



# Using Generalized Estimating Equations to Compare the Effect of Two Methods in the Treatment of Knee Osteoarthritis

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## Authors' contributions

*This work was carried out in collaboration between all authors. Authors AS and AB performed the statistical analysis. Author EB designed the study, wrote the protocol and managed the analysis of the study and approved the final manuscript. Author KKK gathered the data. All authors read and approved the final manuscript.*

## Article Information

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## ABSTRACT

**Background:** We aimed to compare the effect of two different treatment methods on severity pain in patients with severe knee osteoarthritis.

**Materials and Methods:** A total of 40 female patients with severe knee OA were randomly assigned into two parallel groups: An intervention group received standard physiotherapy treatment accompanied by knee traction, and a control group received only standard physiotherapy treatment. Both groups were subjected to a follow-up period of 5 weeks (10 times). Generalized Estimating Equations model was used to estimate the odds of a pain as a function of the groups adjusted for potential confounders.

**Results:** Using intervention as the reference group, the pain odds ratios was 3.17 (95% CI: 1.24—8.09) for control group.

**Conclusion:** We would recommend using of the common physiotherapy treatment accompanied by knee traction instead of common physiotherapy procedure in patients with severe knee OA.

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## 1. INTRODUCTION

Osteoarthritis (OA) is one of the most disabling degenerative diseases affecting in elderly [1] and is considered as one of the five diseases that affected in disability in elder men and women [2]. OA is relatively common in Europe and has been reported to be a major disabling disease in the western world, affecting 10% of men and 18% of women over the age of 60 [3]. Global statistics show that more than 100 million people worldwide suffer from OA [1,2], which is one of the most common causes of disability in the world [3,4]. The most common type is knee OA [1,2]. The disease causes pain, morning stiffness, limited joint movement and lead to severe disability.

Many patients with severe knee OA are denied access to quality treatment. Studies show that 32% of people who suffer from OA need help and support in dealing with this disease for life perform daily activities, and to improve their quality of life [4].

Patients with severe knee OA complain of pain severity and disability. Studies have shown that exercise and stretching positively affect on the disease and can reduce the severity of knee OA pain [5].

Treatment available for this disease can be divided into two categories: Conservative treatment and surgical treatment. Most conservative treatments are associated with poor outcome. New and effective treatment of this disease is surgical joint traction [6,7]. Due to the joint effect of stretching as one of the methods mobilization, drawing of non-surgically treatment is considered to be one of the treatment of severe knee OA. Therefore, the focus of treatment of knee OA is the management of its symptoms with emphasis on self-management therapies such as exercise [8] and complementary and alternative medicine (CAM) therapies, such as massage [7,9].

Severe knee OA increases with the increase in age. Less than half of people with the severe knee OA are treated, so they need to spread awareness about the disease, its prevention and rehabilitation society [8].

Treatment of joint replacement surgery is a common treatment for this group of patients which causes the costs imposed on society and

the exclusion of patients with a number of activities over a life time. In addition, some patients due to age and poor physical condition do not allow this operation.

Physical tension in the joint as a common method used to reduce pain in spine disorders. Also pulling the knee joint as one of the techniques of mobilization is commonly used [7,8-11].

Due to the harmful effects of the disease on patients, it seems that finding a better treatment is necessary. We aim to compare the pain of severe knee OA in patients that were treated by two methods: 1. common physiotherapy treatment; and 2. common physiotherapy treatment accompanied by knee traction. In this illustration we model the relationship between a correlated binary response variable (pain severity) and treatment method, controlling for age and body mass index by using generalized estimating equations (GEE).

## 2. MATERIALS AND METHODS

The assignment of treatments to participants was performed based on random mechanism to compare the pain severity after treatment therapy in patients with severe knee OA (grade 3 & 4 on the Kellgren-Lawrence grading scale). A total of 40 female patients with severe knee OA were recruited from two hospitals in Iran, the 17 Shahrivar Clinic and the Clinic of Rehabilitation Sciences and Physiotherapy. Patients were randomly assigned into two parallel groups: An intervention group received standard physiotherapy treatment accompanied by knee traction, and a control group received only standard physiotherapy treatment. Both groups were subjected to a follow-up period of 5 weeks (10 times). The outcome of this trial was the evaluation of the level of pain (high/low) after treatment which was assessed by visual analog scale. The research protocol has been approved by the Ethic Committee of the Shahid Beheshti University of Medical Sciences, and each patient was asked to provide informed consent. Exact details about gathering data has been mentioned in a study [12].

### 2.1 Statistical Analysis

Since responses were correlated, the Generalized Estimating Equations (GEE) model,

which takes into account the correlated nature of responses, with a logit link and autoregressive correlation structure was used to estimate the odds of a pain as a function of the groups adjusted for age and body mass index. We looked specifically for the group interaction, and we excluded the non-significant terms. The results are presented as the odds ratio and its 95% CI. All analyses were carried out by using SAS software Package, version 9.1.

### 3. RESULTS

At the baseline, the mean BMI were 30.79kg/m<sup>2</sup> (SD=6.14) for intervention and 32.25kg/m<sup>2</sup> (SD=5.57) for control group. The mean age for intervention and control group were 61.25(SD=6.8) and 61.20(SD=8.6), respectively.

We started by fitting a preliminary GEE model including only group to observe the influence of the potential confounders on pain severity. Unadjusted pain odds ratio was 3.01 (95% CI: 1.24-7.30) for control group.

In GEE model controlling for age and body mass index, our test of interaction by group showed that the association between age and pain and between pain and body mass index were not different among groups. In this model, the odds of pain decreased with increasing age: Pain odds ratios was 0.93(95% CI:0.88-0.99) for age. We infer that a 1-year increase in age has 7% decrease among patients in the odds of pain. Comparing two models, we found that the pain odds ratio in patients increased after adjustment for confounding variables. Using intervention as the reference group, the pain odds ratios was 3.17 (95% CI: 1.24—8.09) for control group.

### 4. DISCUSSION

In this clinical trial study the GEE approach was used to carry out logistic regression for correlated dichotomous responses. In the first model (without confounders), unadjusted pain odds ratios was 3.01(95% CI: 1.24-7.03) for control group. Furthermore, we were able to adjust for covariates that might be important confounders in this association. After adjustment for confounding variables, an association was also observed between treatment group and pain. Adjusted pain odds ratios was 3.17(95% CI: 1.24-8.09) for control group. Comparing two models, the influence of the potential confounders included in analysis can be

observed. Unadjusted OR of 3.01 is changed to OR of 3.17 for control group. The added knee stretch to common physiotherapy in patients with severe knee OA, decreased the level of pain.

The etiology of OA is multifactorial. Studies showed that OA onset and progressing are mediated through biomechanical forces acting across the joint and the failed repair of damage caused by excessive mechanical stresses and loading on joint tissues. The negative intra-articular pressure caused by the stretch application not only decrease the subchondral bone, but also improve the exchange of substances between the articular cartilage and synovial fluid and then the trophic situation of articular cartilage may be improved. Better performance of articular cartilage can reduce the pressure on the subchondral bone, and thereby reduce pain and increase range of motion in patients. Inability to repair structural damage in knee OA that caused by excessive stress on the joint cartilage in OA symptoms and this issue, is not considered as the important cause of biomechanical changes in subchondral bone. If the excessive pressure removed appropriately from affected joint then other therapeutic approaches, such as pharmacotherapy might be unnecessary [13].

Notice that the high pressure and abnormal tension is the factor for onset and progressing of OA. So the tension reduces symptoms in patients, through the temporary relief of mechanical stress on their joints. That is consistent with the results of different treatments such as weight loss, in soles inside the shoes, knee braces, surgical osteotomy and stretch joint [13,14].

Using stretch surgically by means of the fixed external tools increases joint space between a few months and reduces the mechanical stress on the bones around the hip joint. After removal of immobilization devices, it increases the distance between the joint surfaces and reduces density of the subchondral bone and thereby storage of growth factors that are effective in cartilage repair is provided. The research conducted on animals showed a partial restoration of the articular cartilage. After using traction, subchondral bone with low-density absorbs the more pressure and causes the less pressure on the cartilage [6,7,15-17].

Felson et al. [18] reported that 5 kg loss in body weight can reduce more than 50% risk of

developing OA. We did not find a statistically significant association between body mass index and pain.

Our findings are subject to several limitations. The sample size is not large. This should be confirmed by further longitudinal studies with large sample size. All participants in our study were female.

Clinical trial study is strength of our study, which means that we can draw definitive conclusions concerning the direction of causality.

## 5. CONCLUSION

In conclusion, we would recommend using of the common physiotherapy treatment accompanied by knee traction instead of common physiotherapy procedure in patients with severe knee OA.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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