, BMI ≥ 22.7 - ≤
Although there was no significant differences between the mean of log duration of illness between subgroup of knee OA, but from figure 1. there were a tendency to show a correlation between increased of grade knee OA with log duration of illness.

From figure 2 which was used the percentage of value of total-BMD to the BMD of young adults, there is also a tendency of correlation between increased of BMD percentage with increased of the grade of knee OA, especially from grade 3 to grade 4. The difference between grade 2 and grade 4 was about 4 %. It also a surprise if we looked for the percentage legs BMD in figure 3, there was a tendency decrease of BMD between grade 3 and grade 4. The difference was about 7 %.

25.4 kg/m$^2$ as middle, and BMI >25.4 kg/m$^2$ as highest. Calculation for OR between grade 2 versus 3 (increased 1 grade) for the lowest to highest was 1.12 (0.36-3.49), and OR between grade 2 versus grade 4 (increased 2 grade) for the lowest to highest was 5.26 (0.59 – 47.20), there was a tendency increase of 5 times between those subgroup (table 6).
Knee OA development increased by 20% per 5-year age increase. Age did not affect the risk of incident of knee OA in longitudinal Framingham study in which the mean age of subjects at baseline evaluation was 70.5 years. Only 2 longitudinal studies from several studies was confirmed the influence of age on the radiographic progression of knee OA, it was study from Schouten et al (OR 3.8; 1.1 to 13.4) and Ledingham et al (OR 1.18; 1.01 to 1.14). In our study although there were no significant influence of age on progression of knee OA in ANOVA test, the OR for increased of 2 grades was nearly twice with increased of 1 grade. This finding showed the possibility of influence of age on progression of the disease, but it must be careful to make an interpretation, because this study was a cross-sectional study.

The influence of gender on knee OA development may be mediated through multiple routes, including hormonal influences on cartilage metabolism, gender variation in the consequences of injury, gender differences in the mechanical environment of the knee (e.g. varus-valgus laxity). Our study confirmed with other longitudinal study that women develop knee OA more frequently. Although gender was confirmed as risk factor for incident of the knee OA, there were no studies found the effect of gender on progression of knee OA, the previous study demonstrate similar findings with our result.

There were no longitudinal studies that explore the impact of duration of illness on incident and progression of knee OA. Only one study found that patient underwent Total Knee Replacement (TKR) began symptom of knee OA 16 years before TKR. Patient underwent TKR was 2 years older than those undergoing Total Hip Replacement (THR). Men developed symptom of knee OA an average of 5 yr before women. Our finding found that the duration of illness was not affect the radiographic progression of OA, although there was a tendency correlation between those factors. In our opinion, it is still needed another longitudinal study to confirm such finding.

A subsequent Framingham study (mean age of subjects, 70.5 years) in subjects free of disease at baseline assessment confirmed that higher BMI increased the risk of incident of OA (OR, 1.6 per 5-unit increase; 95% CI, 1.2 to 2.2) and weight change was directly correlated with risk of OA (OR, 1.4 per 10-pound change in weight). In a longitudinal study of the Chingford population, belonging to the top BMI tertile was associated with an increased risk of incident of knee OA (OR, 2.38; 95% CI 1.29 to 4.39). There were some study confirmed the influence of BMI on progression of knee OA. Study conducted by Schouten et al found that the OR between fourth vs. first quartile was 11.1 (3.3 to 37.3). Spector et al found over one third of middle aged women with unilateral disease will progress to bilateral knee OA within 2 years. Cooper et al found that BMI influenced the radiographic progression of knee OA, BMI middle (22.7 –25.4 kg/m²) will give OR 2.3 (0.8-6.4) compare to lowest BMI (<22.7 kg/ m²). BMI Highest (>25.4 kg/ m²) will give OR 2.6 (1.0-6.8) compare to lowest BMI. Our finding similar with those studies, BMI was significantly associated with the increased of knee OA grading, especially between grades 2 to 4, with the OR 5.26 for the BMI highest
tertile compared to the BMI lowest tertile. We concluded that BMI was risk factors for radiographic progression of OA.

Radin et al\textsuperscript{27} postulated that increased bone mass and thickening of the subchondral bone plate would cause stiffening of the bone, as a consequence, result in cartilage destruction on repeated loading. In a normal healthy joint, it is postulated that the bone assist in high load tolerance by deformation and the formation of micro fractures, but as it thickens the shock absorbing capacity is reduced and shear stresses increase in the articular cartilage, eventually leading to cartilage fibrillation.

Both the Framingham and Chingford studies found that subjects with the knee OA have 5% to 10% higher BMD than those without knee OA\textsuperscript{28,29}. In the Framingham study, women with K-L grade 1 and 2 of the knee had 5% to 9% higher femoral neck BMD than did those with K-L grade 0, with adjustment for age, BMI and smoking\textsuperscript{29}. Women in the Chingford study with knee OA had 7.6% and 6.2% higher BMD at lumbar spine and femoral neck sites, respectively, than did control subjects, with adjustment for age and BMI\textsuperscript{28}. A recent prospective study has confirmed this relationship by showing a higher bone density increases the risk of incident radiographic knee OA in older women\textsuperscript{27}.

On the other hand Chingford longitudinal study found that among women who already have knee OA, those with low BMD and who are losing bone faster exhibit more rapid progression of radiographic changes than those with high BMD and who are losing bone more slowly\textsuperscript{21}, confirming the previous finding from the Framingham prospective study\textsuperscript{22}.

With ANOVA test, this study do not find any significant correlation between T-BMD, L-BMD and T-BMC with the radiographic progression of knee OA, but there a tendency increased of percentage of BMD between grade 2 and 4, the difference was about 4 %. This finding was rather different with other study.

On the other hand the tendency of decreased of percentage legs-BMD between grade 3 and 4 was support the theory that patient with low BMD would have more rapid progression of knee OA. Dequeker et al\textsuperscript{10} tried to explain this situation and said that the increased loss of bone in this location due to local disability of the joint.

This study was a cross sectional study which some of the variables (e.g. T-BMD, T-BMC and L-BMD) were not statistically different between subgroup of K-L grading of knee OA, a longitudinal study was needed to confirm this result.

**CONCLUSION**

In this cross sectional model, BMI was significantly associated with increased of knee OA grading or it could be said that BMI was risk factors for radiographic progression of OA. Subjects who already have knee OA and also have high BMI must be careful about the progressivity of their knee OA.

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**REFERENCES**