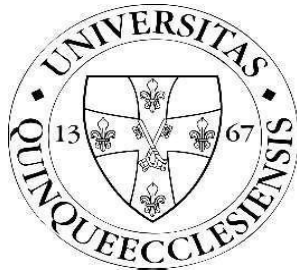


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ACTIVITY LEVEL AND QUALITY OF LIFE AMONG PATIENTS BEFORE
AND AFTER TOTAL KNEE REPLACEMENT SURGERY

Doctoral (Ph.D.) thesis booklet

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Introduction

Knee OA is a chronic age-related progressive musculoskeletal disorder which is a leading cause of disability among elderly individuals [1]. It is associated with various clinical and radiological symptoms. The clinical symptoms of knee OA based on the American College of Rheumatology include pain, crepitus, morning stiffness, low physical activity level, joint instability, swelling, gait deformity, joint effusion, and local inflammation [2-4]. The radiological symptoms based on X-ray are characterized by inflammation, new bone growth (osteophytes), cartilage breakdown, debris in the synovial fluid, and subchondral cysts [5, 6].

The main risk factors for knee OA are age, gender, and body weight [7-10]. It is suggested that with age the thickness of cartilage decreases and its ability to absorb shocks during daily activity decreases. Hence, these changes lead to a breakdown of cartilage cells and new bone growth (osteophytes) [7, 8, 11]. The second important risk factor is gender. Knee OA is more common among women (11%) than men (7%), particularly after the age of 50 years old [8, 11]. Women after 50 years old have low levels of estrogen, which leads to cartilage breakdown and low metabolism [8, 12]. These changes make women have a higher prevalence of knee OA than men. The third important risk factor is body weight. Obesity could increase the risk of developing knee OA three times and increase the progression of knee OA as well [8, 13].

In Hungary, it was estimated that 17% of the Hungarian population had OA based on the European Health Interview Survey 2014 [14]. In addition, Fekete et al., 2020 found that 15.15% of the patients had knee OA (15 out of 99 patients) for more than ten years. Furthermore, Horváth et al., 2011 found that 111 patients (out of 672, 16.5%, 70 women and 41 men) had radiographic knee OA and 2.9% of them had severe knee OA in the south-western part of Hungary [15]. Most of these patients were elderly with a high body mass index (more than 30) [15]. Unfortunately, the quality of life among Hungarian patients with knee OA was the worst compared to other patients from Germany, Spain, and Italy based on the osteoarthritis-specific quality of life scale (OAQoL), which could be related to differences in culture, the provided health services, and duration of illness [16].

Various treatments are currently available to address knee OA that could be conservative or

surgical interventions. The suitable interventions are chosen based on the grade of knee OA, the severity of pain, and activity level limitations [17-19]. Nevertheless, all of the interventions aim to reduce pain, improve the physical activity level, enhance the quality of life, and reduce OA progression [17-19]. The knee brace is the most commonly used conservative intervention for mild and moderate knee OA. Total knee replacement (TKR) is the most commonly used surgical intervention for severe knee OA.

Study objectives

The effects of the knee brace and TKR on pain and activity level are generally measured by both subjective and objective assessment tools. Nevertheless, some questions are still poorly addressed, or insufficient information is available about these two types of interventions. For instance, in Hungary, there are no databases about the activity level of Hungarian patients based on objective assessment tools, as subjective assessment tools (questionnaires) were mainly used to assess pain and activity levels. Therefore, my Ph.D. thesis aimed:

- 1- To evaluate the effects of knee valgus brace on pain and activity levels over different time intervals among patients with medial knee OA.
- 2-To evaluate the long-term effects of total knee replacement surgery on activity level based on ActivPAL.
- 3-To assess the activity level improvement after one year of total knee replacement surgery among patients with severe knee OA using the ActivPAL and the SF-36 questionnaire.
- 4- To report the quality of life among patients with severe knee osteoarthritis who were on the waiting list for total knee replacement surgery.

Sub-study: Effect of using knee valgus brace on pain and activity level over different time intervals among patients with medial knee OA: A systematic review

Background: The Knee valgus brace is one of the accepted conservative interventions for patients with medial compartment knee osteoarthritis to correct the knee varus and increase

functional activity level. The available systematic review and meta-analysis studies evaluated all kinds of knee braces (such as soft, dynamic, valgus, and others) that are used for patients with medial compartment knee OA, but there is no prior study has evaluated the effect of knee valgus brace over a different time interval. Thus, the aim of this study was critically evaluating the studies that only assessed the effect of knee valgus brace on pain and activity level among medial knee OA participants in the last 20 years (from 2000-2020). The time interval of using a knee valgus brace was determined as short-term use (up to 3 months), moderate-term use (more than 3 months and up to 6 months), and long-term use (more than 6 months).

Methods: Five databases were searched to find articles from the year 2000 to the end of November 2020: Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE, PubMed, Web of Science, and Scopus. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) guidelines were used to report the methodology and the results of the systematic review. Two reviewers independently evaluated the available articles for eligibility and assessed quality. The inclusion criteria were: including all types of studies that evaluated the effects of knee valgus brace on pain and functional activities were included and they had to be written in English. Also, they had to meet all of the following criteria:(a) adult participants with medial compartment knee osteoarthritis, (b) participants with pain, morning stiffness, and activity level limitations, (c) the outcomes of pain and/or activity level were measured using any of the following questionnaires: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), visual analogue pain score (VAS), the short form 36 (SF-36) questionnaire, and the Knee injury and Osteoarthritis Outcome Score (KOOS), (d) and publication between January 2000-end of November 2020.

The study was excluded if it (a) looked at evaluating the knee valgus brace combined with another treatment or medication, (b) had children participants, (c) evaluated pain and the activity level with other questionnaires, (d) used different kinds of knee orthoses instead of knee valgus brace, (e) had patients with lateral compartment knee OA or had OA in other joints such as hip or ankle joints. No restrictions if the knee OA was with clinical or/and radiological symptoms. The reporting quality and risk of bias in the included studies were assessed by two reviewers independently according to the Strengthening the Reporting of Observational Studies in

Epidemiology tool (STROBE) for non-randomized controlled studies and the Cochrane risk-of-bias tool for randomized controlled studies.

Results: 24 studies were included (Seven randomized controlled studies and 17 cohort studies) were included in the systematic review with a total of 579 participants. This study found that the effect of knee valgus brace was evaluated by 17 studies for up to three months, by 6 studies for up to six months, and by 3 studies for up to one year. Two studies evaluated two different time intervals. Most of these studies found using a knee valgus brace effective in reducing pain and improving activity level over different time intervals. Pain improved between 12.5%-58.6% and quality of life improved between 10%-40%. However, up to 35% of the participants stopped using the brace due to skin irritation, discomfort, and poor fitting.

The majority of the included studies evaluated the impact of the knee valgus brace for a considerably short-term (less than six months). Thus, limited evidence is available on the long-term use of the knee valgus brace and its associated complications. In addition, the overall biases associated with these results were high, especially the performance bias and detection bias as neither the researchers nor the participants were blind about the given interventions.

Sub-study: Effect of the knee replacement surgery on activity level based on ActivPAL: A systematic review and Meta-analysis study

Background: Total knee replacement (TKR) surgery is the last surgical intervention to deal with severe knee injuries such as advanced knee osteoarthritis [20, 21]. The main outcomes of this surgery are reducing knee pain and increasing the quality of life and the physical activity (PA) level of the patients [21]. The success of this surgery depends on the patients' self-satisfaction in terms of quality of life improvement after the surgery including physical improvement [21, 22]. Several studies have relied on different types of objective monitors (accelerometer or pedometer); however, most of these monitors have low validity and reliability [23-25]. On the other hand, few studies have used high validity and reliability objective monitors to measure PA level among the elderly population. To our knowledge, no systematic review and meta-analysis studies have focused on evaluating the PA level after the surgery based on only high validity and reliability objective monitors such as ActivPAL (PAL Technologies, Glasgow, UK).

Methods: A systematic review and meta-analysis were conducted to evaluate the benefit of TKR surgery alone to enhance physical activity recommendations based on high validity accelerometer. Two independent reviewers evaluated five electronic databases (Cochrane-Central-Register-of-Controlled Trials, EMBASE, PubMed, Web of Science, and Scopus) to find relative studies between January 2000 and October 2021. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) guidelines were used to report the methodology and the results of the systematic review. All English language published studies that evaluated the PA level improvement before and after total knee replacement surgery using the ActivPAL included regardless of the study designs. Moreover, the included articles must meet the following criteria:(a) adult participants with severe knee OA who received the TKR surgery, (b) minimum follow-up time was six months, and (c) the PA level was measured by the ActivPAL only. The study was excluded if (a) it combined total knee replacement surgery with any other interventions, or (b) used another accelerometer.

The reviewers evaluated the quality of reporting according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) tool for non-randomized studies [26, 27]. Moreover, the Risk Of Bias In Non-randomized Studies (ROBINS-I) tool was used to evaluate the risk of bias in non-randomized controlled studies [28]. For non-randomized uncontrolled studies, the National Institutes of Health (NIH) quality assessment tool was used to evaluate the quality of pre-post studies without a control group [29]. The Cochrane Collaboration's Review Manager Program (RevMan version 5.3, Cochrane collaboration, Oxford, UK) was used for data analysis. Weighted mean differences (WMDs) and corresponding 95% confidence intervals (CIs) were estimated by Fixed-effect meta-analysis. The chi-square test for Q and the I^2 quantity were used to test heterogeneity between studies. Significant results were considered if a p-value for the chi-square test ≤ 0.1 and $I^2 \geq 50\%$ [30].

Results: After screening 4427 studies only three studies were included (with a total number of patients was 173 participants with an average age of 63.3 years and an average body mass index of 33.2 kg/m²). Overall, the physical activity improved after the surgery. The results found that the number of steps was significantly improved in the three included studies up to 37.3% and 45.6% after six-months and one-year after the surgery, respectively. In addition, the stepping

time was significantly improved in two studies up to 38.7%. However, these changes did not meet the recommended activity level guideline (150 minutes/week) and that could be related to the patient's health status and his/her activity level before the surgery. No significant changes were seen in sedentary time and standing time after six-months and one-year follow-up. Heterogeneity among studies was low to moderate (0% - 63%).

Main Study: Activity level and quality of life among patients before and after knee replacement surgery: A case- series study

Background: Knee osteoarthritis is a very common age-related disorder. Total knee replacement surgery (TKR) is the last-stage intervention for severe cases to reduce pain and improve the quality of life. Nevertheless, there is no information about the activity level of patients with severe knee osteoarthritis before and after TKR surgery in Hungary. The aim of this study was to evaluate the improvement in quality of life pre-post TKR surgery among patients using subjective and objective assessment tools.

Methods: This study included eight participants (70.8 ± 4.5 years and 30.7 ± 4.3 kg/m²) with severe knee osteoarthritis on the waiting list for total knee replacement (TKR) surgery. The inclusion criteria were the presence of a clinical and radiological diagnosis of osteoarthritis that required total knee replacement surgery. The confirmation of radiological diagnosis was performed by the orthopedic surgeon at the orthopedic clinic, at the University of Pécs, to ensure that participants needed TKR surgery. Participants were excluded if they had hip and ankle injuries in the last five years or if they had co-morbidities or medical conditions that affected physical activity, such as congestive heart failure or cognitive impairment. Ethical approval was obtained from the University of Pécs, and consent was initially collected from the participants.

Physical activity measurement tools: The activity level was evaluated with ActivPAL and the short form (SF-36) questionnaire. ActivPAL (PAL Technologies, Glasgow, UK) is a uniaxial accelerometer (20 g) that calculates the time spent in sedentary, standing, upright, and stepping states, and the number of steps per day for up to 14 days [31-35]. The ActivPAL is recommended to be used with the elderly more than other monitors, such as ActiGraph, because it has a higher validity and reliability to detect body movement at different speeds than

ActiGraph [35, 36]. Before use, the monitor was charged and activated with ActivPAL3™ (version 8.11.9.100). Moreover, the Hungarian version of the short form (SF-36) questionnaire was used to assess QoL. This form is composed of 36 items about eight domains: physical functioning, physical role, bodily pain, general health, vitality, social functioning, emotional role, and mental health. Each domain is scaled between zero (poor health status) and 100 (no problem at all) [37-39].

Intervention and total knee replacement surgery: All of the participants underwent the operation with the medial parapatellar approach that was performed by the orthopedic surgeon. Various prosthetic knee types were used, such as S and N Genesis II, Johnson and Johnson PFC sigma, and Zimmer Nexgen. No compliances were reported after the surgery. The patients stayed five to six days at the hospital after the surgery. Physiotherapy sessions were standardized according to hospital protocols to minimize confounding factors for both inpatient and outpatient periods (for three months only).

Data analysis: For data from the SF-36 questionnaire, the average (\pm SD) of physical functioning, physical role, pain, general health, and the overall QoL score were calculated for each participant at all assessment time points, as these aspects are the most relevant aspects with the study's goal. The data from the ActivPAL were extracted from the monitor using the software. Then, the downloaded files were imported into Excel. The average (\pm SD) sedentary time, standing time, stepping time, and the number of steps were calculated for each participant at all assessment time points during the testing period (seven days). A valid day is defined as 10 hours of continuous activity with less than three hours of interruptions. All data were analyzed by SPSS (SPSS Inc., Chicago, IL, USA, version 24) using a paired sample test. Significant results were considered if the significance (2 tailed) value was less than 0.05 [40]. Only eight patients were included in the paired sample t-tests. The data were normally distributed based on the Kolmogorov–Smirnov test [41].

Results: The activity level based on ActivPAL, the sedentary time and standing time significantly improved among the patients by 12% ($P=0.033$, from 18.3 hours to 16.1 hours) and 65.7% ($P=0.030$, from 3.5 hours to 5.8 hours), respectively one year after TKR surgery. The number of steps also improved by 17.1% ($P=0.11$, from 6270 to 7344 steps) one year after TKR

surgery. Based on the Short Form-36, the overall score, pain, and physical function improved by 50.0% (P=0.050), 23.9% (P= 0.32), and 5.3% (P=0.58), respectively one year after TKR surgery among the included patients. To the best of our knowledge, the main study of the thesis was the first in Hungary which gave details about the number of steps, stepping time and sedentary time among patients with severe knee OA using activPAL.

Sub-study: Quality of life of patients with severe knee osteoarthritis in Hungary: A cross-sectional study

Background: Knee osteoarthritis (OA) is a chronic musculoskeletal disease that is associated with mortality, disability, and low quality of life in Hungary, the quality of life of patients with severe knee OA has not sufficiently investigated. One conference paper reported the quality of life (QoL) among Hungarian patients with severe knee OA before total knee replacement surgery using four different questionnaires, including a homemade questionnaire, the Knee Society Score (KSS), the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and the short form (SF-36) questionnaire [42]. However, the number of participants was not mentioned, and the reported results and methods were not well presented as it was a conference paper. As a result, insufficient data are available about the activity level of Hungarian patients with severe knee OA. Therefore, more information is required in this field to have clear information about their QoL, to identify the most challenging activities for patients with severe knee OA, and to identify whether there are differences in QoL across the included women and men. This cross-sectional study aimed to report QoL of patients with severe knee OA who planned to have TKR surgery after one month. Additionally, this study aimed to evaluate gender differences in terms of QoL.

Methods: Ten patients (6 female, 4 male, 70.6±4 years, 30.7±3.4 kg/m²) with severe knee osteoarthritis were included from an orthopedic clinic in Pécs, Hungary. The SF-36 questionnaire (Hungarian version) was used to assess QoL of the patients one month prior to TKR surgery. The participants were recruited from the Department of Orthopedics (Clinical Center, University of Pécs, Hungary). The inclusion criteria were the presence of radiological and clinical symptoms of knee osteoarthritis, the Kellgren-Lawrence (K-L) scale score ≥ 3 [43], and pain during daily activities. Furthermore, the included participants had to be scheduled for TKR surgery within a

month. The radiological symptoms were confirmed by the orthopedic surgeon at the orthopedic clinic. The exclusion criteria were to have one or more of the following: osteoarthritis in the hip or ankle, knee replacement before, knee surgery in the last five years, hip and ankle injuries in the last five years, and cognitive problems. Ethical approval from the University of Pécs was granted and the consent form was signed by all participants before participation.

All the included participants were briefed about the study, and they were asked to sign the consent form. Then, each participant was asked to complete the Hungarian language SF-36 form questionnaire one month before the surgery. The eight domains of the SF-36 questionnaire were reported, including physical functioning, physical role, bodily pain, general health, vitality, social functioning, emotional role, and mental health [44-47]. It is scored from zero to 100. A low score indicates poor health status and a high score shows better health status [44-47].

For the statistical analysis. The SPSS software (SPSS Inc., Chicago, IL, USA, version 24) was used to calculate descriptive statistics and the Multivariate Analysis of Variance (MANOVA). In the multivariate analysis, all eight domains were dependent variables, and gender was an independent variable. The results were considered significant if the P value was less than 0.05. Other factors such as using walking assistance, diabetes, hypertension, smoking, employment, and marital-status were not recorded because the outcomes were insignificant. The scoring was performed online via the online software Orthotool-kit (<https://www.orthotoolkit.com/sf-36/>).

Results: The participants with severe knee OA reported a low overall average of pain (40.95%), role limitations due to physical health (42.5%), and role limitations due to emotional problems (46.7%) that reduced their QoL. In addition, there are significant differences between women and men in some domains. Women had significantly lower physical functioning and role limitations due to emotional problems than men by 42.8% ($p=0.03$) and 73.3% ($P=0.005$), respectively. Moreover, women had a higher feeling of pain than men; however, the difference was insignificant.

Discussion of the main findings

Based on the systematic review study, the knee valgus brace is an effective conservative intervention to improve the quality of life and reduce pain during daily activities. the knee valgus brace could be suitable for some patients more than others. For instance, Barnes et al., 2002 [48] suggested that patients who have severe Kellgren-Lawrence grade (KL) grade and higher body mass index 28-30 stopped using the knee valgus brace, whereas patients with lower KL grade (grade II) and BMI between 20-24 still use the brace. Obese participants complain of rotation and skin irritation due to poor fitting. Participants with severe knee OA (KL grade IV) were less satisfied with using the knee valgus brace and found it less effective [49, 50]. Thus, using the knee valgus brace could be more recommended and suitable for the patients who have less than 8 degrees of knee varus, less than 20 degrees of knee flexion contracture, mild to moderate knee OA level (KL grade II and III), and their body mass index less than 30 [48, 50, 51]. However, the long-term of using this brace is still not very convenient, and the patients who benefit most from using the brace should be identified with high methodological quality studies.

Based on the meta-analysis study, total knee replacement surgery is an effective treatment for improving patients' quality of life with severe knee injuries. Based on the high validity monitor, the number of steps significantly improved, but the sedentary time did not change significantly. To increase the maximum benefits of the surgery, the sedentary time should be decreased. Hence, long-term follow-ups, rehabilitation programs, and physical interventions are important to enhance the physical outcomes and reduce the sedentary time after the surgery. The participant's health status before the surgery could have an impact on the success of surgical and achieving maximum benefit of the surgery. Nevertheless, further studies are needed to understand the benefit of surgery with or without rehabilitation assessed using high validity monitors.

Based on the case-series study, the included Hungarian patients have better physical activity levels and less pain (less pain or a better QoL in general) based on both objective and subjective tools. The activity level increased between 65.7%-12% based on the ActivPAL and between 50%-5.3% based on the SF-36 questionnaire after one year of the surgery. However the sedentary time decreased from 18.3±1.9 to 16.1±3.1 hours per day, these changes are still not

enough to allow the included Hungarian patients to meet the general physical activity guidelines which could reduce the efficiency of TKR surgery. Hence, long-term follow-up and rehabilitation sessions could be required to reduce the sedentary time and increase the efficiency of TKR surgery. This is the first study in Hungary that used objective and subjective tools. However, the objective assessment tool, ActivPAL, is more sensitive and reliable than the subjective assessment tools. Thus, it is important to include objective assessment tools in the evaluation to reduce recall bias and represent more information about the physical activity level.

Based on the cross-sectional study, The outcomes of this study found that there were significant impairments in some of the sub-scores of QoL. The patients with severe knee osteoarthritis had a low quality of life and severe pain during daily activities which reduced their ability to freely achieve their daily activities. However, the overall scores of social functioning and emotional well-being among participants were the highest in domains with less struggle. Furthermore, women with severe knee OA had significantly higher pain and lower quality of life than men due to their emotional status. Further studies with large sample sizes are needed.

Limitations

The systematic-review study included both randomized and non-randomized studies. The decision to include all types of studies was due to the limited number of randomized studies that focus on the effect of the knee valgus brace on pain and activity level. Also, it was difficult to include only randomized studies as they have some dissimilarities in terms of control group features, the used questionnaire, the study procedure, and the duration of using the brace. In further, this study focused on evaluating activity level through questionnaires (self-reported) not by objective methods, such as activity monitors, because mainly using questionnaires is faster, cheaper, and easier for researchers than using activity monitors. However, future studies could be conducted to evaluate the activity level with objective methods.

The meta-analysis study included three studies that met the inclusion criteria and none of them is a randomized controlled study; therefore, the results of the included studies could be associated with a high risk of bias such as selection bias and performance bias. Also, this study included

only studies that used the ActivPAL and excluded studies with any other interventions with the surgery which limit the results' generalizability.

The case-series study had a small sample size due to the COVID-19 epidemic, few patients were able to visit the hospital and participate in this study. Nevertheless, the participants were recruited from a large hospital that came from different places in Hungary, and the results could be used to calculate the sample size for upcoming studies. Furthermore, a one-year follow-up could not be sufficient to assess the effect of the surgery; however, the results gave a better overview of the PA of patients after the surgery. Hence, further studies with longer follow-ups and more participants are recommended.

The cross-sectional study had a small sample size. This study was a part of the case-series study with a small sample size. The data collection process was performed through the COVID-19 pandemic. Hence, it was difficult to meet more patients to collect more data.

Clinical implication

The findings of the systematic review study could help specialists who work with patients with medial compartment knee OA to provide sufficient information about the knee valgus brace before recommending the knee valgus brace to ensure the best quality of life and pain management. The results of the meta-analysis study will help specialists who work with patients undergoing TKR surgery to restore their activity level, decrease their sedentary time, and increase their satisfactory outcomes after surgery. The results of the main study are crucial for specialists who work with Hungarian patients with severe knee OA to understand their activity level limitations and how to enhance their activity level after surgery. The findings of the last study emphasize the importance of including intensive emotional health care in the treatment strategy for women with severe knee OA in Hungary.

Summary of Novel Findings

1- The systematic- review study aimed to provide a comprehensive overview of the effects of using the knee valgus brace on self-reported pain and activity levels over three different time intervals: short-term, moderate-term, and long-term among patients with medial compartment

knee osteoarthritis. This study found that most of the included studies recommended using the knee valgus brace to reduce pain and enhance the quality of life. However, most of them are short-term studies, and more information about the long-term effects is needed.

2- Using the knee valgus brace could be more recommended and suitable for patients who have less than 8 degrees of knee varus, less than 20 degrees of knee flexion contracture, mild to moderate knee OA level (KL grade II and III), and their body mass index less than 30.

3-The meta-analysis study aimed to address the activity level improvement after at least six months of total knee replacement based on the high validity and reliability accelerometer ActivPAL. This study found that the number of steps significantly increased after surgery; however, the sedentary time after surgery was still high and could reduce the efficiency of surgery. Therefore, to increase the efficiency of TKR surgery, it is important to reduce sedentary time.

4- Moreover, the meta-analysis study suggested that the health status of the patients before the surgery is associated with the outcomes of the surgery. Patients with high activity level before the surgery are more likely to have better physical activity level after the surgery.

5- The case-series study is the primary study for my Ph.D. This study aimed to assess the activity level behavior of patients with severe knee OA and to evaluate the quality of life improvement after one year of total knee surgery. Additionally, we addressed whether the activity level improvement after total knee replacement surgery is sufficient to restore normal activity levels. The results of this study found that the activity level and pain were enhanced one year after surgery; however, the sedentary time after surgery should be reduced more to reach the maximum benefits of surgery. Hence, to enhance the efficiency of the surgery, it is recommended to try to reduce the sedentary time and join a long-term rehabilitation follow-up.

6-To the best of our knowledge, the main study of the thesis was the first in Hungary which gave details about the number of steps, stepping time, and sedentary time among patients with severe

knee OA using activPAL. Using a high avidity objective assessment tool is important to evaluate the PA among patients with knee OA in order to understand their physical activity behaviour.

7- The last study in my thesis was a cross-sectional study that aimed to report the quality of life among the recruited Hungarian patients with severe knee OA and to assess the differences in quality of life based on gender differences. The results of this study found that the included Hungarian patients with severe knee OA had low activity levels and high pain level. Furthermore, the included Hungarian women with severe knee OA had lower functional levels due to emotional problems than the included Hungarian men.

8- It is important to include intensive emotional treatment in the rehabilitation strategy for patients with severe knee OA in Hungary to enhance their quality of life.

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