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Knee Osteoarthritis Functional Classification Scheme – Validation of Time Dependent Treatment Effect. One Year Follow-Up of 518 Patients

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Abstract

Objective: The purpose of the current study was to validate time dependent changes of a novel functional classification for patients with knee osteoarthritis (KOA), following a home-based biomechanical treatment (HBBT).

Methods: A retrospective analysis of 518 patients with KOA was conducted. All patients were classified using a novel knee osteoarthritis functional grade (KOFG) classification for KOA, based on spatio-temporal gait analysis. Patients were re-classified after 3 months and 1 year of HBBT to examine and validate this classification using time-dependant changes. The time dependent changes in the classification were compared to gold-standard self-assessment questionnaires, WOMAC and short form 36 (SF-36).

Results: The changes in KOFG were demonstrated over time, with most changes occurring after 3 months of treatment with consolidation of the effect at 12 months. For example, of 427 patients that were classified in KOFG 2-4 grade at baseline, 44.9% and 51.5% had lower (better) KOFG grades at 3 and 12 months of treatment, respectively. The changes in KOFG were validated with WOMAC and SF-36 questionnaires showing a significant correlation between KOFG changes and changes in WOMAC and SF-36. SF-36 pain sub-scale showed an improvement of 33.0% and 38.0% following 3 months and 12 months of treatment, respectively (p values <0.0001).

Conclusions: The results of the current study validate the knee osteoarthritis functional grade classification scheme as a tool to assess time dependant changes in KOA as well as its sensitivity to assess treatment effect. The KOFG can offer a more robust mode of reporting clinical results in describing the natural history and time-dependent treatment results of patients suffering from knee OA and should be considered as an additional outcome measure in future studies.

Keywords: Knee Osteoarthritis; Function; Classification; Gait

Introduction

Knee osteoarthritis (KOA) is among the most common degenerative diseases, affecting 15% of the world population, causing significant pain and functional limitation [1,2]. The risk of mobility impairments caused by KOA alone is greater than due to any other medical condition in people over 65 [3]. It leads to social, psychological and economical burdens, with substantial financial consequences [4]. It is estimated that by 2030 30% of the people over 60 and 50% of the people over 80 would suffer from KOA [5,6]. Along with the aging of the world population KOA is expected to be a great burden on the global health expense.

Several classification schemes for KOA have been proposed. The American College of Rheumatology has published clinical criteria and classification for KOA [7]. Kellgren and Lawrence have published their classification of OA based on x-ray films [8,9], which was shown to correlate with clinical function as represented in standard questionnaires [10,11]. However, x-ray based classification is lacking since it represents the disease in the knee articular surface, rather than the function of the diseased joint. Functional assessment and classification of patients with KOA is lacking, even though previous gait analysis studies have shown that KOA alters gait patterns [12-19], and that gait changes are associated with KOA disease severity [20-25]. Only one study by Elbaz et al presented a functional classification for KOA severity based on spatio-temporal gait analysis. They have found that KOA functional severity can be classified according to stride length and cadence into four distinct severity groups.

Their data showed that knee osteoarthritis functional grade (KOFG) correlated with clinical questionnaires and Kellgren and Lawrence classification [26]. This functional classification is an objective, reproducible tool to assess the actual effect of the disease on patients' function. However, this classification has not yet been validated as a tool to report time-dependant clinical outcome of KOA treatment. It is important to determine the sensitivity of such a classification as a tool to assess time-dependant changes in functional severity as well as assessing treatment effect in terms of functional severity classification.

Several methods have been proposed to treat KOA. Operative treatment includes tibial osteotomy, knee replacement – unicompartment or total knee replacement [27,28]. Non-operative treatments include nonsteroidal anti-inflamatory drugs (NSAID's) glucosamine and chondroitin supplements, physical therapy, and intrarticular injections of either steroids or hyaluronic acid [29-31]. In addition, biomechanical treatments for knee OA are also proposed with the purpose of reducing pain, improving function and halting disease progression. These treatments aim to unload the diseased articular surface by using wedged insoles, foot orthoses, special shoes or valgus braces. Other treatments have been designed to modify neuromuscular patterns, with a specific goal of improving gait patterns [32-33]. A home-based biomechanical treatment (HBBT) (AposTherapy) has been recently proposed for the treatment of KOA [34-38].

The purpose of the current study was to further validate time-dependent changes of the novel functional classification for patients with KOA. We examined changes over time in patients that were treated with HBBT for 12 months using the KOFG classification and compared them to gold-standard outcome measures, WOMAC and SF-36.

Methods

The study presented is a retrospective cohort study based on one clinic dataset (Hertzelia, Israel). After receiving ethics committee approval, we analysed the clinic's database for patients that fulfilled the following inclusion criteria: age above 18, bilateral knee osteoarthritis diagnosed by the referring physician (as defined by the American College of Rheumatology), patients that completed one year follow-up and had a complete set of clinical questionnaires and spatiotemporal gait analysis. Since this was a retrospective study the ethics committee waived the need for individual consent forms.

The initial dataset included 852 patients. Exclusion criteria were: Arthroscopy six months from beginning of treatment, neuropathy, status post cerebral vascular accident (CVA), severe back pain, fibromyalgia, oncologic disease, rheumatic arthritis, joint replacement surgery, high tibia osteotomy, and severe osteoarthritis in other joints. Final data set included 518 patients.

Patients were referred for treatment by their primary care physician. They were initially assessed by a physical therapist and completed spatio-temporal gait analysis and pre-treatment (baseline) clinical questionnaires including the short form 36 (SF-36) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). After the completion of the pre-treatment assessment, patients commenced the HBBT (AposTherapy).

The biomechanical foot-worn device was individually calibrated to each patient by a physiotherapist certified in the therapy. The principle of device calibration was to achieve minimal pain while walking (See Figure 1). For example, in KOA with medial compartment disease, as was the case for most of our patients, the pod-element under the hindfoot is shifted laterally from the neutral position.

This shifts the COP in the foot laterally, thereby reducing the magnitude of the knee adduction moment acting on the knee joint. This is done until the patient reports minimal pain during initial contact.

The forefoot pod-element is shifted medially from the baseline position until the patient reports minimal pain during mid-stance to toe-off. Once the desired alignment is achieved, the patient should report immediate pain relief while walking. Following calibration patients received home-based exercise guidelines. During the first three weeks patients were instructed to wear the calibrated biomechanical system for 30 minutes, while doing their daily activities (overall accumulating 10-15 minutes' walk).

Patients were then instructed to gradually increase their wearing time reaching 2 hours a day following 3 months of treatment. After three months, patients were encouraged to add outdoor walking, starting with 10 minutes and reaching 30 minutes a day. Patients were asked to come back to follow-up meetings at the clinical center after 3 weeks, 3 months, 6 months, 9 months and 12 months. During these follow-up meetings patients were re-assessed and, if needed, the biomechanical device was re-calibrated.

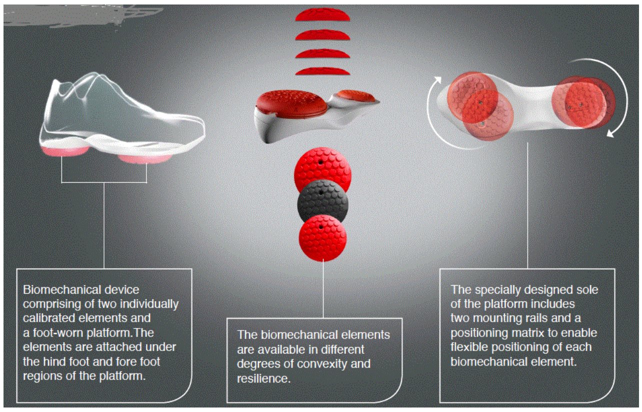

Figure 1: The Biomechanical device.

The outcome measurements included the Knee osteoarthritis functional grade (KOFG) classification [26], the WOMAC [39,40] and the SF-36 [41,42]. Spatio-temporal gait analysis was done by computerized mat (GaitMat system, E.Q., Inc. Chalfont, PA) [43]. The gait analysis measurements were then used to calculate the KOFG which is based on the minimal stride length between left and right (cm) and cadence rate (steps/minute).

The KOFG is a four-grade scale with 1 being the best function and 4 the worst function. The classification scheme differs between men and women. The KOFG has been described elsewhere and has been validated both in correlation to clinical and radiological data [26].

Statistical Analysis

The statistical analysis was performed by an experienced biostatistician, on R © version 3.0.3, (2014, Vienna, Austria). Categorical data are presented as count (percent). Continuous data are presented as mean (± standard deviation).

Chi-square test was used to compare the KOFG between time points (baseline, 3 months and 12 months). Analysis of variance was used to compare the results of the clinical questionnaires results between time points. Tukey's pairwise comparisons were used to test the difference between specific time-points.

In order to test for trend within each time point a comparison was made of the clinical questionnaires between the KOFG grades at each time point. Hypothesis testing was done using the Jonckheere-Terpstra

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test to evaluate for trend. This enabled us to study if better KOFG leads to better clinical outcome at each time point. All reported p values are two-sided. P value below 0.05 was considered to be statistically significant.

Results

The study population included 518 patients, of which 336 (64.8%) patients were females and 182 (35.1%) patients were males. Average age was 63.4 (±12.9) year old. In 377 patients, there was data available about which of the knees was more symptomatic; left in 163 patients (43.2%), right in 178 patients (47.2%) and bilateral in 36 patients (9.5%). In cases where this data was not available, the knee with the more severe KOFG was chosen for analysis.

Data about radiographic changes and classification by the Kellgren and Lawrence classification was available for 80 patients. Of the 80 patients 13 (16.3%), 32 (40.0%), 21 (26.3%) and 14 (17.5%) were graded as x-ray arthritis grades of 1,2,3 and 4, respectively.

Table 1 presents the classification of KOFG patients at baseline, 3 months and one year of follow-up. It can be seen that at baseline the KOFG distribution is a symmetric bell shaped with 17.6%, 36.9%, 32.5% and 13.1% in grades 1-4, respectively. This however changes with time to a distribution with a right tail as more patients have lower KOFG (better functional condition).

At three months the frequencies are 26.7%, 45.4%, 22.82% and 5.22% for grades 1-4, respectively. At one year of follow-up this trend towards better KOFG is further improved with distribution of 32.9%, 43.33%, 18.9% and 5.0% for grades 1-4, respectively. These differences in distributions between baseline, 3 months and one year of follow-up are statistically significant (p value < 0.0001).

	Grade 1	Grade 2	Grade 3	Grade 4
Baseline	91 (17.60%)	191 (36.94%)	168 (32.50%)	68 (13.15%)
3 months	138 (26.69%)	235 (45.45%)	118 (22.82%)	27 (5.22%)
12 months	170 (32.88%)	224 (43.33%)	98 (18.96%)	26 (5.03%)
Overall P value<0.0001; p value <0.0001 for comparing baseline to 3 months and comparing baseline to 12 months for both; p value = 0.141 for comparing 3 months and 12 months follow-up.				

Table 1: Functional gait classification.

Comparing the KOFG according to grade at baseline shows that the greatest improvement in KOFG occur between treatment initiation and 3 months of follow-up, however, the improvement remains at 12 months and no further deterioration occurs (see Figure 2).

Examining the number of grades changed between baseline to 12 months follow-up it can be seen that in baseline KOFG of 1, 88.9% remained in grade 1. Of the patients originally at KOFG of 2, 33% of the patients improved to KOFG of 1. Considering patients that were in KOFG 3 at baseline, 62.1% improved to KOFG of 2 or 1. In patients at KOFG of 4 at baseline improvement rates were 25.1% and 42.6% to KOFG of 1or 2 (pooled) and KOFG of 3, respectively. This represents a total of 67.7% of patients showing improvement in KOFG of 4 at baseline.

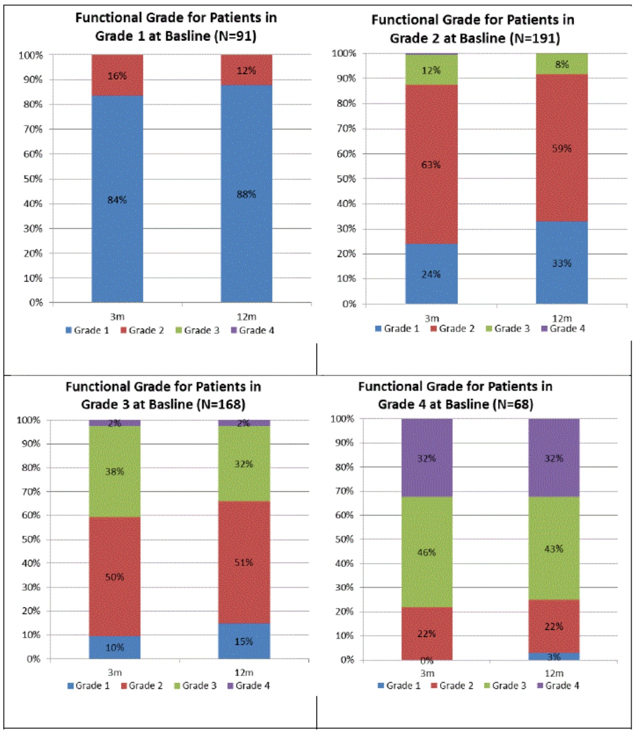

Figure 2: Functional grade at follow-up according to grade at baseline. Comparing 3 months and 12 months after treatment initiation, p values were 1, 0.154, 0.386 and 0.558 for KOFG at baseline of 1, 2, 3 and 4 respectively (Figures 2a-2d, respectively).

Changes in clinical questionnaires (SF-36 and WOMAC) are summarized in Table 2. Examining the clinical questionnaire trends as KOFG can be observed. SF-36 showed that the greatest improvement occurred from baseline to 3 months in all domains (see Figure 3).

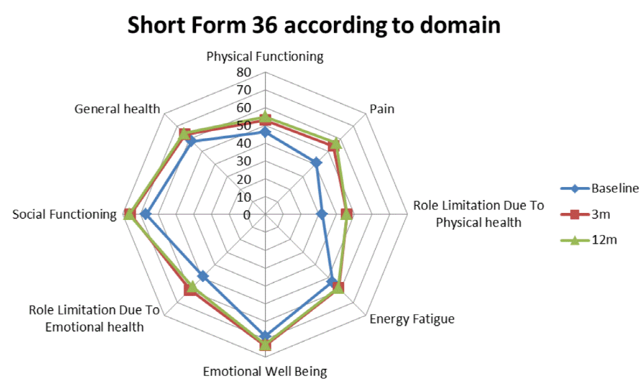

Figure 3: Short form 36 according to domain by follow-up time. Overall ANOVA p values for all domains p values<0.0001. It can be seen that there is an improvement in all domains between baseline and 3months and that that improvement is maintained in 12 months after treatment initiation. For specific pairwise p values see table 2.

These differences are statistically significant (p value=0.001 for all domains). From 3 months of treatment to 12 months it can be seen that the SF-36 was stable and presents similar clinical results.

The WOMAC clinical questionnaire showed a similar trend for major improvement between baseline and 3 months follow-up. This improvement was statistically significant (p value<0.0001).

However, from 3 months to 12 months there was a milder improvement, although no WOMAC category suggests worsening.

	BL	3m	12m	P value BL-3m	P value BL-12m	P value 3m-12m
Short Form 36 Domains:						
Physical Functioning	46.2 (± 0.92)	53.0 (± 0.93)	54.9 (± 0.98)	<0.0001	<0.0001	0.334
Pain	40.9 (± 0.92)	54.4 (± 0.90)	56.6 (± 0.98)	<0.0001	<0.0001	0.222
Role limitation d/t Physical health	32.0 (± 1.58)	45.8 (± 1.72)	45.8 (± 1.74)	<0.0001	<0.0001	0.999
Energy/Fatigue	53.4 (± 0.76)	58.5 (± 0.77)	58.2 (± 0.80)	<0.0001	<0.0001	0.919
Emotional well being	68.4 (± 0.77)	73.5 (± 0.69)	73.0 (± 0.73)	<0.0001	<0.0001	0.883
Role limitation d/t emotional health	49.1 (± 1.85)	59.9 (± 1.79)	57.3 (± 1.87)	<0.0001	<0.0001	0.585
Social functioning	66.9 (± 1.13)	75.6 (± 0.96)	76.2 (± 1.00)	<0.0001	<0.0001	0.917
General Health	58.1 (± 0.69)	63.4 (± 0.72)	64.4 (± 0.75)	<0.0001	<0.0001	0.649
Total SF-36 score	51.6 (± 0.73)	59.4 (± 0.74)	59.8 (± 0.82)	<0.0001	<0.0001	0.884
WOMAC						
WOMAC - pain	46.1 (±1.00)	30.6 (±0.95)	27.1 (±1.00)	<0.0001	<0.0001	0.034
WOMAC - function	42.7 (±1.02)	30.6 (±0.96)	27.7 (±1.05)	<0.0001	<0.0001	0.111
WOMAC - stiffness	47.4 (±1.33)	33.4 (±1.18)	29.3 (±1.18)	<0.0001	<0.0001	0.045
WOMAC - total score	43.8 (±0.98)	30.8 (±0.93)	27.7 (±1.02)	<0.0001	<0.0001	0.066
Table 2 presents the mean (± standard error) of short form 36 (SF-36) and WOMAC clinical questionnaires. Reported P values are Tukey's pairwise p values. BL=Baseline, 3m=3 months, 12m= 12 months.						

Table 2: Clinical questionnaires outcomes at pre-treatment and following 3 and 12 months of treatment.

Table 3 presents the WOMAC total score at each time point according to KOFG grade. In each time point improved KOFG is associated with better clinical outcome, i.e., lower WOMAC total score.

This was shown to be statistically significant (all p values < 0.0001).

	KOFG 1	KOFG 2	KOFG 3	KOFG 4	P value
Baseline	30.1 (± 2.04)	41.7 (± 1.56)	48.6 (± 1.66)	56.2 (± 2.53)	<0.0001
3 months	20.7 (± 1.44)	29.2 (± 1.29)	41.6 (± 1.97)	49.9 (± 4.24)	<0.0001
12 months	17.9 (± 1.36)	27.6 (± 1.48)	38.8 (± 2.56)	51.6 (± 4.55)	<0.0001
This shows that at each time point better KOFG was associated with better clinical score.					

Table 3: Mean (± standard error) WOMAC total score according to KOFG at each time point.

Discussion

In this manuscript we examined the time-dependent validity of a recently published functional classification for KOA population in assessing response to treatment. Patients in this study were treated for one year with a HBBT. The results of the study showed that the KOFG classification scheme offers an objective measurement tool for the assessment of function in KOA population and is also a valid tool to assess time-dependent treatment effect. It has been shown that changes in KOFG followed the trend in changes in clinical questionnaires. Even more so, in all time points better KOFG score were associated with better clinical outcome.

The use of gait as a modality to assess the functional severity of knee OA and the outcome of knee OA treatments are becoming abundant. However, to date, this was not yet translated into a clinical treatment and into clinical decision making. This study is the first to report the clinical outcome of a certain treatment modality in terms of KOFG. We believe that categorizing KOA function into four distinct severity grades enables the clinician and researcher a better-defined tool to quantify the severity of disease and to assess the impact of an intervention than just stating the change in gait analysis parameters. This is further emphasized by the correlation between the clinical and functional outcome as reported by Elbaz et al. [26] Additionally, Elbaz et al. have only studied the relations between the KOFG and the clinical outcome at a cross-sectional evaluation. This paper validated the classification as a tool to objectively assess time-dependent response to treatment in terms of the actual functional condition of the patient. It is important to have a strong, objective, sensitive tool that assesses changes in function, especially for patients with KOA whom daily function is significantly compromised by the disease. By adopting this tool and using it as an outcome measure in future studies, an accurate comparison of the effect of different treatment modalities with regards to function can be performed.

The KOFG was sensitive to evaluate the effect of an intervention used to treat KOA (HBBT) over one year of treatment and was validated using gold-standard questionnaires. It has been shown that within 3 months of treatment patients improved by an average of 1.49-1.89 points in all the WOMAC questionnaire's subcategories (in a 0-10 scale). This improvement is favourable to the improvement of 0.18 to 0.77 and no improvement in patients treated by NSAIDS or Glucosamine, respectively (in a 0-10 scale) [29,30]. Furthermore, the improvement in WOMAC-pain and WOMAC-function met the OMERACT-OARSI clinical response to treatment [44]. With regards to the KOFG, 51.5% of the patients in KOFG 2-4 grades improved by at least one functional grade, shifted from a worse functional grade to a better one.

This study has several drawbacks; the first is that it lacks a control group. Our study presents a treatment cohort study without a control group and as such it does not allow the estimation of treatment efficacy compared to other treatments or no treatment. Previous studies have reported a placebo effect in knee OA studies, especially for pain, stiffness and self-reported function [45]. Although without a control group we cannot estimate the placebo effect, we believe that the effect of treatment is beyond the placebo effect as the effect size of the treatment was larger than the effect size that was reported for the placebo effect. For example, the reported effect size for alleviating pain in the placebo group was 0.5 [45], whereas in the current study the effect size for alleviating pain was 0.83. Another drawback is that we included only patients that completed one year of follow-up and treatment. This might present a selection bias. We hope to report in the future of a case-control study comparing treatment with the biomechanical gait training device to a control group. Thirdly, this was a retrospective analysis of an existing database. One of the inclusion criteria was that patients will have a complete set of data for all time points. However, this criterion does not allow to determine drop-out rates. A prospective study will also address this limitation and will enable to determine drop-out rates. Finally, only part of the study population had radiographic assessment of their degenerative changes. Ideally, baseline x-rays for all patients would have given a clearer presentation of the population, however we assume that the 80-available data are good representatives of the study population. Furthermore, additional radiographic assessment following treatment could have provided interesting information regarding the changes over time. Future studies should consider x-ray as an outcome measure, alongside changes in functional classification.

Conclusion

The results of the current study validate the knee osteoarthritis functional grade classification scheme as a tool to assess time dependant changes in KOA as well as its sensitivity to assess treatment effect. The KOFG can offer a more robust mode of reporting clinical results in describing the natural history and time-dependent treatment results of patients suffering from knee OA and should be considered as an additional outcome measure in future studies.

Role of the Funding Source

This study was not funded

Conflict of Interest

RD, AM and AE hold shares in AposTherapy.

GS is a salaried employee of AposTherapy.

AH, NS, YB and NH are co-researchers in a number of studies. They do not receive and are not entitled to any financial compensation from AposTherapy.

This research work has been submitted to OARSI Congress, where all abstracts are published in a special supplement issue in Osteoarthritis and Cartilage. This work was not published as a full-length article.

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