Knee Joint Stability and Functional Ability in Patients with Osteoarthritis of the Knee

Martin van der Esch
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Knee Joint Stability and Functional Ability in Patients with Osteoarthritis of the knee.

By Martin van der Esch

The research presented in this thesis is part of the research program of the EMGO Institute. The studies were carried out at the Department of Physiotherapy, the Department of Rehabilitation Medicine and Psychology of the Jan van Breemen Institute and The Department of Rehabilitation Medicine of the VU University Medical Center, Amsterdam, The Netherlands.

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Knee Joint Stability and Functional Ability in Patients with Osteoarthritis of the Knee

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door

Martin van der Esch

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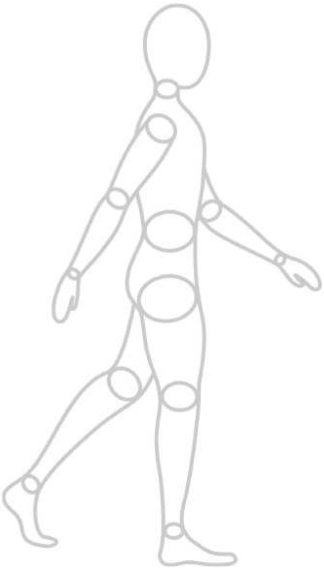
Chapter 1

GENERAL INTRODUCTION



Osteoarthritis

Osteoarthritis (OA) of the knee is a major problem because of its high prevalence and substantial impact on functional ability (1-5). The risk of a reduction in functional ability attributable to knee OA alone is as great as that due to cardiac disease and greater than that due to any other medical disorder in the elderly (2). In The Netherlands, more than 335.000 of the 16 million inhabitants (i.e., more than 21 in 1000 inhabitants) have knee OA (5). Its incidence in general practice in The Netherlands is 1.5/1000 per year and increases with age. OA is also more common in women than in men (6,7). Given the trend towards an aging population, one may expect that prevalence and incidence will increase in the near future.

Functional ability in knee OA patients

Osteoarthritis (OA) of the knee is characterized by disability in daily functioning, primarily in activities related to mobility, e.g. walking, stair-climbing, and transfers (such as rising from a chair, rising from bed, getting into and out of a car)(1-4). Even in the early phase of the disease process, reduced functional ability is already present (8). In a systematic review, it was found that functional status and pain in knee OA patients had deteriorated at three year follow up (9). Therefore, it can be concluded that reduced functional ability starts in the early phase of the disease and is progressive.

Determinants of functional ability in knee OA patients

A number of determinants for developing reduced functional ability in knee OA patients have been defined in epidemiologic studies (1,10-18). Traditionally, reduced functional ability in knee OA patients has been attributed to degeneration of cartilage and bone. However, this relationship is far from clear. Dougados et al. showed an increased risk of functional deterioration associated with progressive cartilage degeneration (19), while Dieppe et al. showed no association (20). The relationship between articular degeneration and functional ability is weak. Therefore, other determinants may better explain the reduction in functional ability in knee OA patients.

From a clinical perspective, the most common and dominant symptom that occurs in knee OA is joint pain. Joint pain is increased by joint use and relieved by rest (9). However, as OA progresses, pain may become more persistent and may also occur at rest and at night. In the chronic state of the disease, knee pain arises in response to a complex interaction between internal and external factors leading to enhanced sensitization of the peripheral and central nervous system. Pain has been found to increase the risk of reduced functional ability in knee OA patients (9).

Muscle strength in knee OA patients has been shown to be an important determinant of functional ability (21,22). The peri-articular knee muscles are an integrated component of the knee joint and provide knee joint movement. The muscles absorb forces and loads generated during walking and contribute to the control of body position and movement (23). Furthermore, sufficient muscle strength is necessary for adequate functional ability. Muscle weakness has been found to increase the risk of reduced functional ability in knee OA patients (13,21,22).

Exercise therapy, particularly exercises with the aim to improve muscle strength, has been shown to be an effective intervention for improving the daily functioning of patients with knee OA (13,21-24) and has been advocated in knee OA treatment guidelines (25,26). However, on average the beneficial effects of exercise therapy are moderate and there is also considerable heterogeneity in its effectiveness between patients. Furthermore, the effect is not sustained in the long term (27). Therefore, there is a need for further optimization of exercise therapy, by both improving the content of therapy and by adequate selection of patients in whom improvement can be expected.

One potential area for optimization of exercise therapy is joint stability. Improvement of joint stability to increase functional ability has been mentioned in clinical guidelines (25,26). According to the model in Figure 1 an unstable knee joint may result in reduced functional ability. However, the role and function of joint stability in relation to functional ability is not well understood.

Stability is a key component of the mechanical environment of the normal knee joint. Stability of the knee is achieved through the interaction of the passive restraint system (ligaments, capsule) and the active neuromuscular system (muscle strength, proprioception) (23,28-30). In the unloaded state, knee stability is provided by the ligaments, capsule and other soft tissues. It is theorized that in the loaded state, during standing and walking, stability is achieved through the interactions between these tissues, the geometry of the femoral condyles, and tibiofemoral contact forces at the joint surface generated by muscle contraction and gravity. Under loaded, dynamic conditions, stability of the knee depends on peri-articular muscles, proprioceptive systems and cortical awareness of the tone or tension in the joint muscles. The processing of proprioceptive input by the central nervous system results in the contraction of peri-articular muscles, which stabilize the joint.

Instability may be defined as the inability of the joint to maintain a position or to control movements under differing external loads, resulting in abnormal displacement in the varus-valgus direction of the tibia with respect to the femur. The terms varus and valgus refer to a movement or position of the tibia from the center of the knee in the frontal plane (30). In this thesis, we discuss the knee joint instability that results from non-contractile laxity, and instability that results from neuromuscular deficits, including proprioceptive deficits. More precisely, instability is the patient's inability to keep the femoral condyles centered in the varus-valgus direction at the tibia plateau. The cause of this inability may be due to the impairment of one single independent physical factor or it may be multifactorial, consisting of ligament and capsule laxity, and neuromuscular impairments including muscle weakness and proprioceptive deficits.

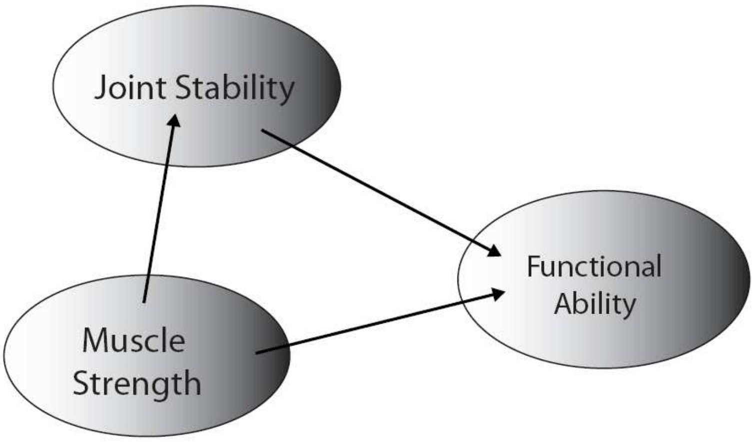


Figure 1. The theorized relationship between muscle strength, joint stability and functional ability in knee osteoarthritis patients.

In this thesis it is hypothesized that joint stability affects functional ability. More specifically, impairments in a number of factors involved in the process of knee joint stabilisation are hypothesized to affect functional ability. These factors are (i) muscle weakness, (ii) non-contractile joint laxity due to inadequate passive restraint by ligaments and capsule, (iii) neuromuscular deficits such as inaccuracy of joint proprioception, and (iv) varus-valgus motion during walking (27-30). (Figure 2). These factors may influence independently and directly functional ability. However, considering the important role of muscle strength, it is also of interest to study the influence of laxity, proprioception and varus-valgus motion during walking on the relationship between muscle strength and functional ability.

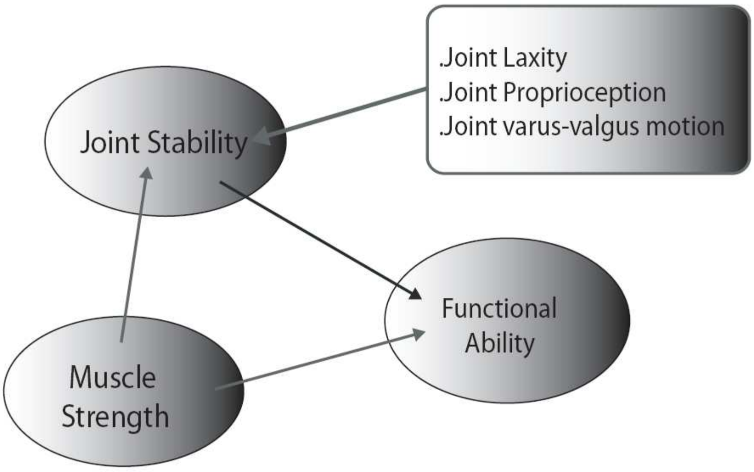


Figure 2. Joint laxity, joint proprioception and joint varus-valgus motion as determinants of joint stability in knee osteoarthritis patients.

Joint laxity is defined as the displacement or rotation of the tibia with respect to the femur in the varus-valgus direction under medial or lateral load (31). In the unloaded state, knee stability is provided by the ligaments, capsule, and other soft tissues. In OA knees laxity may be due to a loss of articular cartilage and/or bone height, chronic capsuloligamentous stretch, or combinations of ligamentous, meniscal, muscular, and capsular pathology. Previous studies have suggested that joint laxity is related to functional ability in knee OA (18,32). However, only 1 study has been found concerning the influence of knee joint laxity on the relationship between muscle strength and functional ability (32).

Proprioception (i.e., joint movement sense) is defined as the conscious and subconscious perception of the movement of a joint in space, and influences the awareness of both the position and movement of the joint (33). Knee joint proprioception therefore encompasses both the sense of joint position and the sense of motion. These senses derive from neural inputs arising from mechanoreceptors in joints, muscles, tendons and associated tissue (34). Joint mechanoreceptors have the ability to detect the actual joint position and joint motion. Sensory feedback through knee joint mechanoreceptors, i.e. proprioceptors, modulates and activates knee muscles (23). Poor proprioception has been reported for patients with knee OA (34-44). Studies have shown conflicting findings on the relationship between proprioception and functional ability in knee OA patients (36-40). Some results suggest that deficits in proprioception are not large enough to have an impact on functional ability (36,39), whereas other results suggest that poor proprioception is associated with worse functional status (33,35,38,39). The influence of poor proprioception on the relationship between muscle strength and functional ability has not been studied in knee OA patients.

Varus-valgus motion of the knee is defined as the movement and position of the knee in the varus-valgus direction during the loading response phase and the midstance phase of the gait-cycle in knee OA patients. Supposedly, in an adequate walking pattern varus-valgus motion is minimal due to an adequate neuromuscular system and low laxity of the passive restraint of the knee (30). It is presumed that knee OA patients minimize varus-valgus motion during walking by using greater magnitudes of muscle activity. It can therefore be assumed that the presence of high varus-valgus motion and muscle weakness result in restricted functional ability. No studies were found showing the influence of high varus-valgus motion during walking on functional ability in knee OA patients.

Assessment of determinants of functional ability in patients with knee OA

In this thesis muscle strength, joint laxity, joint proprioception, and varus-valgus motion of the knee have been measured as determinants of functional ability.

Muscle strength. Muscle strength is assessed for flexion and extension of the knee using an isokinetic dynamometer (EnKnee; Enraf-Nonius, Rotterdam, the Netherlands). Strength of the quadriceps and hamstrings are measured isokinetically at 600/second. The reproducibility of this measurement of muscle strength has been established (45).

Joint laxity. Laxity of the knee is assessed using a device, which measures the angular deviation of the knee in the frontal plane. Varus-valgus movement is assessed in an unloaded situation. In an unloaded state the muscles around the knee are relaxed. It is supposed that an external load at the knee in the varus-valgus direction is responsible for a movement in the frontal plane. During testing, the knee was flexed at 20o to relax the cruciate ligaments. An external load stresses the capsule and collateral ligaments, with movement in the frontal plane expressing laxity. The method of assessing varus-valgus laxity is based on that described by Sharma et al (31). The information on reproducibility of the measurement of knee laxity is currently very limited and based on small numbers of patients. In the study of Sharma et al only intra-reliability scores were presented (31). Information regarding inter-rater reliability and agreement parameters is presently unavailable. Therefore, there is a need for examining the reproducibility of the measurement of laxity in the knee.

Knee joint proprioception. To assess proprioception of the OA knee (i.e. the threshold to detection of passive motion) a device is designed following Sharma et al. (35) and Pai et al (38). The device consists of a chair with a computer-controlled motor and transmission system and two attached free moving arms. Each arm supports the patients' shank and foot and moves in the sagital plane. The joint of each arm is moved by a computer controlled stepper-motor and transmission system for angular displacement. The foot/ankle is attached with an air splint to the footrest, which is a moving component of the apparatus. Angular motion is detected by angular displacement and force transducers. Attached to the chair is an upward-bending tray, to prevent visual input of the moving knee. Two handheld buttons are attached to the tray. The seat of the chair consists of a gel-pad with the aim to prevent any vibrating sensation and movement of the skin. This provides a measurement of angular displacement, while eliminating or minimizing visual and auditive stimuli, vibrations, cutaneous tension, and pressure cues to limb motion. Although two studies have measured proprioception in patients with knee OA (35,38), information on the reproducibility of the methods used to assess proprioception is rarely provided, particularly concerning the agreement parameters no information is available yet. Therefore, knowledge of the reproducibility of proprioception measures is needed to establish the utility of these measures in scientific research and clinical practice.

Varus-valgus motion. Varus-valgus motion of the knee joint is assessed by two different measurement systems: an optoelectronic camera system and a multi-component force plate. Varus-valgus motion is assessed during a loaded and dynamic functional ability (i.e. walking). When walking, the knee moves rotationally in the frontal plane (i.e., varus-valgus). A whole step (i.e., starting at the heel strike phase of the step and ending at the toe off phase of the step) is used for collecting data. Forces in the foot are detected in relation to knee joint position. The ground reaction forces are measured with a force plate that is imbedded in a walking track. The movement of the knee in the frontal plane is measured with a 3-dimensional movement analysis system. Movements and positions of the knee are measured in degrees.

Functional ability. Functional ability is assessed in two ways: by observation and by self-report (questionnaire). In assessing observed functional ability the 100 meter walking test and the Get Up and Go (GUG) test are used (46). The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire is used as a self-report measure of function. The WOMAC is a disease-specific measure of pain, stiffness, and physical function for knee OA patients, The WOMAC includes 5 items related to pain, 2 items related to stiffness, and 17 items related to physical function. Each item is scored on a 5-point Likert scale. Reliability and validity of the WOMAC have been established (47,48).

Aim of this thesis

The overall research question addressed in this thesis is: Is knee joint stability a determinant of functional ability in patients with osteoarthritis of the knee?

Three factors involved in the process of knee joint stabilization are the focus of the studies described here. Firstly, knee joint laxity is studied, with the following research questions:

Is knee joint laxity of influence on the strength of the relationship between muscle strength and functional ability? **(Chapter 2)**

When measuring knee joint laxity in knee OA patients, what are the intra- and inter-rater reliability and the intra- and inter-rater agreement parameters? **(Chapter 3)**

Is knee joint laxity related to structural joint change (joint space narrowing and osteophyte formation) and joint malalignment in knee OA patients? **(Chapter 4)**

Is knee varus-valgus laxity higher in women than in men in knee OA patients? **(Chapter 5)**

Secondly, this thesis focuses on the following questions in relation to proprioception:

Is knee joint proprioception related to functional ability and does poor proprioception aggravate the impact of muscle weakness on functional ability? **(Chapter 6)**

When measuring knee joint proprioception in knee OA patients and healthy subjects, what are the inter- and intra-rater reliability and the inter- and intra-rater agreement parameters? Additionally, what are the effects of variations in measurement procedure on measurement error? **(Chapter 7)**

Finally, varus-valgus motion of the knee joint is studied in an attempt to answer the following questions:

Is varus-valgus motion of the knee a valid measure of knee joint stability? **(Chapter 8)**

Is high varus-valgus motion associated with reduced functional ability in knee OA patients? Furthermore, in knee OA patients with high varus-valgus motion, is muscle weakness associated with a more severe reduction in functional ability than in knee OA patients with low varus-valgus motion? **(Chapter 9)**

An overall discussion of the findings in this thesis is provided in **Chapter 10**.

Chapters 2-9 were originally written as separate articles for publication in international peer reviewed scientific journals. Therefore, some overlap between chapters is inevitable, especially with regard to the description of the methodology. The general introduction as well as the general discussion offers an overview providing the links between the different studies. In the end of the general discussion the overall conclusion of the whole study project is presented.

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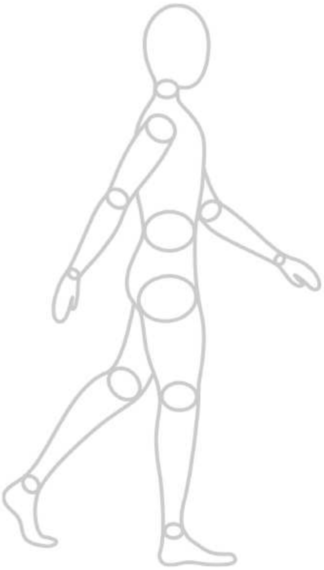
Chapter 2

JOINT LAXITY AND THE RELATIONSHIP BETWEEN MUSCLE STRENGTH AND FUNCTIONAL ABILITY IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE



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ABSTRACT

Objective. To establish the impact of knee joint laxity on the relationship between muscle strength and functional ability in osteoarthritis (OA) of the knee.

Methods. A cross-sectional study of 86 patients with OA of the knee was conducted. Tests were performed to determine varus-valgus laxity, muscle strength and functional ability. Laxity was assessed using a device that measures the angular deviation of the knee in the frontal plane. Muscle strength was measured using a computer-driven isokinetic dynamometer. Functional ability was assessed by observation (100-meter walking test) and self-report Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)). Regression analyses were performed to assess the impact of joint laxity on the relationship between muscle strength and functional ability.

Results. In regression analyses, the interaction between muscle strength and joint laxity contributed to the variance in both walking time ($P = 0.002$) and WOMAC score ($P = 0.080$). The slope of the regression lines indicated that the relationship between muscle strength and functional ability (walking time, WOMAC) was stronger in patients with high knee joint laxity.

Conclusion. Patients with knee OA and high knee joint laxity show a stronger relationship between muscle strength and functional ability than patients with OA and low knee joint laxity. Patients with OA, high knee joint laxity, and low muscle strength are most at risk of being disabled.

Keywords: Osteoarthritis, Knee, Disability, Laxity, Muscle strength

INTRODUCTION

Osteoarthritis (OA) of the knee is a common musculoskeletal disorder (1). Patients with OA of the knee frequently report limitations in their ability to perform activities of daily living (functional ability), such as stair climbing, walking and household chores (2-4).

Muscle strength has been shown to be a determinant of the ability to perform daily activities in patients with OA of the knee (5,6). Available evidence from studies on the effectiveness of muscle strengthening for knee OA demonstrates consistent improvement in ability after the intervention (7-9). However, the magnitude of the effect varies considerably between patients. These differences may be attributable to factors that interfere with the relationship between muscle strength and functional ability, i.e., muscle strengthening may be more effective in some patients than in others (10,11). Joint laxity is one factor that may contribute to this difference in efficacy.

Joint laxity is defined as the displacement or rotation of the tibia with respect to the femur in the varus-valgus direction (10). Joint laxity may affect the relationship between muscle strength and functional ability. However, 2 opposing hypotheses exist concerning how the relationship between muscle strength and functional ability is influenced. One hypothesis is that in patients with a high knee joint laxity, there is a *stronger* relationship between muscle strength and functional ability. This hypothesis is based on the assumption that in patients with high laxity, muscle activity around the knee compensates for the absence of ligamentous control due to impairments of the passive restraint system. Taking on this dual role increases the importance of muscle strength for adequate functioning, which is reflected in a stronger relationship between muscle strength and functioning. Studies in patients with anterior cruciate ligament (ACL) deficiency have shown that the loss of stability provided by ligaments and capsule can be compensated by increased muscle activity (11,12). The pattern of increased muscle activation was also found in patients with OA of the knee (13). Compared with age-matched healthy adults and compared to young adults, patients with OA of the knee had higher muscle activity during the execution of daily activities. Therefore, in lax knee joints the role of muscle strength becomes more important, resulting in a stronger relationship between muscle strength and functional ability. The other hypothesis is that in patients with high knee joint laxity, there is a *weaker* relationship between muscle strength and functional ability (14). This hypothesis is based on the assumption that in patients with high laxity, muscle activity can no longer stabilize the knee, resulting in inadequate control of joint motion. In these patients, functional ability will be affected regardless of the level of muscle strength, resulting in a weaker relationship between muscle strength and function. In view of these 2 opposing hypotheses, the objective of this study was to establish the influence of knee joint laxity on the strength of the relationship between muscle strength and functional ability.

PATIENTS AND METHODS

Patients

A total of 86 patients diagnosed with OA of the knee were included in the study. Inclusion criteria were OA of the knee (uni- or bilateral), aged between 40 and 85 years, and with consent to participation. Knee OA was diagnosed according to the clinical criteria of the American College of Rheumatology (15). Exclusion criteria were as follows: polyarthritis, presence of rheumatoid arthritis or other systemic inflammatory arthropathies, knee surgery within the last 12 months or a history of knee arthroplastic surgery, intra-articular corticosteroid injections into either knee within the previous 3 months, and/or inability to understand the Dutch language.

Measures

Demographics. A series of demographic variables were obtained including age, sex, height, weight, and duration of complaints.

Muscle strength. Muscle strength was assessed for flexion and extension of the knee using an isokinetic dynamometer (EnKnee; Enraf-Nonius, Delft, the Netherlands). Quadriceps and hamstrings strength were measured isokinetically at 60^0/second.
A single tester assessed all patients according to a standardized protocol. Patients were seated on a bench and secured to the testing device through

the use of chest, pelvis, and thigh straps. The ankle pad of the dynamometer was placed 2 cm proximal to the medial malleolus to allow ankle dorsiflexion during the tests. The mechanical axis of the dynamometer was aligned with the approximate axis of the knee through the lateral epicondyle of the femur. Patients rested their hands on the sides of the bench.

During isokinetic testing at 60^0/second, range of motion was limited to 20-80^0 for joint protection. Following instruction, patients performed 4 warm-up repetitions, beginning with submaximal contractions and building to maximal contractions. Following a 30-second rest, patients performed 3 maximal test repetitions. Right-left order of testing was alternated between patients. The tester verbally encouraged the patients to achieve maximal torque. The maximum score of the 3 repetitions was used to indicate maximum flexion or extension strength. The mean of flexion and extension strength of the left and right leg were computed to obtain mean muscle strength. Subsequently, mean muscle strength (in Nm) was divided by the patient's weight to control for the correlation between muscle strength and weight. Thus, a measure of overall leg muscle strength in Nm/kg was obtained, which was used in the analyses.

Joint laxity. Varus-valgus laxity was measured using a previously described device and protocol that provide thigh and lower-leg immobilization, a stable knee angle in flexion of 20^0, and fixed varus and valgus load (16). Laxity was measured (in degrees) as the movement in the frontal plane after varus and valgus load. A weight of 1.12 kg was used to load the lower leg. This weight was attached to the free-moving arm by a cord. The cord was attached 0.68 m from the pivot of the arm, resulting in a net moment on the knee of 7.7 Nm. This load could be applied to the lower leg both medially and laterally, resulting in varus or valgus movement in the knee joint.

All measurements of laxity were performed by the same examiner (MvdE) in adherence to a protocol, including the use of anatomic landmarks for patient positioning, patient instructions and the examiner's position. Right-left order of testing was alternated between patients. Three consecutive measurements were made. The mean (in degrees) laxity of the right and left knees obtained from these 3 measurements was used for analysis. The intraclass correlation coefficients (ICCs) for intrarater and interrater reliability of the measurements with this device in healthy persons were 0.80 and 0.88, respectively (17).

Functional ability. Functional ability was assessed with both a standardized physical performance test and a self-report questionnaire (Western Ontario and McMaster University Osteoarthritis Index (WOMAC)). As a performance-based measure of function, a 100-meter walking test was used (18). The time to walk a 20-meter level and unobstructed corridor 5 times (100 meters in total) was measured. Patients were instructed to walk the distance as fast as possible. On the command "go", patients walked along the level of the corridor. They were instructed not to stop before crossing the finish line. A stopwatch was used to measure in seconds the time from the command "go" until patients crossed the finish line. The examiner was standing at the finish line during the test. Patients who used canes while walking were permitted to use them during the test. All patients were wearing walking shoes.

The Dutch version of the WOMAC was used to assess self-reported functional ability (19). The WOMAC is a disease-specific measure of pain, stiffness, and physical function for individuals with OA of the knee (20). The WOMAC, with a possible range of 0-96, includes 5 items related to pain, 2 items related to stiffness, and 17 items related to physical function. Each item is scored on a 5-point Likert scale. Reliability and validity of the WOMAC have been established (21). Higher scores on the WOMAC represent greater limitations in function. The ICC for Dutch WOMAC physical functioning was 0.92 (19).

Pain. Average overall pain in the past week and average current knee pain were measured using a 100-mm visual analogue scale.

Radiography. Radiographs of the knee were scored by an experienced reader using the grading scales proposed by Kellgren and Lawrence (22,23). The radiographs of 7 patients were missing.

Statistical analysis. Because functional ability (i.e., walking ability and WOMAC physical function score) was specific to the person, knee-specific data (i.e. muscle strength and joint laxity) were averaged across right and left knees for analyses involving functional ability.

First, Pearson's correlation coefficients were computed to establish the bivariate relationship between joint laxity and muscle strength and between joint laxity and functional ability (i.e., walking time and WOMAC physical function). Second, multiple regression analyses were performed to assess the relationship between muscle strength and functional ability and the impact of laxity. Multiple regression analyses were used to assess which factors were independently associated with functional ability. An interaction variable between muscle strength and laxity was added to the model to assess the role of laxity as a modifier of the relationship between muscle strength and functional ability. The independent variables muscle strength and joint laxity were centered around the mean (24). Centering allows for a meaningful interpretation of main effects when interaction is present in the model. Other independent variables in the analysis comprised age, sex, duration of symptoms, and current pain. The significance level for exclusion from the final regression model was set at $P < 0.10$; regression coefficients were considered to be significant at $P < 0.05$. All analyses were performed using SPSS software, version 11.5 (SPSS, Chicago, IL).

RESULTS

Characteristics of the study sample are listed in Table 1. The mean varus-valgus laxity between the left and right knees correlated with each other ($r = 0.78$, $P < 0.001$). Between the left and right knees, quadriceps strength and hamstrings strength correlated with each other ($r = 0.79$, $P < 0.001$ and $r = 0.83$, $P < 0.001$, respectively). The mean ± SD total muscle strength as an average of flexion and extension strength was 0.74 ± 0.35 Nm/kg, with a Pearson's correlation coefficient of 0.85 ($P < 0.001$) between the average of quadriceps and hamstrings strength of the left knee and the average of quadriceps and hamstrings strength of the right knee.

Table 1. Characteristics of patients with knee osteoarthritis (N =86)*

Characteristics	Value
Sex, no. (%)	
Female	65(76)
Male	21(24)
Age, years	63.6 ± 9.1 (46-83)
Body mass index,kg/m^2	31.6 ±6.4 (22.6-59.5)
Duration of complaints, years	18.6 ± 14.0 (1-70)
Overall current pain (0-10)	3.7 ± 2.8 (0-10)
Overall pain in the last week (0-10)	5.3 ± 2.7 (0-10)
Frequency of pain during the day, no. (%)	
Seldom	3 (3.5)
Occasionally	15(17.4)
Regular	24 (27.9)
Frequently	10(11.6)
Continuous	34 (39.5)
Walking time, seconds	105.2 ± 39.6 (40-270)
WOMAC-Pain score	10.9 ± 5.1 (0-24)
WOMAC-Stiffness score	3.7 ± 2.1 (0-8)
WOMAC-PF score	32.4 ± 13.8 (1-57)
Varus-valgus laxity, degrees	
Left knee	6.9 ± 3.4 (1.6-18.9)
Right knee	6.9 ± 3.2 (1.0-17.0)
Isokinetic quadriceps strength, Nm/kg	
Left knee	0.82 ± 0.46 (0.03-2.49)
Right knee	0.90 ± 0.48 (0.03-2.47)
Isokinetic hamstrings strength, Nm/kg	
Left knee	0.61 ± 0.29 (0.03-1.50)
Right knee	0.63 ± 0.30 (0.11-1.61)
Muscle strength †	0.74 ± 0.53 (0.05-2.02)
K/L grade, no. (%) of knees	
Right (n=79)	
Grade 0	7 (8)
Grade 1	7 (8)
Grade 2	39(45)
Grade 3	24 (28)
Grade 4	2 (2)
Left (n=79)	
Grade 0	5 (6)
Grade 1	11(13)
Grade 2	35(41)
Grade 3	20(23)
Grade 4	8 (9)

* Values are the mean ± SD (range) unless otherwise indicated.
WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.
K/L = Kellgren/Lawrence.
† Averaged left/right and extension/flexion.

Bivariate relationships between joint laxity, muscle strength, and functional ability. Joint laxity was moderately associated with walking-time (r = 0.25; $P < 0.05$) and not associated with the WOMAC physical function score (r = 0.03, $P = 0.799$). Negative correlations were found between joint laxity and total muscle strength (r = -.034, $P < 0.05$) and between total muscle strength and walking time (r = -0.50, $P < 0.001$). Similarly, total muscle strength correlated negatively with the WOMAC physical function score (r = -.061, $P < 0.001$).

Multivariate relationships between joint laxity, muscle strength, and functional ability. To analyze the relationship between functional ability and total muscle strength, a multiple regression model was constructed: Functional ability = $b_0 + b_1 * \text{muscle strength} + b_2 * \text{laxity} + b_3 * \text{laxity} * \text{muscle strength}$.

The model explaining the total variation of walking time was as follows (see Table 2): Walking time = 97.41 – 72.73 muscle strength + 0.70 laxity – 12.24 muscle strength * laxity (F = 13.89, $P < 0.001$, $R^2 = 0.35$; N = 81). This means that 35% of the total variation of walking time is explained by muscle strength, laxity and their interaction. The independent variable muscle strength (b_1= -72.73, $P < 0.001$) and the interaction between muscle strength and joint laxity (b_3=-14.24, $P = 0.002$) were significantly associated with walking time. When laxity equals 0 (0 = mean of 6.9°) and muscle strength increases by 1Nm/kg, then the walking time will decrease with 72.73 seconds. However, when laxity increases by 1° (1 = 7.9°) and muscle strength increases by 1Nm/kg (= 1.74 N/kg), then the walking time will decrease by 84.27seconds.

The model explaining the total variation of WOMAC physical function was as follows (see Table 2): WOMAC physical function = 30.98 – 31.49 muscle strength – 1.04 laxity – 2.34 laxity*muscle strength (F = 19.94, $P < 0.001$, $R^2 = 0.43$; N = 81). This means that 43% of the total variation of WOMAC physical function is explained by muscle strength, laxity and their interaction. The independent variables muscle strength (b= -31.49, $P < 0.001$), joint laxity (b= -1.04, $P < 0.05$) and the interaction between these 2 variables (b = -2.34, $P = 0.08$) were associated with the WOMAC physical function score, although the interaction was not statistically significant at the $P < 0.05$ level. This means that when laxity equals 0 (0 = mean of 6.9°) and muscle strength increases by 1Nm/kg (0 = mean of 0.74 Nm/kg), then the WOMAC physical function score will decrease with 21.48. However, when laxity increases by 1° (1 = 7.9°) and muscle strength increases by 1 Nm/kg, then the WOMAC physical function will decrease by 34.87. To visualize the interaction between muscle strength and joint laxity, laxity was dichotomized into low and high laxity using the median-split method (Figure 1).

Table 2. Results of the regression of functional ability (walking time and WOMAC physical function) on muscle strength and joint laxity*.

	Walking time†		WOMAC physical function‡	
Variables§	b* (SEE)	P	b*(SEE)	P
Intercept	97.41		30.98	
Muscle strength	-72.73 (12.89)	0.000	-31.49 (4.48)	0.000
Laxity	0.70 (1.17)	0.549	-1.04 (0.41)	0.012
Muscle strength x laxity	-12.24 (3.79)	0.002	-2.34 (1.32)	0.080

* WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.
b = unstandardized regression coefficient.
† $R^2 = 0.35$, F=13.89, $P < 0.001$.
‡ $R^2 = 0.43$, F=19.94, $P < 0.001$.
SEE = Standard Error of the Estimate.
§variables centered around the mean.

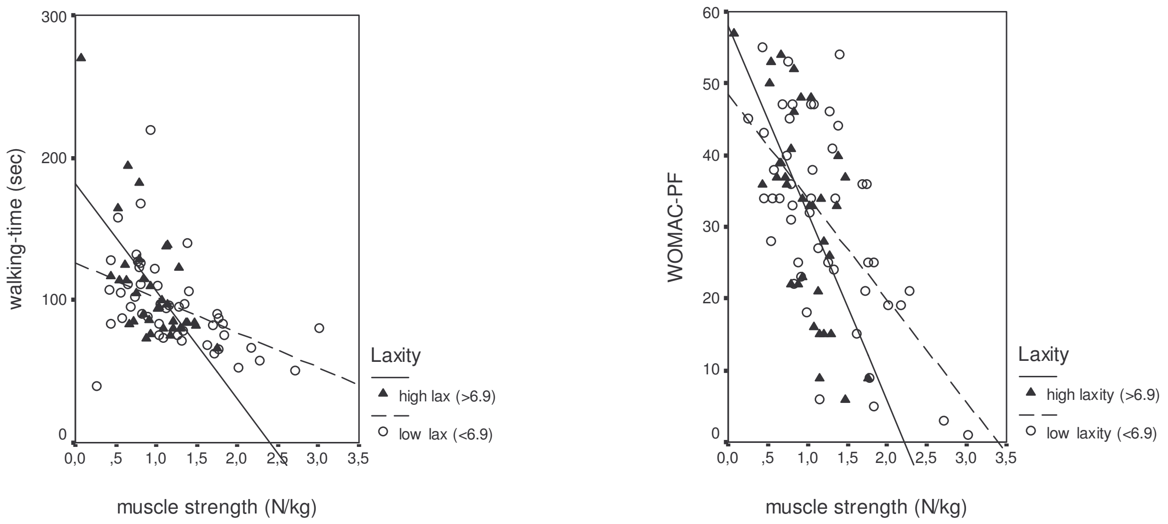

Figure 1A. **Figure 1B.**
The relationship between functional ability and muscle strength in a low-laxity group ($<6.9^0$) and a high-laxity group ($>6.9^0$).
A: walking time vs. muscle strength. B: WOMAC physical function vs. muscle strength.
WOMAC-PF = Western Ontario and McMaster Universities Osteoarthritis Index physical function.
Sec = seconds

These analyses were repeated in a more extensive model, with the demographic variables from Table 1 as controlling variables. The results of those analyses were consistent with the results published here.

DISCUSSION

Two opposing hypotheses of the influence of joint laxity on the relationship between muscle strength and functional ability were tested in patients with OA of the knee. Our results confirm the first hypothesis, i.e., high joint laxity is associated with a stronger relationship between muscle strength and functional ability.

The results of the present study may be explained by the results presented by Hortobagyi et al (13). In that study patients with OA had a significantly higher coactivity of knee muscles than age-matched healthy adults and young adults. Patients with knee OA revealed increased muscle coactivation while executing activities of daily living. Coactivation is considered to provide active stabilization of the knee in the absence of adequate stabilization by the passive restraint system (ligaments and capsule) (11,12). It is likely that coactivation of muscles will only succeed in stabilizing the knee joint when there is sufficient muscle strength. This means that muscle strength is a prerequisite for successful joint stabilization through muscle coactivation. Therefore, we hypothesize that coactivation will be more successful in providing joint stability and subsequently in maintaining functional ability in patients with high muscle strength than in patients with less muscle strength, indicating a close relationship between available muscle strength and successful stabilization through muscle coactivation. This would mean that in patients with high knee laxity, differences in muscle strength result in relatively large differences in functional ability compared to patients with low-laxity knee joints. Comparable results were found in a study by Doorenbosch and Harlaar (11), where subjects with an ACL deficiency, i.e., high anterior-posterior laxity, compensated the loss of passive stability (laxity) by developing higher coactivation levels of knee muscles, i.e., active stabilization. Similarly, the results of McNair and Marshall (12) support the hypothesis that higher levels of co-contraction of quadriceps and hamstrings during movements in patients with ACL deficiency provide an active stabilization of the knee to compensate for the loss of the passive structure.

Our results are not in agreement with conclusions presented by Sharma et al (9,10,14). In one of those studies (14), it was stated that high laxity was associated with a weaker relationship between muscle strength and functional ability in patients with knee OA (supporting the second hypothesis).

A likely explanation of this discrepancy is the difference in analytical approach. The conclusions of Sharma et al were based on a comparison of the correlations between muscle strength and disability in a high-laxity and low-laxity group. Between these 2 patient groups, there was a small difference in correlation between quadriceps strength and WOMAC physical function (r = -0.27, 95% confidence interval(95% CI) -0.46, -0.05 in the low-laxity group and r = -0.19, 95% CI -0.40, 0.04 in the high-laxity group) and between hamstrings strength and WOMAC physical function (r = -0.30, 95% CI -0.39, 0.03 in the low laxity group and r = -0.21, 95% CI -0.42, 0.02 in the high-laxity group). Given these 95% CIs, it is not likely that the differences in correlation reported by Sharma et al were statistically significant. Additionally, for our particular research question, the use of regression coefficients is preferable. First, using a regression model with an interaction term of muscle strength and laxity allows for one analysis using data from all patients, whereas a correlational analysis similar to the approach used by Sharma et al would require dividing the research group into patients with high and low laxity based on an arbitrary cutoff point. Secondly, the *P* value of the regression coefficient of the interaction term provides an immediate insight into the statistical significance of the impact of laxity on the relationship between muscle strength and functional ability.

It should be noted that there are some differences between the populations and measurement equipment and protocols of our study and the study by Sharma et al (14). Our patients were on average more disabled (higher WOMAC physical function score), although age, sex, body mass index, pain and OA severity were similar. With regard to the measurement protocols and equipment, there are differences between the studies in measuring laxity and muscle strength. In our measurement of laxity, we applied a different method of leg fixation to the device, used a lower torque, which was also applied in a different manner, and used an electronic sensor to assess varus-valgus rotation rather than an analogous device. In our study, muscle strength was measured isokinetically with a lower velocity (60°/second as opposed to 120°/second). Muscle strength was also corrected for body weight and expressed in SI units rather than feet/pound. However, although these differences may have influenced the results, we believe that the statistical analysis is the main reason for the different conclusions.

The direct relationship between laxity and functional ability was found to be weak (walking time) or absent (WOMAC physical function). Therefore, although laxity is an important factor in instability of the knee (25), the direct effect of laxity in functional ability seems to be relatively limited.

Some issues need to be addressed concerning the methods used in this study. First, the interrelationship of joint laxity between left and right knees in patients with OA of the knee was established and showed a high correlation. Consequently, joint laxity of left and right knees of the same patients were averaged and used in subsequent analyses. Second, the inter-relationship of muscle strength between left and right knees was established, also showing also a high correlation. The results of the muscle strength measurements were averaged in the same manner and were used in subsequent analyses. This indicated that both knee joint laxity and muscle strength are characteristics of a specific patient, instead of characteristics of a specific knee. This finding has been reported previously for muscle strength (5).

In considering the implications of this study for exercise therapy, it is useful to consider some limitations first. One limitation is that an adequate level of joint laxity is unknown In the absence of a known cutoff point to separate normal angular deviation under load from abnormal deviation (laxity) the differentiation between high and low laxity is only relative. The second limitation of this study is that it was a cross-sectional study of 86 patients from 1 rehabilitation center and causal conclusions were not allowed. Nevertheless, our results support the use of exercise therapy in patients with OA with high knee joint laxity. Based on the results presented here, patients with high laxity can be predicted to benefit from interventions aimed at increasing muscle strength.

In conclusion, patients with OA with high knee joint laxity show a stronger relationship between muscle strength and functional ability than patients with OA with low knee joints laxity. Patients with OA with high knee joint laxity and low muscle strength are most at risk of being disabled.

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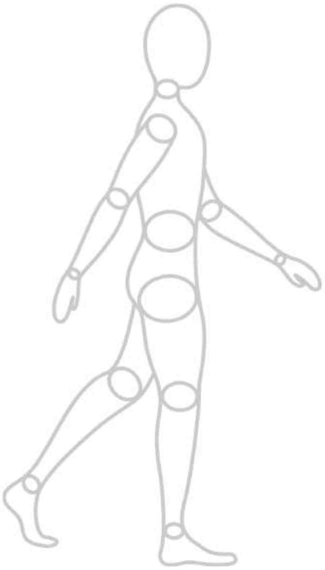
Chapter 3

REPRODUCIBILITY OF KNEE JOINT LAXITY MEASUREMENTS



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ABSTRACT

Objective. To determine reproducibility of frontal plane knee joint laxity measurement through the assessment the intra- and inter-rater reliability coefficients and the intra- and inter-rater agreement coefficients.

Methods. Two raters independently assessed the laxity of the knee joint in the frontal plane by three repeated measurements. Fourteen days later the assessment was repeated. Complete data were obtained from 20 healthy subjects. Laxity was assessed using a device which consisted of a chair with a free-moving arm that supported the subject's lower leg. Medial and lateral loads were applied, resulting in a varus and valgus movement in the knee joint. The intra- and inter-rater reliability coefficients (Intraclass Correlation Coefficients (ICC)) were estimated, as were the intra- and inter rater agreement parameters (the Standard Error of Measurement (SEM) and the Minimal Detectable Difference (MDD)).

Results. Adequate intra-rater reliability (ICC>0.80) was calculated for each rater's measurements of laxity. The inter-rater reliability was less adequate (ICC=0.65) when calculated using the first day's measurements. However, inter-rater reliability was adequate (ICC=0.88) when calculated using the day 14 measurements. The intra-rater measurement error calculated across occasions was 1.3^{0} for individual subjects. This resulted in a MDD of 3.7^{0}. The inter-rater measurement error, i.e. the SEM and MDD, was higher (1.5^{0} and 4.3^{0} , respectively).

Conclusion. Intra-rater reliability of knee joint laxity measurement is good. Adequate training of the raters establishes the basis for good inter-rater reliability. In clinical trials, it is preferable for one trained rater to perform the laxity measurement. The measurement of knee joint laxity is limited due to its relatively high measurement error in individual subjects; therefore, the measurement should be restricted to group assessment rather than individual patient assessment.

Keywords: Reproducibility, Reliability, Knee joint laxity, Osteoarthritis.

INTRODUCTION

Frontal plane knee joint laxity may play an important role in knee osteoarthritis (OA). Laxity can be defined as the angular deviation of the tibia-femoral joint in the frontal plane after varus-valgus load is applied (1,2). Laxity is related to radiographic progression and to poor functional outcome (3-8). Although laxity has been identified as an important factor in OA of the knee, detailed information on clinimetric properties of its measurement is unavailable.

Measuring laxity equates to measuring small differences in varus-valgus deviations. To detect minimal differences in laxity, high-precision measurement with high reproducibility is essential.

Reproducibility concerns the degree to which repeated measurements in a constant situation provide similar answers. For the quantification of reproducibility, two types of measures can be distinguished: measurements of reliability and measurements of agreement. Reliability parameters assess whether persons in a group can be distinguished from each other, despite measurement errors (9). Reliability is expressed as the intraclass correlation coefficient (ICC), ranging from 0 to 1 (9). A high ICC represents a sufficient distinguishing capacity of the instrument regardless of measurement error. In order to identify precise measurement, the absolute measurement error has to be taken into account. Expressing the measurement error in scale points is often referred to as agreement. Agreement parameters assess how close the results of the measurements are within individual subjects by estimating the absolute measurement error in repeated measurements (10,11). Agreement in measuring joint laxity is expressed as the standard error of measurement (SEM) in degrees and the minimal detectable difference (MDD) in degrees.

Currently, there is very limited information regarding the reproducibility of the measurement of knee joint laxity. In two studies (4,5) the reliability was tested on four and five patients, respectively, with an intra-rater reliability of 0.92 (ICC). Sharma et al (1,2,6,7) presented reliability scores ranging from 0.84 to 0.90 (ICC). Information regarding inter-rater reliability and agreement parameters is presently unavailable. For this reason, there is an evident need to examine the reproducibility of the measurement of laxity in the knee.

The objective of this study was to establish (i) the intra- and inter-rater reliability and (ii) the intra- and inter-rater agreement parameters of the measurement of knee joint laxity.

METHODS

Subject. Twenty healthy young volunteers (10 males, 10 females) participated in the study. The mean ± SD age of the subjects was 22.9 ± 3.0 yr. The inclusion criteria were no current knee pain; no previous injury in the hip-knee region; no analgesics or anti-depressive medication; and, for women, regular menstrual cycles for the 3 months prior to the study. All of the above criteria may influence the degree of laxity. Ethical review board approval was obtained, and all participants provided written informed consent.

Design. Two raters (a physical therapist and a human movement scientist), both trained in clinical measurements by a clinician, independently performed all the laxity measurements. The subjects were scheduled for the two experimental sessions (day 1 and 14). On both occasions the raters measured the subjects. Each rater measured the same knee of each subject three times. In 10 subjects the right knee was measured and in 10 other subjects the left one.

Each rater made three consecutive measurements and the subjects remained seated and fixed between measurements. The deviation in the subject's knee was recorded digitally. After the first rater had assessed the joint laxity, all fixations points were removed and the subject stood up. Subsequently the second rater seated, fixed and assessed the same subject. To avoid bias, the second rater waited in an other room while the first rater performed the measurements.

After 14 days the procedure was repeated; the order of raters was reversed. Both raters were blinded to the results of the reproducibility analyses of the day 1 measurements.

Equipment. An electronic device (Fig.1) was used to measure knee varus-valgus laxity. A chair with an attached free-moving arm, which supported the subject's lower leg, was used to seat the subject. The subject was seated comfortably in the measurement chair, which had a back support. The device was constructed in such a manner that throughout the study the knee joint was held in 20^0 of flexion.

The thigh, lower leg and ankle were fixed to the device. No medial or lateral movement of the lower leg and thigh or internal and external rotation of the hip was possible using these fixation techniques. The thigh and lower leg were fixed at five places. The foot and distal part of the lower leg were fastened to the arm sing clamps at the ankle and at the distal part of the leg (Fig. 1; points1 and 2). Below the knee the lower leg was fixed to the device with a Velcro bandage (Fig. 1; point 3). The distal/lower part of the thigh was fixed using two clamps (Fig 1; point 4). The upper thigh was fastened to the chair using a Velcro bandage (Fig.1; point 5).

The joint of the arm moved with minimal friction. The axis of rotation of the free- moving arm was centrally located directly under the tibiafemoral joint of the subject (i.e., the middle of the popliteal fossa). To supply a steady moment to the knee of 7.7 Nm, a dead-weight was used. This weight was attached to the free-moving arm by a cord. The cord was attached 0.68 m from the axis of rotation of the arm. This load could be applied to the lower leg both medially and laterally, resulting in varus or valgus movement in the knee joint. An electronic measurement system digitally recorded the end point of the varus or valgus movement, after 4 s. Laxity of the knee joint was calculated as the sum of the varus and valgus deviations in degrees (7,8).

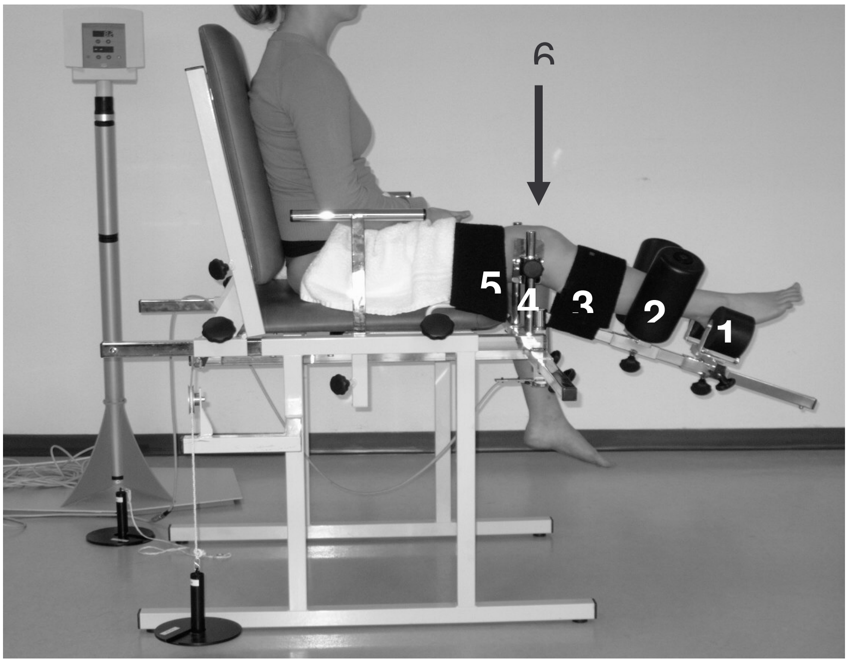

Figure 1.

Experimental set up for the assessment of knee joint laxity showing the measurement chair with five fixations and the position of the meter in line with the valgus-varus rotation axis of the knee. 1 and 2, ankle and lower leg clamps; Velcro bandage for lower leg; 4, two clamps at the femur condyles; 5, Velcro bandage for thigh; A, free-moving arm; B, axis of rotation; C, dead weight.

Joint laxity measurement. All measurements of laxity were performed in accordance with our protocol, including the use of anatomical landmarks for patient positioning, patient instructions and the examiner's position.

Anatomical landmarks of the knee were palpated to localize the medial and lateral joint spaces and the middle of the fossa poplitea. These anatomical structures give an indication of the position of the varus-valgus rotation axis of the tibia-femoral joint of the knee. The electronic meter was positioned in line with the varus-valgus rotation axis (Fig. 1; point 6).

To avoid increased muscle tone resulting from pain during the fixation or measurement, subjects were instructed to relax as much as possible and to report the onset of pain.

Raters were seated behind the patient and applied the load slowly by hand to the lower leg in a standardized manner.

Analysis. The mean score in degrees for laxity obtained from the three measurements was used for analysis. Reproducibility was assessed using the following sources of variance: subject, rater, time of measurement and interaction between these variables. To express reproducibility, the following parameters were established(11,12).

Intra-rater reliability. The ICC (2,k) was calculated as the ratio of variance between subjects within one rater, in relation to the relative measurement error (including all sources of variance: rater, subject, time of measurements, and the absolute measurement error).

Intra-rater agreement. The SEM concerns the absolute measurement error in measuring an individual. It assesses the proximity of the scores on repeated measures (10,11). The amount of measurement error can be expressed as the SEM. The SEM was derived by taking the square root of the error variance of the following sources of variance: time of measurement, interaction between subject and time of measurement, interaction between rater and time of measurement, and interaction between subject, rater and time of measurement. The SEM was calculated across both occasions. The SEM was used to calculate the MDD. The MDD is the smallest measurable difference that can be interpreted as a real difference between two measurements, i.e. beyond zero (10,11). To compute the MDD as the 95% confidence limit of the SEM, the SEM has to be multiplied by 1.96 (for the 95% interval (ICC)) and by the square root of 2 for the difference scores ($1.96 \times \sqrt{2} \times SEM$). The MDD expresses the uncertainty of the difference between two observed scores (14).

Inter-rater reliability. The ICC was calculated as the ratio of variance between (rater, subject, time of measurement, and the absolute measurement error) between subjects and between the two raters, in relation to the relative measurement error.

Inter-rater agreement. The SEM was calculated to establish the absolute measurement error across raters and occasions, calculated according to the generalizability theory (9). The SEM was derived by taking the square root of the error variance of the following sources of variance: rater, time of measurement, interaction between rater and subject, interaction between rater and time of measurement, interaction between subject and time of measurements, and the interaction between subject, rater, time of measurement. The SEM was used to calculate the MDD. The MDD was also calculated across raters and occasions.

In order to visualize the difference between raters against the corresponding mean of the two raters for each subject, a limit-of-agreement plot was constructed, as proposed by Bland and Altman (15).

For reliability, an ICC >0.70 was regarded as adequate (16). Confidence intervals were presented as an indication of the precision of the point estimate. To calculate the ICC, the SEM and the MDD, a two-way random effects model of analysis of variances (ANOVA) was performed, using the Statistical Package for the Social Sciences (SPSS) version 12.0. Windows (SPSS, Chicago, IL, USA).

RESULTS

Subjects. The study sample consisted of 20 healthy subjects. The demographic data of subjects are presented in Table 1. For rater A, the mean scores in knee joint laxity on the first (day 1) and second assessment (day 14) were 5.5^0 and

6.5^0, respectively. For rater B, the mean scores were 5.5^0 and 6.5^0 at day 1 and 14, respectively.

Table 1
Characteristics of subjects (*n*=20)

Variable		
Mean (S.D.) age (yr)	22.85 (2.96)	
Sex: % female	50%	
Mean (S.D.) weight (kg)	68.2 (8.5)	
Mean (S.D.) length (m)	1.78 (0.09)	
Mean (S.D.)knee joint laxity		
- Rater A at day 1 and day 14	5.5 (2.3)°	6.2 (2.6)°
- Rater B at day 1 and day 14	5.5 (2.6)°	6.5 (2.4)°

Intra-rater reliability. The ICC for rater A was 0.84 (95% CI 0.61, 0.94) and 0.93 (95% CI 0.81, 0.97) for rater B.

Intra-rater agreement. Generalized across occasions by the same fixed rater, the measurement error, expressed as the SEM, was 1.35^0 and the MDD was 3.73^0 (Table 2).

Inter-rater reliability. The ICC was 0.65 (95% CI 0.13, 0.86) for the assessment on day 1 and 0.88 (95% CI 0.70, 0.95) for the assessment on day 14.

Inter-rater agreement. The SEM was 1.55^0 and the MDD 4.30^0, generalized across raters and occasions. This result represents the absolute measurement error when a subject has been measured on a first occasion by a rater and the same subject is also measured by a second rater on a second occasion by a second rater. The agreement coefficients are presented in Table 2.

Table 2
Intra- and inter-rater agreement coefficients

	SEM	MDD (95% CI)
Intra [a]	1.35	3.73 (2.66-6.37)
Inter [b]	1.55	4.30 (3.21-6.50)

[a] generalized across occasions by the same fixed rater.
[b] generalized across occasions and raters.

Figure 2 shows the difference between raters on day 14, plotted against the mean value of both raters for each subject for laxity of the knee joint. No systematic variation in the differences over the range of measurement was found amongst the subjects. The width of the limits of agreement suggests that there was considerable random variation.

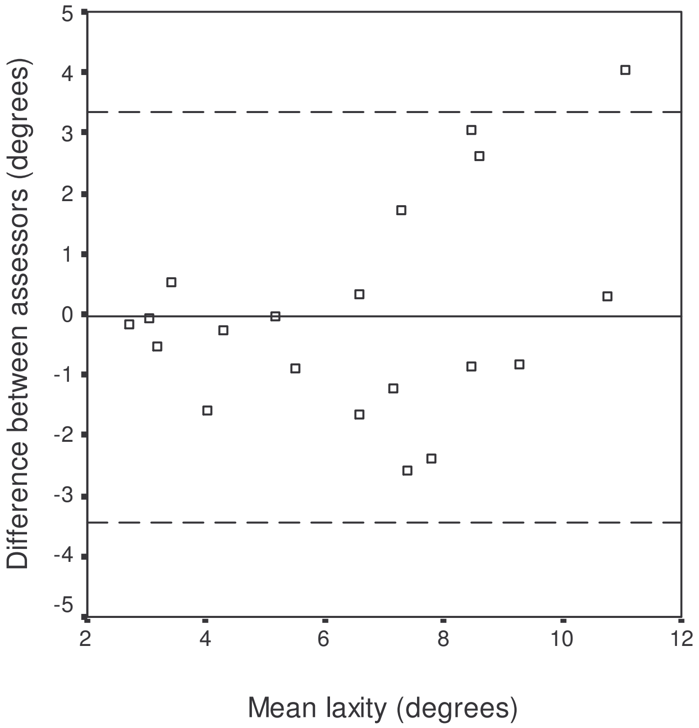

Figure 2.
Differences between raters on day 14 plotted against the mean value of both raters for each subject for varus-valgus laxity of the knee joint. Solid line shows the mean difference (-0.026); dashed lines show the 95% limits of agreement (3.38 en –3.44).

DISCUSSION

In this study the reproducibility of knee joint laxity measurement was quantified using generalized reliability parameters and agreement parameters in healthy, stable subjects. The ICC as an intra-rater reliability coefficient expresses the measured variance within one rater on two occasions . In our study the ICCs were found to be adequate for both raters (0.84 and 0.93, respectively). The ICC as an inter-rater reliability coefficient expresses the measured variance between two raters on the first and second occasions. The ICC was low (0.65) on the first occasion (day1) and adequate (0.88) on the second occasion (day 14). Measurement of intra-rater agreement parameters is important in quantifying measurement error. In our study the intra-rater SEM was 1.3^0. When the measurement was repeated by the same rater on the same subject the MDD was 3.7^0. This expresses (with an uncertainty of < 5%) that a difference between two measurements of less than 3.7^0 is attributable to measurement error and can therefore not be interpreted as a real difference. Only a difference in measurements made by the same rater exceeding 3.7^0 is likely to signify a real change in laxity.

Inter-rater agreement parameters express the absolute measurement error when a rater measures an individual subject on one occasion and a second rater measures the same subject on a second occasion 14 days later. In our study the inter-rater SEM was 1.5^0. This indicates the absolute measurement error generalized for occasions and raters. The MDD was 4.3^0, which indicates that this is the smallest difference between two measurements made by different raters at different times that can be interpreted as a genuine change.

To assess reproducibility we used healthy, stable subjects. It was assumed that the biological variation in the group, i.e. the variability in laxity of the knee joint, was small. The raters were well instructed, trained and measured in accordance with a given protocol. Compared with other studies involving clinical subjects (1,2,4,5,) our intra-rater reliability coefficients were lower. The heterogeneity of the population in previously conducted clinical studies could explain the difference from our study. A small range of laxity in healthy subjects makes the distinction between subjects more difficult, compared with a patient population with higher variability. In a patient population the subjects are easier to rank, because the difference between subjects is greater than the difference between subjects in a healthy population. Consequently, the ICC will be lower in healthy subjects than the ICCs in clinical studies. To compare the inter-rater reliability, no other studies are available. The inter-rater reliability coefficient was substantially higher on day 14 compared with day 1. In the day 14 session reliability was good. Although the raters had some previous experience in knee assessment, it is conceivable that experience gained through the knee measurements in this study resulted in a higher reliability coefficient. The increased experience could explain the higher reliability on day 14.

Inter-rater reliability was lower than intra-rater reliability. Therefore, using one trained rater to perform all laxity measurements is recommended.

One source of error could be the fixation of the lower leg and thigh of subjects. The lower leg and thigh were fixed in five places. Possible reasons for variation in the fixation points which can account for measurement variance are: (i) small differences in the positioning of the leg during fixation between raters and between occasions, and (ii) possible pain in the lower leg and thigh during the measurement. In our study a load of 7.7 Nm was used. Sharma et al (1,2) used a load of 12 Nm. In a study applying this load to patients with OA of the knee, we found that a load of 12 Nm induced pain in some patients (8). Hence, we decided to reduce the applied load to 7.7 Nm. This reduced load was not painful for any of the patients tested. However, it is recommended that the patient's exposure should be limited to the minimum number of measurements readings needed to obtain a reliable result, and that attention should be paid to possible discomfort or pain during the measurements, in order to prevent any adverse effects. Although the mean scores of laxity in our study are similar to those in the Sharma et al study (1,2,7), the subjects are not comparable because of the technical differences between the devices and the different loads used in the measurement.

Our results suggest that laxity measurements are of limited use in clinical practice, because of considerable measurement error. However, in research precision can be increased by including more subjects. For clinical trials related to laxity, an adequate number of subjects should be included, based on a power analysis.

In conclusion, these results on reproducibility of the knee joint laxity measurement indicate that the intra-rater reliability is good. The inter-rater reliability is less adequate on the first test occasion and good on the second test occasion. In a setting in which both raters are well trained, it is possible to achieve acceptable inter-rater reliability. The interpretation of results of the measurement of frontal plane knee laxity at the individual level is limited because of measurement error.

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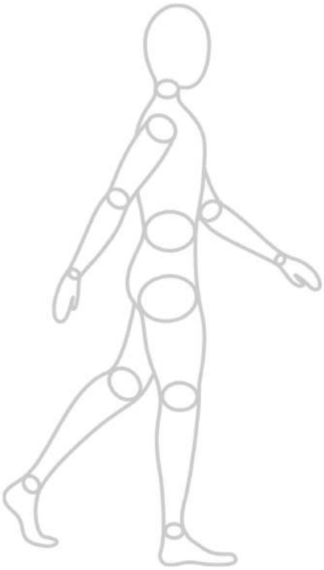
Chapter 4

GENDER DIFFERENCE IN VARUS-VALGUS LAXITY IN OSTEOARTHRITIS OF THE KNEE



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In recent years, knee joint varus-valgus laxity has been identified as an important factor in osteoarthritis (OA) of the knee. Varus-valgus laxity is defined as the displacement of the tibia relative to the femur in the frontal plane ('varus and valgus rotation') (1). High joint varus-valgus laxity has been identified as a risk factor for progression of osteoarthritis (1,2) and as a predictor of poor functional outcome (3,4). Clinical experience indicates that women with OA of the knee show more varus-valgus laxity than men. However, gender related differences among patients with OA of the knee have not been studied. Therefore, the aim of this study was to test the hypothesis that varus-valgus laxity in knee OA patients is higher in women than in men.

The study group consisted of 86 patients (21 men and 65 women) diagnosed with OA of the knee. Patients were selected randomly from the population of an outpatient rheumatology rehabilitation centre in the Netherlands. Inclusion criteria were OA of the knee (uni- or bilateral), age between 40 and 85 years, and informed consent to participation. OA of the knee was diagnosed according to the clinical criteria of the American College of Rheumatology (5). Exclusion criteria were: polyarthritis, presence of rheumatoid arthritis or other systemic inflammatory arthropathies, knee surgery within the past 12 months or a history of knee arthroplastic surgery, intra-articular corticosteroid injections into either knee within the previous 3 months, and/or inability to understand the Dutch language.

Varus-valgus laxity was measured using a previously described device and protocol (4,6). The intraclass correlation coefficient (ICC) for intra-rater reliability of the measurements with this device in healthy persons ranged from 0.84 to 0.93, the ICC for inter-rater reliability ranged from 0.65 to 0.88 (7). The mean laxity of the left and right knee was used as a measure of the patient's knee joint laxity . This was justified because 89% of total variance in knee joint laxity was between-patient variance, that is less than 11% of variance in knee joint laxity was due to differences between laxity of the left and right knee within patients. Radiographs of the knee were scored by an experienced radiologist using the grading scales proposed by Kellgren & Lawrence (K/L)(8). The radiographs were missing from seven patients. An unpaired t-test was used to assess gender differences in knee joint laxity. Additionally, unpaired t-tests and Mann-Whitney U-tests were used to establish gender differences in age, body mass index (BMI), and severity of radiological joint damage. A multiple linear regression analysis was performed to assess the relationship between varus-valgus laxity and gender while controlling for age, BMI, and radiographic OA.

Characteristics of the study sample are listed in Table 1.

Table 1. Characteristics of study participants, grouped according to sex (N =86).

		Male (n = 21)	**Female** (n = 65)	**P-value**
Age (years)		64 ± 7.3	63 ± 10	0.684
Body mass index (kg/m^2)		30.9 ± 7.3	31 ± 6.5	0.612
Varus-valgus laxity, mean of left and right knees (°)		4.6 ± 2.2	7.7 ± 2.9	<0.001
Varus-valgus laxity, left knee (°)		4.6 ± 2.5	7.7 ± 3.3	<0.001
Varus-valgus laxity, right knee (°)		4.6 ± 2.2	7.8 ± 3.1	<0.001
Aligned/malaligned , no of knees				
		N =21	N = 65	
Right		16/5	38/27	0.070
Left		15/6	37/28	0.073
K/L grade, no. of knees				
Right		N = 20	N = 59	0.382 *
	Grade 0	-	7 (10.8%)	
	Grade 1	2 (9.5%)	5 (7.7%)	
	Grade 2	15 (71.4%)	24 (36.9%)	
	Grade 3	3 (14.3%)	21 (32.3 %)	
	Grade 4	-	2 (3.1%)	
Left				0.141 *
	Grade 0	-	5 (7.7%)	
	Grade 1	2 (9.5%)	9 (13.8%)	
	Grade 2	9 (42.9%)	26 (40.0%)	
	Grade 3	6 (28.6%)	14 (21.5%)	
	Grade 4	3 (14.3%)	5 (7.7%)	
Missing		1	6	

Values are the mean ± SD or n (%).

* Determined by the Mann-Whitney U test. All other p-values determined by the unpaired t-test. K/L, Kellgren and Lawrence.

Age, BMI and radiographic OA were not significantly different between women and men. Mean (± SD) joint varus-valgus laxity was 7.7° ± 2.9° for women and 4.6° ± 2.2° for men. A Student's t-test showed a significant difference between women and men for varus-valgus laxity of the knee joint ($p < 0.001$). In a regression analysis controlling for age, BMI and radiographic OA, gender significantly affected the level of laxity ($b = 3.25$, $r^2 = 0.26$, $p < 0.001$). Of the controlling variables only age contributed significantly to laxity ($b = 0.08$, $p = 0.039$).

This study shows significantly higher knee joint varus-valgus laxity in women than in men. To our knowledge this is the first study documenting the gender difference in varus-valgus laxity in patients with OA of the knee. It is unknown whether varus-valgus laxity difference also exists in normal knees of healthy individuals. The difference in varus-valgus laxity between men and women could be explained by free circulating sex hormones, oestrogen and progesterone. These hormones have been mentioned as an explanation of the greater incidence of ligamentous anterior-posterior laxity in women than men (9). In studies of healthy women it was found that anterior-posterior joint laxity is directly correlated with the menstrual cycle (10), indicating that oestrogens might also induce higher varus-valgus laxity. This would imply that a gender difference in laxity is already present prior to the onset of OA. Whether this difference is modified by the presence of OA-induced (peri-)articular changes is unclear.

Because of the gender difference reported in this study, researchers should be aware of gender as a potential source of bias in studies of knee OA. Whether or not to control for gender in studies on varus-valgus laxity, depends on the particular research question and underlying theory that is being studied. In conclusion, women with knee OA have higher joint varus-valgus laxity than men.

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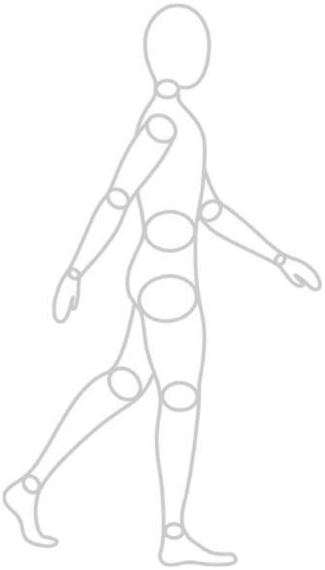
Chapter 5

STRUCTURAL JOINT CHANGES, MALALIGNMENT AND LAXITY IN OSTEOARTHRITIS OF THE KNEE



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ABSTRACT

Objective. To assess the relationship between (i) structural joint changes (i.e. joint space narrowing and osteophyte formation) and laxity and (ii) joint malalignment and laxity in osteoarthritis (OA) of the knee.

Methods. A cross-sectional study was carried out on 35 outpatients with osteoarthritis of the knee. Weight-bearing radiographs of the knees were used to assess joint space narrowing (JSN) and osteophyte formation. Knee joint laxity was assessed using a device that measures the angular deviation of the knee in the frontal plane (varus-valgus laxity). Malalignment was assessed using a goniometer. All analyses were performed using knees as units of analysis (i.e. 70 knees).

Results. The mean laxity of 70 knees was 8.0° ± 4.1°. Knees with minute JSN were significantly more lax than knees with no JSN. There was no significant relationship between osteophyte formation and laxity. Malaligned knees were significantly more lax than aligned knees.

Conclusion. Both joint space narrowing and malalignment are related to laxity. These results support the premise that biomechanical factors play a role in the degeneration of the OA knee joint.

Keywords: Osteoarthritis, Knee, Radiography, Laxity, Malalignment

INTRODUCTION

OA of the knee is characterized by structural joint changes, including joint space narrowing (JSN) and osteophyte formation. It has been hypothesized that JSN, osteophyte formation, and laxity are interrelated (1-3). Laxity can be defined as the displacement or rotation of the tibia with respect to the femur in the varus-valgus direction (1,4). The loss of articular cartilage decreases the distance between the tibiofemoral surfaces, reducing the restraining capabilities of capsule and ligaments; this induces laxity. Conversely, laxity may influence the mechanical environment of the joint: because of laxity, the passive restraint system may not be able to respond adequately to abrupt external forces (1,5). This may lead to OA progression (JSN and osteophyte formation). Previous studies have shown inconclusive results (1,6,7). The relationship between the severity of structural change in OA and laxity, as hypothesized in the biomechanical model described above, is in need of further replication.

Malalignment (i.e. any shift from a neutral or collinear alignment of the hip-knee-ankle angle) may be related to laxity of the knee joint (5,8,9). Malalignment increases medial and lateral knee compartment forces. These biomechanical forces can result in increased tear stresses and compression stresses in the passive restraint system of the knee (i.e. ligaments, capsule and other soft tissue). As a result, the passive restraint system may increase in length, reducing its restraining capabilities and enhancing laxity. However, the relationship between malalignment and laxity in osteoarthritis of the knee has not yet been assessed.

The purpose of the present study was to assess the relationship between (i) structural joint changes (JSN and osteophyte formation) and laxity and (ii) joint malalignment and laxity, in OA of the knee.

PATIENTS AND METHODS

Patients.

Thirty-five patients diagnosed with knee OA were included in the study. Patients were selected randomly from the population of an outpatient rheumatology rehabilitation center in the Netherlands. Inclusion criteria were

OA of the knee (uni- or bilateral), age between 40 and 85 years, and consent to participation. OA of the knee was diagnosed according to the clinical criteria of the American College of Rheumatology (10). Exclusion criteria were: polyarthritis, rheumatoid arthritis, or other systemic inflammatory arthropathy, knee surgery within the past 12 months or a history of knee arthroplastic surgery, intra-articular corticosteroid injections into either knee within the previous 3 months, and inability to understand the Dutch language.

Measures.

Demographics. A series of demographic variables were obtained including age, gender, height, weight, and duration of complaints.

Laxity. To assess laxity of the knee a device was designed following Sharma et al (1). The device consisted of a chair with an attached free moving arm (Figure 1). The arm supported the patient's shank and moved the shank across the transverse axis of the knee joint, in the frontal plane. The joint of the arm moved with minimal friction. The foot and distal part of the leg were fastened to the arm. The thigh was fastened to the chair. No medial or lateral movement of the femur or internal and external rotation of the hip was possible using this fixation technique. Throughout the study the knee was held flexed at 20^0. First, the examiner applied a fixed medial load of 7.7 Nm, resulting in a varus rotation of the knee in the frontal plane. Subsequently, the same load was applied laterally, resulting in a valgus rotation of the knee. A digital device recorded the end point of the varus or valgus deviation. The laxity of each knee was calculated as the sum of the varus and valgus deviations (1).

All laxity measurements were performed by the same examiner (MvdE) in adherence to a protocol, including the use of anatomic landmarks for patient positioning, patient instructions and the examiner's position. Three consecutive measurements were made. The highest score for laxity obtained from these three measurement was used in the statistical analyses.

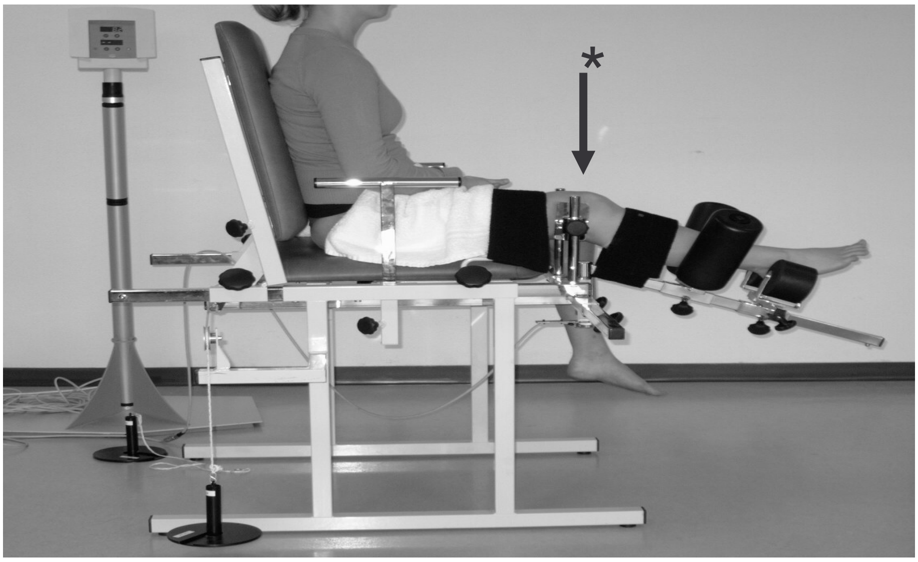

Fig. 1. Experimental set-up for the assessment of knee joint laxity showing the measurement chair with five fixations and (*) the position of the meter in line with the valgus-varus rotation axis of the knee.

Radiographic assessment. Weight-bearing, anteroposterior radiographs of the knee joints were obtained following the Buckland-Wright protocol (11). All radiographs were obtained in the same unit by one trained technician. One experienced reader (HW) assessed the radiographs using a radiographic line drawing atlas (12).

To assess JSN, the interbone distance at the narrowest points of the medial and lateral tibia-femoral compartments and the distance at the narrowest point of the patella and femur were measured as recommended (12). A four-grade (0-3) scale was used: (0 = no JSN; 1 = minute JSN; 2 = definite JSN; 3 = ankylosis). To assess osteophytes a similar rating scale was used: (0 = no osteophyte; 1 = minute osteophyte; 2 = definite osteophyte, moderate size; 3 = large osteophyte). The medial and lateral compartments of the tibiofemoral joint, and the patella-femoral joint were graded separately. After grading the compartments for JSN and osteophytes, the highest grade per knee for both JSN and osteophytes were used for analysis (1,13).

Alignment. Alignment was assessed with a goniometer. The measurement was found to be reliable (14). In the frontal plane the angle between the thigh and shank was measured in degrees, with the axis of the arm of the goniometer at the transversal axis of the knee. One arm of the goniometer was positioned in line with the thigh (from the anterior iliac spine to the middle of the patella) and the other arm in line with the shank (from the middle of the patella to the middle of the line between the medial/lateral malleolus). The rotation axis was in the middle of the patella (15). The measurement was carried out in a non-weight-bearing position, with the knee extended. The test was carried out by an experienced physical therapist (MvdE), adhering to a protocol. Knees were considered `aligned' if the angle was less than 5° in a varus or valgus direction and `malaligned'' if the angle was 5° or more.

Statistical analysis. All analyses were performed using knees as units of analysis (i.e. n = 70). First, a one-way univariate analysis of variance (ANOVA) was used to assess the relationship between JSN and laxity and between osteophyte formation and laxity. Second, knee laxity was compared in aligned and malaligned knees using a Student's *t*-test. Finally, the relationship was tested between JSN and (mal)alignment, and between osteophyte formation and (mal)alignment using a X^2-test. Results were considered statistically significant if p-values were below 0.05. All analyses were performed using SPSS version 11.5 software (Chicago, IL, USA).

RESULTS

Patients. Mean ± SD age was 66.5 ± 10.3 years; most participants were female (74%). Further demographic data for the study population were: height 164.4 ± 9.7 cm, weight 82.3 ± 14.1 kg, and body mass index (BMI) 30.4 ± 4.6 kg/m^2. Mean ± SD time since diagnosis of OA was 10 ± 10 years.

Radiographic features. Frequency distributions of JSN grades and osteophytes grades are shown in Table 1.

3	3	4	9.6	3.0.	0	-	3	8

Table 1. Characteristics of OA knees according to joint space narrowing and osteophyte formation grade.

	Frequency distribution		Knee joint laxity (°)		Aligned		Malaligned	
	n	%	Mean	SD	n	%	n	%
Joint space narrowing								
0	13	19	5.3	3.0	11	32	2	5
1	31	44	9.3	4.7	17	50	14	39
2	16	23	8.0	2.8	6	18	10	28
3	10	14	8.0	3.7	0	-	10	28
Osteophyte formation								
0	9	13	8.0	3.7	8	23	1	3
1	44	63	8.0	3.9	23	68	21	58
2	14	20	7.4	3.2	3	9	11	31

Laxity of the knee joints. Mean ± SD laxity was $8.0^{\circ} \pm 4.1^{\circ}$, range 2.0°-19.5° . The mean ±SD laxity in left knees was $7.9^{\circ} \pm 4.2^{\circ}$ and in right knees $8.2^{\circ} \pm 4.1^{\circ}$, with a Pearson's correlation coefficient of $r = 0.81$ ($p < 0.001$) between the knees.

Relationship between radiographic features and laxity. Laxity per JSN grade and osteophyte grade is shown in Table 1. Laxity differed significantly between the JSN grades ($F = 3.20$, $p = 0.029$). Post-hoc testing showed a statistically significant difference between JSN grades 0 and 1 ($p = 0.003$). There was also a non-significant trend towards a difference in laxity between JSN grades 0 and 2 ($p = 0.070$). No significant differences were found between other combinations of grades. The difference in laxity between the osteophyte grades was not statistically significant ($p = 0.783$).

Alignment of the knee joint. Of the 70 knees, 36 knees were malaligned (19 valgus, 17 varus).

Relationship between alignment and laxity. The difference in laxity between aligned and malaligned knees was statistically significant ($t = -2.99$; $p = 0.004$), with a mean ± SD laxity of $6.6^{\circ} \pm 3.9^{\circ}$ for aligned knees and $9.4^{\circ} \pm 3.9^{\circ}$ for malaligned knees. No statistically significant difference in laxity was found between valgus and varus knees ($p = 0.19$).

Relationship between radiographic features and malalignment. Both increased JSN and increased osteophyte formation was associated with increased malalignment ($p < 0.001$). The relationship between radiographic features and alignment is shown in Table 1.

DISCUSSION

This study shows that both JSN and malalignment of the knee are associated with laxity. The relationship between JSN and laxity has been examined previously (1,6,7). Sharma et al (1) found an association between joint space width and varus-valgus laxity; narrowing of the joint space was associated with an increase in laxity. Wada et al (6) also reported a positive relationship between joint space narrowing and laxity in the knee joint. Our results confirm that laxity is increased in patients with minute JSN, compared to those with no JSN. In patients with definite JSN, the same trend was found.

The present study did not find a statistically significant relationship between osteophyte formation and joint laxity. A possible explanation is that there are two opposing processes: (i) laxity may enhance the osteoarthritic process, through intraarticular displacements, shear stress and suboptimal distribution of forces; and (ii) osteophytes may have a stabilizing effect on the knee joint.(1,7).

A second purpose of our study was to examine the relationship between malalignment and laxity. We found that malalignment is associated with joint laxity. In malaligned knees laxity was higher than in aligned knees. Our study is the first to demonstrate the hypothesized association between malalignment and laxity in osteoarthritis of the knee.

Limitations of our study include the fact that the study group comprised only 35 patients, including only a few cases with severe OA. The relative dominance of knees with mild OA might explain why that the association between JSN and laxity was found for minute JSN (grade 1) only, and not for definite JSN (grade 2) and ankylosis (grade 3). Our cross-sectional study does not allow causal conclusions: longitudinal studies are required to establish causal relationships. In view of our results such studies are warranted.

In conclusion, both joint space narrowing and malalignment both are related to laxity. These results support the premise that biomechanical factors play a role in the degeneration of the osteoarthritic knee joint.

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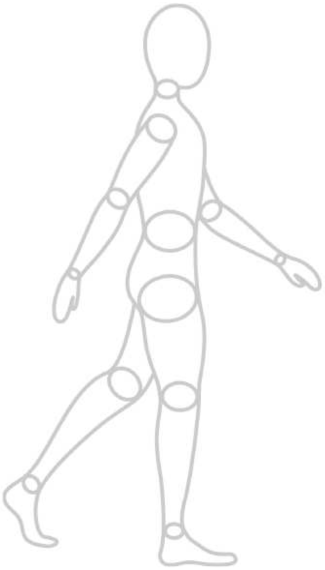
Chapter 6

JOINT PROPRIOCEPTION, MUSCLE STRENGTH AND FUNCTIONAL ABILITY IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE



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ABSTRACT

Objective. To test the hypotheses that poor knee joint proprioception is related to limitations in functional ability, and poor proprioception aggravates the impact of muscle weakness on limitations in functional ability in osteoarthritis (OA) of the knee.

Methods. Sixty-three patients with symptomatic OA of the knee were tested. Proprioceptive acuity was assessed by establishing the joint motion detection threshold (JMDT) in the anterior-posterior direction. Muscle strength was measured using a computer-driven isokinetic dynamometer. Functional ability was assessed by the 100-meter walking test, the Get Up and Go (GUG) test, and the Western Ontario and McMaster Universities Osteoarthritis Index physical function (WOMAC-PF) questionnaire. Correlation analyses were performed to assess the relationship between proprioception, muscle strength, and functional ability. Regression analyses were performed to assess the impact of proprioception on the relationship between muscle strength and functional ability.

Results. Poor proprioception (high JMDT) was related to more limitation in functional ability (walking-time: $r = 0.30$, $P < 0.05$; GUG-time: $r = 0.30$, $P < 0.05$; WOMAC-PF: $r = 0.26$, $P < 0.05$). In regression analyses, the interaction between proprioception and muscle strength was significantly related to functional ability (walking time, $P < 0.001$ and GUG time, $P < 0.001$) but not to WOMAC-PF score ($P = 0.625$). In patients with poor proprioception, reduction of muscle strength was associated with more severe deterioration of functional ability than in patients with accurate proprioception.

Conclusions. Patients with poor proprioception show more limitation in functional ability, but this relationship is rather weak. In patients with poor proprioception, muscle weakness has a stronger impact on limitations in functional ability than in patients with accurate proprioception.

Keywords: Osteoarthritis, Knee, Disability, Proprioception, Muscle strength

INTRODUCTION

Osteoarthritis (OA) is a widely prevalent, chronic, disabling condition. Clinically, OA of the knee is characterized predominantly by pain and limitations in the ability to perform activities of daily living, such as stair climbing, walking and household chores (1). These limitations are partly due to muscle weakness (2-5). It has been suggested that functional ability is also affected by poor proprioception (6-13).

Knee joint proprioception encompasses the sense of joint position and the sense of motion. These senses partially derive from neural inputs arising from mechanoreceptors in joints, muscles, tendons and associated tissue (7,14). Joint mechanoreceptors have the ability to detect the actual joint position and joint motion. Sensory feedback through knee joint mechanoreceptors, i.e. proprioception, modulates and activates knee muscles (15-17). Theoretically, knee joint proprioception is essential for accurate modulation and activation of muscles, thus providing adequate neuromuscular control of knee joint position and joint movement, and ultimately the performance of physical tasks. When proprioceptive acuity decreases, functional ability can only be maintained if there is sufficient muscle strength to compensate for the decrease in accuracy of modulation and activation of muscles. This implies that functional ability will be more strongly affected in the presence of both proprioceptive inaccuracy and muscle weakness.

Reduced proprioception has been reported in people with knee OA (7-13,18-23). Some studies have addressed the relationship between proprioception and functional ability in knee OA patients (8-13), but these studies showed conflicting findings. Some results suggest that deficits in proprioception are not large enough to have an impact on disability (9,10), whereas other results suggest that poor proprioception is associated with worse functional status (8,11-13). Thus, we hypothesized that proprioception is related to functional ability in 2 ways: poor proprioception is directly associated with limitation in functional ability, and poor proprioception aggravates the impact of muscle weakness on limitation of functional ability.

PATIENTS AND METHODS

Patients

Sixty-three patients diagnosed with OA of the knee were included in the study. Patients were registered and recruited in an outpatient rheumatology rehabilitation clinic in The Netherlands. Inclusion criteria were age between 40 and 85 years, unilateral or bilateral knee OA diagnosed according to the clinical criteria of the American College of Rheumatology (24), and consent to participation in the study. Exclusion criteria were: polyarthritis, presence of rheumatoid arthritis or other systemic inflammatory arthropathies, knee surgery within the last 12 months or a history of knee arthroplastic surgery, intra-articular corticosteroid injections into either knee within the previous three months, and/or inability to understand the Dutch language. There were no patients with a history of knee ligament deficiency in our study population based on medical file and information obtained from the patients themselves.

Measures. A series of demographic variables were obtained including age, sex, height, weight, and duration of symptoms (Table 1). Radiographs of the knee were scored in a blinded fashion by an experienced radiologist using the grading scales proposed by Kellgren & Lawrence (K/L)(25,26). Weight-bearing, anteroposterior radiographs of the knee joints were obtained following the Buckland-Wright protocol (27). Average overall pain in the past week and current average knee pain were measured using a 100-mm visual analog scale.

Functional ability was assessed with 2 standardized physical performance-based tests (the 100-meter walking test and the Get Up and Go test) and a self-report questionnaire (Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)).). The walking test required subjects to walk as fast as possible a total of 5 times continuously up and down a level 20-meter corridor. A stopwatch was used to measure the time it took to complete the 100-meter distance, commencing from a verbal cue to start walking to culmination of the 5th pass.

The Get Up and Go (GUG) test was performed as described by Hurley et al (10). To perform the test, subjects were seated on a standard-height chair with armrests. On the command “go” subjects stood up without help of their arms and walked along a level, unobstructed corridor as fast as possible. A stopwatch was used to measure the length of time it took the subject to get up from the chair and walk 15 meters. Patients wore their own shoes during testing and were permitted to use a cane if they required it for walking. A longer time to complete the GUG test represented greater functional limitations. The intraclass correlation coefficients (ICCs) for the intratester and the intertester reliability were both 0.98 (28).

The Dutch version of the WOMAC was used (29). The WOMAC is a disease specific measure of pain, stiffness, and physical function for individuals with OA of the knee. The WOMAC physical function (PF), with a possible score range of 0-68, was used to assess self-reported physical function. Each item was scored on a 5-point Likert scale, with higher scores representing greater limitations in function. Reliability and validity of the WOMAC has been established (29), and the Dutch WOMAC-PF has an ICC of 0.92 (29).

Muscle strength was assessed for flexion and extension of the knee using an isokinetic dynamometer (EnKnee; Enraf-Nonius, Rotterdam, the Netherlands). Quadriceps and hamstrings strength were measured isokinetically at 60^0/second. A single tester assessed all patients according to a standardized protocol. Patients were seated on a bench and secured to the testing device through the use of chest, pelvis, and thigh straps. The ankle pad of the dynamometer was placed 2 cm proximal to the medial malleolus to allow ankle dorsal flexion during the tests. The mechanical axis of the dynamometer was aligned with the axis of the knee through the lateral epicondyle of the femur. Patients rested their hands on the sides of the bench.

During isokinetic testing at 60^0/second, range of motion was limited to $20\text{-}80^0$ to protect the knee joint. Following instruction, patients performed 4 warm-up repetitions, beginning with submaximal contractions and building to maximal contractions. Following a 30-second rest, patients performed 3 maximal test repetitions. Right-left order of testing was alternated between patients. During testing the patient placed their hands on the sides of the isokinetic dynamometer to avoid compensatory movement of the trunk. The tester verbally encouraged the patients to achieve maximal torque. The mean strength for the quadriceps and hamstrings muscles (in Nm per kg body weight (Nm/kg)) of the right and left maximum voluntary contraction obtained from 3 measurements was used for analysis. The mean of the right and left knee were averaged to obtain a measure for total muscle strength around the knee at the patient level (4,30).

Knee joint proprioception was assessed using a knee joint motion detection task. Proprioception was measured as the threshold for detection of knee joint motion, expressed as the joint motion detection threshold (JMDT) (11). A device was constructed, consisting of a left and right stepper motor, a left and right transmission and linkage system, seating adjustment components, left and right angular displacements, 2 force transducers and 2 stop buttons. This device provided knee angular displacement and precise measurement of the angular displacement with a resolution of 0.1^0. Visual and auditory stimuli, mechanical vibrations, cutaneous tension, and pressure cues were minimized. The method of assessing proprioception was based on those described in the studies of Sharma et al (8) and Pai et al (11).

Subjects were seated in a chair with a back support and both lower legs were supported on 2 separate lever arms (Figure 1). The chair was in a semi-reclined position. Each subject was seated with knees at 90^0 flexion and the hips in 70^0 flexion. The knees were hanging over the edge of the chair, which was 5 cm proximal to the popliteal fossa. The axis of rotation was aligned with the tibiofemoral joint's axis of rotation. An ankle cuff minimized extraneous movements. An ankle cuff strapped around the lower leg, just above the malleoli minimized extraneous movements. To eliminate any contribution from cutaneous receptors and to avoid skin contact with clothing and the lever arm, the lower leg was placed on a free moving foot rest, which is a component of the lever arm. To minimize visual cues, patients were sitting behind an upward-bending tray, which prevented them from seeing movement of their knees. A stepper motor with low resonance and vibration was used to minimize auditory and vibration cues, and patients were seated on a thick cushion to eliminate vibration cues.

Each subject was given standard instructions informing them that a random leg would be tested. Both legs were moved to a starting position of 30^0 knee flexion. After stopping the movement, a random delay occurred before motion onset. Following this delay, computer-controlled constant angular motion of 1 knee was initiated at a velocity of 0.3^0/second.The patient pushed a button after definite detection of knee joint position change: the right button after detecting knee joint position change in the right knee and the left button for the left knee. Each subject underwent several practice trials. The order of the leg tested was randomly chosen. The angular displacement between the starting position and the position at the instant of pushing the button was recorded. The threshold for detection of knee joint movement was defined as the difference, in degrees, between the actual onset of motion and the subject's detection of knee joint position change or motion. High JMDT meant a great difference between the actual onset of motion and the subject's detection and expressed poor proprioception. Low JMDT meant a small difference between the actual onset of motion and the subject's detection and expressed accurate proprioception .

The mean JMDT of the right and left knees obtained from 3 measurements was used for analysis. The mean of the right and left knee were averaged representing total proprioception (see Results section for further details). ICCs for intrarater reliability for the assessment of participants with and without OA by a single experienced tester were 0.91 and 0.87, respectively.

Figure 1.
Experimental setup for the measurement of proprioception in knee osteoarthritis, as measured by the joint motion detection threshold.

Statistical analysis. Because functional ability (i.e., walking time, GUG time and WOMAC-PF score) was specific to the person, and muscle strength and proprioception were knee-specific data, a linear mixed model was used to account for the dependency of left and right knee data within subjects.

Pearson's correlation coefficients were computed to establish the bivariate relationship between proprioception and muscle strength; between muscle strength and functional ability; and between proprioception and functional ability (i.e., walking-time, GUG-time and WOMAC-PF). A regression analysis was used to assess the relationship between muscle strength, proprioception and functional ability. An interaction variable between muscle strength and proprioception was added to the regression analysis, to assess the role of proprioception as a modifier of the relationship between muscle strength and functional ability. To adjust for the dependency of proprioception of the left and right knees, the mean of both measurements and the difference between both measurements were added to the regression analyses. The same approach was used for muscle strength measurements of the left and right knees. This approach controls for the independent contribution to the regression model of the left and right knee data of proprioception and muscle strength, respectively. The variables proprioception and muscle strength were centered around the mean (31). Centering allows for a meaningful interpretation of main effects when interaction is present in the model. Other independent variables in the analysis comprised age, sex, duration of symptoms and current pain. Results were considered statistically significant at $P < 0.05$. All analyses were performed using SPSS software, version 12.0 (SPSS, Chicago, IL).

RESULTS

The characteristics of the study sample are listed in Table 1. Mean ± SD proprioception, expressed as JMDT was 4.95° ± 2.98°. The mean ± SD JMDT in left knees was 4.76° ± 3.44° and in right knees 5.14° ± 3.14°, with a Pearson's correlation coefficient of 0.64 ($P < 0.001$) between JMDT of the left and right knees. The median was 4.3°. The ICC for the 3 trials was 0.88 for the left knee, and 0.87 for the right knee. For that reason the mean of the 3 measurements was used in further analyses. A linear mixed model analysis of proprioception established variance in proprioception scores of 0.36 within subjects and 0.62 between subjects (ICC = 0.63). This means that 63% of the variance in proprioception scores occurs between patients and 37% occurs at the knee level (within patients).

Mean ± SD total quadriceps strength was 0.99 ± 0.57 Nm/kg; in left knees, the strength was 0.97 ± 0.62 Nm/kg and in right knees 1.02 ± 0.59 Nm/kg, with a Pearson's correlation coefficient of 0.80 ($P < 0.001$) between quadriceps strength of the left and right knee. Mean ± SD total hamstrings strength was 0.67 ± 0.34 Nm/kg; in left knees the hamstrings strength was 0.65 ± 0.34 Nm/kg and in right knees 0.69 ± 0.35 Nm/kg, with a Pearson's correlation coefficient of 0.90 ($P < 0.001$) between hamstrings strength of the left and right knee. Total muscle strength as an average of quadriceps and hamstrings strength was 0.83 ± 0.45 Nm/kg, with a Pearson's correlation coefficient of 0.94 ($P < 0.001$) between quadriceps and hamstrings muscle strength of the left knee and quadriceps and hamstrings muscle strength of the right knee. A linear mixed model analysis of total muscle strength established variance within subjects of 0.12 and between subjects of 0.75 (ICC = 0.86). Mean ± SD walking time was 97.5 ± 35.6 seconds, GUG time was 13.6 ± 7.0 seconds, and WOMAC-PF score was 29.7 ± 14.1 with a theoretical maximum score of 68 points.

Bivariate relationships between JMDT, muscle strength and functional ability. Poor proprioception (i.e., high JMDT) was related to greater limitation in functional ability (walking-time $r = 0.30$, $P < 0.05$; GUG time $r = 0.26$, $P < 0.05$; WOMAC-PF $r = 0.26$, $P < 0.05$). Poor proprioception (i.e., high JMDT) was associated with muscle weakness ($r = -0.42$, $P < 0.001$). Muscle weakness was related to limitation in functional ability (walking-time $r = -0.66$, $P < 0.001$; GUG time $r = -0.61$, $P < 0.001$; and WOMAC-PF score $r = -0.55$, $P < 0.001$).

Table 1. Characteristics of patients with knee osteoarthritis (N =63)*

Characteristics	Value
Sex, no. (%)	48(76)
Female	15(24)
Male	
Age, years	60 ± 7.5 (45-79)
Body mass index,kg/m^2	30.2 ±6.5 (22.4 –56.6)
Duration of symptoms, years	5.7±7.6 (1-47)
Overall current pain (0-10 scale)	3.8 ± 2.5 (0-9.3)
Overall pain in the last week (0-10 scale)	4.8 ± 2.6 (0-9.3)
Walking time, seconds	97.5 ± 35.6 (59.7-209.1)
GUG‡-time, seconds	13.6±7.0 (6.9-43.0)
WOMAC pain score	11.2 ± 6.1 (0-32)
WOMAC stiffness score	4.0 ± 1.9 (0-8)
WOMAC physical function score	29.7 ± 14.1 (4-56)
Proprioception (JMDT), degrees	
Left knee	4.76 ± 3.44 (0.90-19.43)
Right knee	5.14 ± 3.14 (1.33-16.50)
Isokinetic quadriceps strength, Nm/kg	
Left knee	0.97 ± 0.61 (0.08-2.78)
Right knee	1.02 ± 0.59 (0.09-2.66)
Isokinetic hamstrings strength, Nm/kg	
Left knee	0.65 ± 0.34 (0.04-1.54)
Right knee	0.69 ± 0.35 (0.08-1.90)
Muscle strength †	0.67 ± 0.34 (0.06-1.62)
K&L grade, no. (%) of knees	
Right (n=62)	
Grade 0	0
Grade 1	45 (71)
Grade 2	10(16)
Grade 3	6 (11)
Grade 4	1 (2)
Left (n=63)	
Grade 0	2 (3)
Grade 1	39(62)
Grade 2	9(14)
Grade 3	11(18)
Grade 4	2 (3)

* Values are the mean ± SD (range)unless otherwise indicated.
GUG = Get Up and Go test; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; JMDT = joint motion detection threshold; K/L = Kellgren/Lawrence.
† Total strength averaged left/right and extension/flexion.

Multivariate relationships between JMDT, muscle strength and functional ability.

To analyze the relationship between functional ability, total muscle strength and proprioception, a multiple regression model was constructed:

Functional ability = b_0 + b_1 x muscle strength + b_2 x proprioception+ b_3 x muscle strength x proprioception.

The difference between the left and right data of the variables proprioception and muscle strength did not add to regression model. For that reason only the variables representing the mean score for proprioception and muscle strength at the patient level were used.

The model explaining the total variation of walking-time was as follows: walking-time = 91.73 – 68.13 x muscle strength – 1.56 x proprioception– 11.61 x muscle strength x proprioception (F = 23.23, $P < 0.001$, $R^2 = 0.54$; N = 63). This means that 54% of the total variation of walking-time is explained by muscle strength, proprioception and their interaction. Muscle strength (b = -68.13, $P < 0.001$) and the interaction between muscle strength and proprioception (b = -11.61, $P = 0.000$) were significantly associated with walking-time. Thus, muscle weakness was found to be associated with more severe limitation in functional ability. In the presence of poor proprioception, muscle weakness was associated with even more severe deterioration of functional ability. When the mean proprioception (JMDT) of right and left knees equals 0 (0= mean of 4.95^0) and muscle strength decreases by 1 Nm/kg, then the walking-time increases by 68.13 seconds. When the proprioception (JMDT) of right and left knees is 1^0 lower than the mean, and muscle strength decreases by 1Nm/kg then the walking time increases by 56.52 seconds. However, when a decrease of muscle strength of 1 Nm/kg occurs in patients with 1^0 above the mean of proprioception (JMDT), then the walking-time increases even more by 79.74 seconds.

The model explaining the total variation of the GUG time and the WOMAC-PF score is presented in Table 2. For GUG time, the results were similar to the results obtained with walking time. This means that muscle weakness was associated with a higher GUG time. In the presence of poor proprioception, muscle weakness was associated with even higher GUG time. Muscle strength was the only significant independent variable in the regression analysis on the WOMAC-PF score.

Table 2. Results of the regression of functional ability (walking time, GUG time, and WOMAC physical function) on muscle strength and joint proprioception*

	Walking time‡		GUG§		WOMAC physical function¶	
Variables†	b (SEE)	*P*	b (SEE)	*P*	b (SEE)	*P*
Intercept	91.73		11.91		29.19	
Muscle strength	-68.13 (8.90)	0.000	-13.99 (1.70)	0.000	-18.23 (4.37)	0.000
Proprioception	-1.56 (1.27)	0.225	-0.513 (0.24)	0.039	0.01 (0.62)	0.987
Muscle strength x proprioception	-11.61(3.10)	0.000	-3.05 (0.59)	0.000	-0.94 (1.51)	0.534

*GUG = get Up and Go test; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; b = unstandardized regression coefficient; SEE = standard error of the estimate.
† variables centered around the mean.
‡ $R^2 = 0.54$, F=23.23, $P < 0.001$
§ $R^2 = 0.57$, F=25.76, $P < 0.001$
¶ $R^2 = 0.30$, F=8.81, $P < 0.001$

To visualize the interaction between muscle strength and proprioception, proprioception was dichotomized in poor proprioception (high JMDT) and accurate proprioception (low JMDT), using the median-split method. The demarcation between high and low JMDT was 4.3°. The results are shown in Figure 2.

Figure 2A

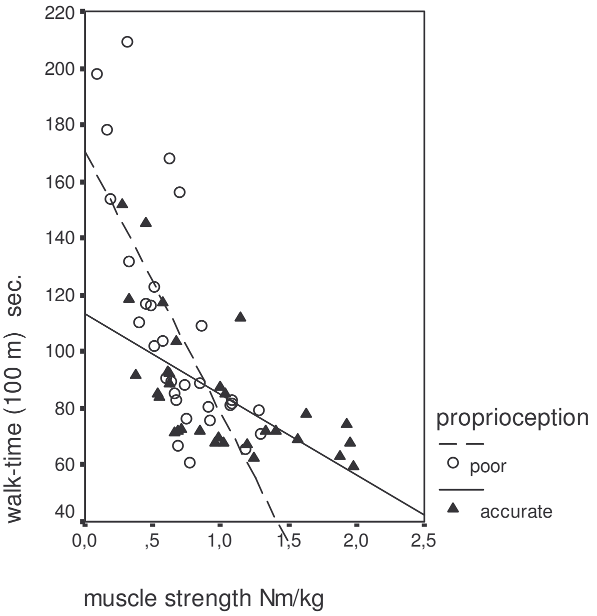


Figure 2B

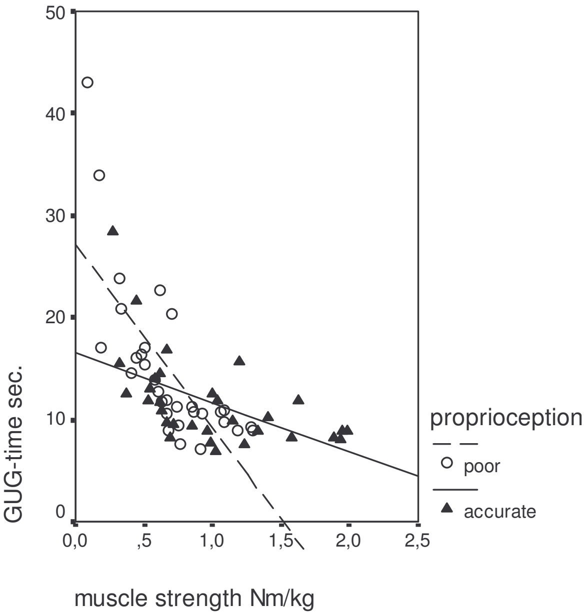
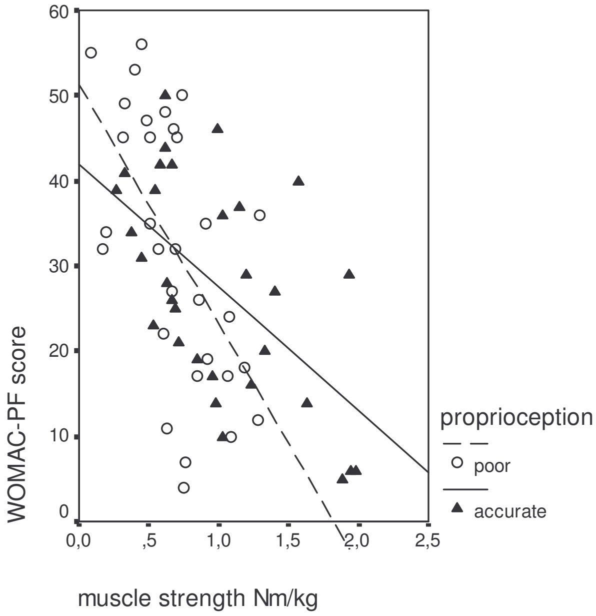


Figure 2C

Figure 2. A,B,C
Relationship between functional ability and muscle strength in an accurate proprioception (low Joint Motion Detection Threshold < 4.3^0) group and a poor proprioception (high Joint Motion Detection Threshold > 4.3^0) group. Sec = seconds; GUG = Get Up and Go test; WOMAC-PF = Western Ontario and McMaster Universities Osteoarthritis Index physical function. Dotted line and circle = poor proprioception; solid line and triangle = accurate proprioception group.



These analyses were repeated in a more extensive model, with the demographic variables from Table 1 as controlling variables (age, sex, duration of symptoms, current pain). The results of those analyses showed that sex (women vs. men) (b = -28.90, $P = 0.002$) added to the explained total variation of walking-time ($R^2 = 0.61$, $P < 0.000$). The inclusion of sex in the model did not affect the significance of the regression coefficients listed in Table 2. The addition of other control variables did not change the significance of the regression coefficients of muscle strength and proprioception. The results also showed that current pain (b = 3.02, $P < 0.001$) added to the explained total variation of the WOMAC-PF ($R^2 = 0.54$, $P < 0.001$). However, current pain had no influence on the significance of the regression coefficients listed in Table 2.

DISCUSSION

We hypothesized that proprioception is related to functional ability in two ways. First, poor proprioception is directly related to limitation in functional ability. Second, poor proprioception aggravates the impact of muscle weakness on limitation of functional ability (i.e., walking time, GUG time and WOMAC-PF score). Our results show that poor proprioception has a weak direct relationship with limitations in functional ability. This relationship was only present in bivariate analyses. In multivariate regression analyses, the main effect of proprioception on functional ability was not significant for walk time and WOMAC-PF score, and although statistically significant, the main effect of proprioception on GUG time was minimal. Thus, the direct effect of proprioception on functional ability can be considered to be weak. However, the interaction between muscle strength and proprioception contributed significantly to the variance in functional ability (i.e., walking time and GUG time, but not WOMAC-PF). These results suggest that in the absence of adequate motor control through a lack of accurate proprioceptive input, muscle weakness affects a patient's functional ability to a greater degree.

Using a similar measurement of proprioception, Pai et al (11) found a significant correlation ($r = 0.367$, $P = 0.030$) between proprioception and the WOMAC-PF score, which is in agreement with our bivariate results. A comparison with other studies is hampered by differences in measurement protocols, equipment and statistical analyses (9,10,13,32,33). The main difference is the operationalization of proprioception. Some studies used joint motion sense as measure of proprioception (8,11), whereas other studies used joint position sense (9,10,13,32,33). In our study proprioception was measured as joint motion sense. Therefore, it is difficult to compare the results of our study with studies using joint position sense as a measure of proprioception.

To our knowledge, this is the first study to evaluate the impact of proprioception on the relationship between muscle strength and functional ability. It was theorized that knee joint proprioception is essential for accurate modulation and activation of muscles. When proprioceptive acuity decreases, functional ability can only be maintained if there is sufficient muscle strength to compensate for the decrease in accuracy of modulation and activation of muscles. Thus, it was predicted that functional ability will be more strongly affected in the presence of both proprioceptive inaccuracy and muscle weakness. In support of this theory, we found larger differences in functional ability due to differences in muscle strength in patients with a poor proprioception, compared with patients with accurate proprioception.

Although the direct relationship between proprioception and functional ability is weak, it appears that proprioception indirectly influences functional ability through modulation of the relationship between muscle strength and functional ability.

It can be hypothesized that poor proprioception can be compensated by adequate muscle strength; in patients with poor proprioception, an increase of muscle strength would result in a bigger improvement in functional ability than in patients with adequate proprioception. If this hypothesis can be proven, this would support the use of exercise therapy in OA patients with poor proprioception. Although exercise therapy has been found to be effective in patients with knee OA, this does not apply to all patients with knee OA (2,3). Identifying subgroups of patients expected to benefit more from exercise therapy would increase the efficiency of care. Based on the results presented here, it can be hypothesized that patients with poor knee proprioception may benefit more from interventions aimed at increasing muscle strength. Patients with poor proprioception may have more benefit from exercise therapy than patients with adequate proprioception.

Poor proprioception is not a local process. In a study of patients with unilateral OA, Sharma et al found no between-knee difference in proprioception, suggesting that poor proprioception is a more generalized process (8). Our results seem to support this conclusion. Although we found difference in proprioception between left and right knees, 63% of the variance in proprioception occurred at the patient level. Furthermore, in the multivariate analyses on the relationship between proprioception, muscle strength and functional ability, the difference between left and right knees did not contribute to the regression model. Although proprioception differs between left and right knees, poor proprioception seems to be predominantly the result of generalized processes.

It is useful to consider some limitations of this study. One limitation is that the cut-off between adequate (i.e., low JMDT) and poor (i.e., high JMDT) proprioception is unknown. In our multivariate analyses continuous data were used. Scatter plots were provided to visualize the results in low and high JMDT groups. The JMDT data were dichotomized by the median-split method (median 4.3°). High JMDT (i.e., > 4.3°) means a great difference between the actual onset of motion and the subject's detection, expressing poor proprioception. Low JMDT (i.e., < 4.3°) means a small difference between the actual onset of motion and the subject's detection, expressing accurate proprioception. It should be noted, however, that it is not known whether the cut-off value of 4.3 ° is clinically meaningful. The second limitation of this study was that it was a cross-sectional study, meaning causal conclusions were not allowed.

In a previous study on knee joint laxity in OA (34), patients with high knee joint laxity showed a stronger relationship between muscle strength and functional ability than OA patients with low knee joint laxity. This suggests that high knee joint laxity and impaired proprioception have a similar influence on the relationship between muscle strength and functional ability. It should be noted that joint laxity measured in the present study was not significantly correlated with joint proprioception (r = 0.083, *P* = 0.515; (data not shown)). This indicates that different processes are responsible for the relationships found in these 2 studies. In conclusion, patients with poor proprioception show more limitation in functional ability, but this relationship is rather weak, and in patients with poor proprioception, muscle weakness has a stronger impact on limitations in functional ability than in patients with accurate proprioception.

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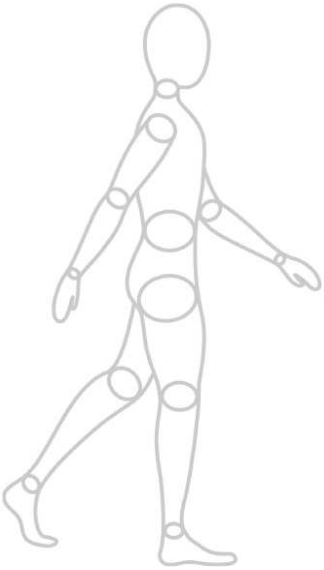
Chapter 7

REPRODUCIBILITY OF THE MEASUREMENT OF KNEE JOINT PROPRIOCEPTION IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE AND HEALTHY SUBJECTS



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ABSTRACT

Objective. To estimate the inter- and intra-rater reliability and agreement of instrumented knee joint proprioception measurement in subjects with knee osteoarthritis (OA) and healthy subjects; to assess the effect of variations in the measurement procedure on agreement parameters.

Methods. Proprioception was measured by a computer-controlled knee angular motion-detecting device in a movement detecting task. The angular displacement between the starting position and the position at the instant of movement detection by the patient was recorded. Two raters independently assessed knee joint proprioception. After 14 days the assessment was repeated. Complete data were obtained from 24 patients with knee OA and 26 healthy subjects. The inter- and intra-rater reliability coefficients (Intraclass Correlation Coefficients (ICC)) and inter- and intra-rater agreement measures (Standard Error of Measurement (SEM) and Minimal Detectable Difference (MDD)) were calculated. Additionally, the effect of changing the velocity of angular displacement and applying headphone music during the measurement on the absolute error (i.e., SEM and MDD) was estimated at the second occasion.

Results. Inter-rater reliability was good in subjects with knee OA and healthy subjects (ICC 0.91 and 0.89, respectively). Interrater agreement was higher in subjects with knee OA than in healthy subjects (SEM 2.13° versus 0.43°, MDD 5.90° versus 1.19°). Intrarater reliability was good in subjects with knee OA and healthy subjects (ICC 0.91 and 0.86, respectively). The intrarater agreement (SEM and MDD) was 2.26° and 6.26° in subjects with knee OA and 0.39°, 1.08° in healthy subjects. The original measurement and the 2 variations in measurement showed comparable measurement errors for subjects with knee OA and healthy subjects.

Conclusions. In knee OA subjects and healthy subjects, knee proprioception measurement shows adequate intra- and interreliability. However, the absolute measurement error is rather high. Therefore, this measurement has limited value in the assessment of individual subjects, but can be recommended for scientific research in groups of individuals.

Keywords: Reproducibility; Proprioception; Osteoarthritis; Knee

INTRODUCTION

Knee osteoarthritis (OA) is a leading cause of limitations in daily functioning in the elderly (1). Inaccurate proprioception has been suggested to be a risk factor for the development of limitations in function in patients with knee OA (1-3). Proprioception can be defined as the conscious and unconscious perception of joint movement and joint position (4-6). Proprioception is decreased in patients with knee OA compared with elderly controls (7-12). Although many studies have measured proprioception in patients with knee OA (1,7, 8,10-27), information on the reproducibility of the methods used to assess proprioception is rarely provided.

Reproducibility concerns the degree to which repeated measurements of a stable characteristic provide similar results. For the quantification of reproducibility, 2 types of measures can be distinguished: reliability and agreement (28-30). Reliability parameters assess whether persons in a group can be distinguished from each other, despite measurement errors (28). Reliability is expressed as the intraclass correlation coefficient (ICC). Agreement parameters assess how close the results of the measurements are within individual subjects by estimating the absolute measurement error in repeated measurements (29, 30).

Adequate reliability and agreement indicate that a measurement is appropriate to use both in scientific research to describe characteristics in groups of patients and in clinical practice to adequately assess individual patients. However, when agreement is lower (i.e., considerable measurement error is present), the assessment can still be sufficient for use in groups of patients, but may be too imprecise to adequately define the individual patient's level of proprioceptive accuracy. Therefore, knowledge of the reproducibility of proprioception measures is needed to establish the utility of these measures in scientific research and clinical practice. Although information has been presented concerning the reliability parameters of the measurement of joint proprioception (13,15), information concerning the agreement parameters is as yet unavailable.

The goal of this study was to estimate the inter- and intra-rater reliability and the inter- and intra-rater agreement of instrumented knee joint proprioception measurement in subjects with knee OA and in healthy subjects. An additional goal was to assess the effect of variations in the measurement procedure on agreement parameters.

SUBJECTS AND METHODS

Design

Two measurement sessions were carried out within a timeframe of 2 weeks. Two raters (both physical therapists and trained to perform the proprioception measurement) independently performed the measurements. Both raters were blinded for the outcome of all other measurements. Rater 1 and rater 2 measured proprioception at day 1. At day 14 rater 1 repeated the measurement. Additionally at day 14 rater 1 performed the measurement using 2 different protocols, to assess the impact of protocol variations on the measurement agreement. Measurements were performed both in subjects with knee OA and in healthy subjects.

Subjects

Subjects with osteoarthritis of the knee were recruited in an outpatient rheumatology and rehabilitation clinic in the Netherlands. The inclusion criteria was: OA diagnosed according to the clinical ACR criteria (31). These criteria include pain and a minimum of 3 of the following criteria: age > 50 years, morning stiffness ≤ 30 minutes, crepitus on active movement of the knee joint, palpable or visible bony enlargement, bony tenderness at the knee joint margins, and no palpable warmth of synovium. The exclusion criteria were as follows: presence of prosthesis at the lower extremity, steroid injection within 2 months prior to inclusion, presence of neurologic disorders (e.g., stroke, Parkinson’s disease, or poliomyelitis), presence of other rheumatoid or orthopedic disorders, recent (< 1 year) history of a lower extremity fracture, history of ligament deficiency, insufficient control of the Dutch language, and hearing problems.

Healthy subjects were recruited from a student population of an allied health faculty. The exclusion criteria were presence, or history, of a severe injury of the lower extremity; a history of knee surgical procedure, or waiting list for knee operation; the presence of any neurological, rheumatoid, or orthopedic disorders; and insufficient control of the Dutch language. Ethical review board approval of the Slotervaart Hospital in Amsterdam was obtained, and all participants provided written informed consent.

Equipment

To assess proprioception (i.e., the threshold to detection of passive motion) of the knee, a device was designed following the recommendations of Sharma (5) and Pai et al (12). The device consisted of a chair with a computer-controlled motor and transmission system and 2 attached free-moving arms (Figure 1). Each arm supported the subject's shank and foot and moved in the sagital plane. The joint of each arm was moved by a computer controlled-stepper motor and transmission system for angular displacement. The foot/ankle was attached with an air splint to the footrest, which was a moving component of the apparatus (32). Angular motion was detected by angular displacement and force transducers. Attached to the chair was an upward-bending tray, to prevent visual input of the moving knee. Two handheld buttons were attached to the tray. The seat of the chair consisted of a gelpad to prevent any vibrating sensation and movement of the skin. This device provides a measurement of angular displacement, while eliminating or minimizing visual and auditory stimuli, vibrations, cutaneous tension, and pressure cues to limb motion.

Subjects were seated in a semi-reclining position with the back supported and the knee hanging over the edge of the apparatus, which is 5 cm proximal to the popliteal fossa. The knees were placed in 900 flexion and the hips in 700 flexion.

MEASUREMENT OF KNEE JOINT PROPRIOCEPTION

The measurement procedure consisted of a knee joint movement detection task. Standard instructions were given to each subject. Each time, the leg was moved to a starting position of 30^{0} knee flexion. Upon reaching this position, movement stopped. Following a random delay, the knee was then extended further with an angular velocity of 0.3^{0}/second. Participants were instructed to push a handheld button at the moment of definite detection of knee joint position change. The angular displacement between the starting position at

30^{o} flexion and the position in the extension direction at the instance when the button was pushed was recorded as the measure of knee joint proprioception (32). This means that a low value (i.e., a small difference between the knee joint angle at onset of movement and the knee joint angle at the moment of detection knee joint position change) indicates good proprioception.

The participants were asked to put on short pants, take off shoes and socks. After attaching the foot/ankle to the footrest with an air splint, participants were told that the test could begin. A training session was started after standardized instruction was given. The participants were told: "Both legs will be moved to the start position, when both legs stop the test begins. At that exact time the rater will say "yes" and point a finger in the air. After a random time period, movement of one of the legs will occur. When you feel movement in the knee joint please push the handheld button, corresponding to the side of knee movement." The participants were asked to concentrate during the entire measurement. Then the measurement was started. When a detection mistake was made, the test was repeated. Measurements were performed 3 times per leg (i.e., 6 times per participant), by both rater 1 and rater 2 on day 1. The order of the 6 repetitions was randomized to ensure that participants would not know beforehand which of the 2 legs would be tested in a specific measurement. At day 14, rater 1 performed the same measurement. The average of the 3 measurements per leg per occasion (day 1 or day 14) of the standard procedure (in degrees) was used to estimate the reproducibility (comprising both reliability and agreement) of this measurement of knee joint proprioception between raters (interrater reproducibility) and occasions (intrarater reproducibility). A detailed description of these analyses is provided below.

Additionally, at day 14, 2 variations in the measurement of knee joint proprioception were performed by the same rater. In the first variation, the angular velocity was reduced from 0.3^{0}/second to 0.1^{0}/second. In the second variation, participants listened to music through headphones during the measurement to eliminate any remaining auditory input related to the onset of knee joint movement (i.e., the sound of the device's stepper-motors starting). Both variations were also performed 3 times per leg and the order in which participants left and right leg were tested was randomized. The 3 separate measurements per leg of the standard procedure at day 14 and the 2 variations in measurement were used to calculate the within-session agreement parameters at day 14 (see statistical analyses below)

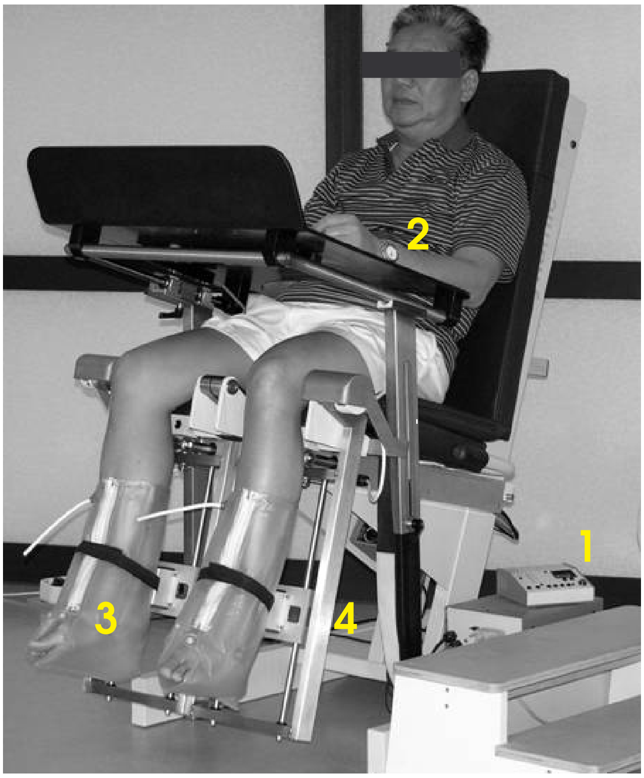

Figure 1. The instrumented knee joint proprioception measurement. Experimental set-up for the assessment of knee joint proprioception, showing the measurement chair control mechanism, handheld button, air splints, and footrest (the moving component of the apparatus).

Statistical analyses

For all analyses, the following sources of variance were used: participant, rater, time of measurement, knee and interaction between these variables. To express reproducibility between raters the following parameters were estimated (30). To express reproducibility between 2 occasions (day 1 and 14) of the proprioception measurment by rater 1, intrarater reliability and intrarater agreement were estimated (30).

Inter-rater reliability and agreement. The ICC (2,1) was calculated as the ratio of variance between participants and between the 2 raters and total variance. The standard error of measurement (SEM) was calculated by taking the square root of the error variance consisting of the following sources of variance: participants; rater; knee; interaction between participant and knee;

interaction between participant and rater; and interaction between participant, rater, and knee. The SEM was used to calculate the minimal detectable difference (MDD). To compute the MDD as the 95% confidence interval limits of the SEM, the SEM has to be multiplied by 1.96 (for the 95% interval) and by the square root of 2 for the difference scores (1.96x√2xSEM) (33, 34).

Intrarater reliability and agreement. The ICC (2,1) was calculated as the ratio of variance between subjects within one rater and total variance. The (SEM) was calculated by taking the square root of the error variance of the following sources of variance: participant; time of measurement; knee; interaction between participant and knee; interaction between participant and time of measurement; interaction between participant, knee, and time of measurement. The SEM was calculated across both occasions (35).

Impact of variations in measurement on intrarater agreement. In addition, at day 14 the within-session SEM and MDD of the 3 repeated measurements were calculated for the original measurement and the 2 variations in measurement performed by rater 1, taken into account the following sources of variance: participant, knee and the interaction between participant and knee. For reliability, an ICC of >0.70 was regarded as adequate (36). To calculate the ICC, the SEM and the MDD, a two-way random effects model of analysis of variances (ANOVA) was performed, using (SPSS) software for windows, version 12.0.1 (SPSS, Chicago, IL).

RESULTS

A total of 24 (8 men, 16 women) subjects with knee OA participated in the study. Mean ± SD age was 61.3 ± 9.8 years, weight 84.5 ± 17.9 kg, height 1.68 ± 0.09 meters, and body mass index (BMI) was 30.2 ± 7.1 kg/m^2. A total of 26 (10 men, 16 women) healthy subjects participated in this study. Mean age ± SD was 20.6 ± 3.1 years, weight 69.4 ±12.3 kg, height 1.75 ± 0.08 meters and BMI was 22.5 ± 2.9 kg/m^2.

Mean ± SD values for the proprioception measurement, generalized over the 2 raters and the 2 occasions were 8.88° ± 6.82° for subjects with knee OA and 1.87° ± 1.24° for healthy subjects. To assess reproducibility parameters, the mean of the 3 repeated measurements per leg per session was used. The within-session correlation at day 1 for rater 1 and rater 2 were 0.821 and 0.876, respectively.

The inter- and intrarater reliability (as expressed by the ICC) and agreement (as expressed by the SEM and MDD) are presented in Table 1. Reliability was high in both subjects with knee OA and healthy subjects. Intra- and interrater reliability were comparable with each other. Likewise, intra- and interrater agreeement were comparable.

The within-session intrarater agreement as expressed by the SEM and MDD at the second session are presented in Table 2. The difference in SEM and MDD between the 2 measurements variations compared with the original measurement were minimal.

Table 1. Inter-/intrarater reliability and agreement of the proprioception measurement insubjects with knee OA and healthy subjects*

	Subjects with knee OA			Healthy subjects		
	ICC (95%CI)	SEM degrees	MDD degrees	ICC (95%CI)	SEM degrees	MDD Degrees
Interrater	0.91 (0.84-0.95)	2.31	5.90	0.89 (0.81-0.94)	0.43	1.19
Intrarater	0.91 (0.84-0.95)	2.26	6.26	0.86 (0.77-0.86)	0.39	1.08

* OA = osteoarthritis ; ICC = intraclass correlation coefficient ; 95% confidence interval ; SEM= standard error of measurement; MDD= minimal detectable difference.

Table 2. Within-session intrarater agreement of the original proprioception measurement and the 2 variations of proprioception measurements in subjects with knee OA and healthy subjects*

Measurement of proprioception	Subjects with knee OA		Healthy subjects	
	SEM degrees	MDD degrees	SEM degrees	MDD Degrees
Original	1.75	4.85	0.39	1.08
Slow speed	1.61	4.46	0.34	0.94
Music	1.89	5.24	0.39	1.08

* See table 1 for definitions

DISCUSSION

The goal of this study was to estimate the inter- and intrarater reliability and inter- and intrarater agreement of the instrumented knee joint proprioception measurement in subjects with knee OA and in healthy subjects. An additional goal was to explore the effects of a change in angular velocity and the addition of headphone music on agreement coefficients.

Reliability was found to be adequate both within and between raters, for both subjects with OA and healthy subjects. Reliability estimates were almost equal in subjects with OA and healthy subjects. However, the slightly higher reliability observed in OA patients can be explained by a larger variance in measurement results and therefore higher ICCs (5,10).

In healthy subjects, inter- and intrarater agreement parameters were better than in subjects with OA, indicating a lower measurement error for the procedure in healthy subjects than in OA subjects. Measurement error for healthy subjects was 0.4°, whereas it was 2.2° in subjects with OA. This finding suggests that in subjects with OA within-person variability has a considerable impact on the level of agreement in the assessment of proprioception. Due to a decrease in proprioceptive accuracy, OA subjects may be less likely to detect repeatedly knee joint position change at the same degree of angular deviation. In addition to OA subject variance, the level of agreement in the assessment of proprioception is also influenced by intra-rater variance. Therefore, both within- and between-subject differences in proprioception must be interpreted with caution in subjects with OA. Even a considerable difference in result between 2 measurements may not be indicative of a genuine difference in proprioceptive accuracy, but instead is likely to be an expression of general proprioceptive inaccuracy. This is also reflected by the rather large MDDs (>4°) found for the population of OA subjects.

In addition to subject and rater variance, other sources of error could have been responsible for variation in outcome. One source of error could have been the fixation of the foot/ankle of subjects. Small differences in the positioning and fixation of the leg between the 2 raters and between the 2 sessions (day 1 and day 14) could have been a reason for variation in measurement outcome. A second source of error could have been the environmental circumstances at the time of the measurement. The subjects' attention can be influenced by surrounding noises. A third source of error could have been the alertness of the subjects during the measurement. Changes in alertness might influence the timing of detection of knee motion. Therefore, to minimize the impact of these potential sources of error, the protocol was standardized to a high degree, the 2 raters were specifically trained to be mindful of subject positioning and instructing, and subjects were measured during the same time of the day on both occasions. We therefore believe that these potential sources of error did not have a major impact on the SEM and MDD.

Variations in measurement procedure had no impact on intrarater agreement. In the first variation, the angular velocity during the measurement was reduced from 0.3°/second to 0.1°/second. However, the measurement error between the original and the variation in measurement did not changed substantially. This is not in accordance with previous studies, in which proprioceptive acuity was found to improve with increasing velocities of joint movement (37-39). An explanation for this difference in results could be the calculation of the SEM and MDD. In our analyses the SEM was measured with the variables subject, knee and the interaction between subject and knee as random variables, resulting in an absolute measurement error. This absolute measurement error represents more precisely the within-subject differences.

The second variation in the measurement procedure, music by headphones, did not substantially affect the agreement of the measurement. This means that the auditory cue of the starting up of the stepper motor ndicating the start of knee joint movement did not lead to substantially different results, compared with a condition where this cue was absent.

Many studies have measured proprioception in patients with knee OA (1, 7, 8, 10-27), however, information on the reproducibility of the methods used to assess proprioception is rarely provided. The studies providing information on reproducibility all used a different method for the measurement of knee joint proprioception; weight bearing or non-weight bearing, start position flexion or extension and a velocity of angular displacement of 0.1º/second to 5º/second. All these factors could have influenced the reproducibility. In general, the measurement of proprioception can be divided into 2 categories: by the detection of joint movement (i.e., joint movement sense) and by the detection of joint position (i.e., joint position sense). Our findings concern joint movement reliability and do not apply to joint position sense measurements. It can be expected that joint movement sense and joint position sense are related with each other, i.e., that both are expressions of proprioception. Future research could examine the relationship between these 2 joint senses.

The results of our study are in agreement with the study by Sharma et al (21). A similar device and measurement procedure for the detection of joint movement were used. The measurement was found to have high intra-rater reliability, which is in line with our results. However, no information was presented concerning the interrater reliability, agreement and variations in measurement. In the study by Marks et al (15) the joint position sense was measured, whereas in our study the sense of joint movement was measured. Although Marks (15) previously reported high reliability for the measurement of knee joint proprioception, these results are difficult to compare due to the considerable differences in the measurements of proprioception used in the study by Marks and our own study.

It is believed that the knee joint position during the proprioception measurement influences on the accuracy of the measurement. It has been demonstrated that proprioception is more accurate in the middle range than at the end-range (40). In our study, subjects were measured from a starting position of 30o flexion, which is a position commonly present in daily life (e.g., during walking and other transfers). Measurements were made while the knee moved towards extension, i.e., towards the end of the range of motion. It is possible that this has resulted in an underestimation of the degree of proprioceptive accuracy in some patients with OA.

In conclusion, in persons with knee OA and healthy subjects the measurement of knee proprioception shows adequate intra- and interreliability. The absolute measurement error is rather high. Therefore, this measurement has limited value in the assessment of individual patients, but can be recommended for scientific research in groups of patients.

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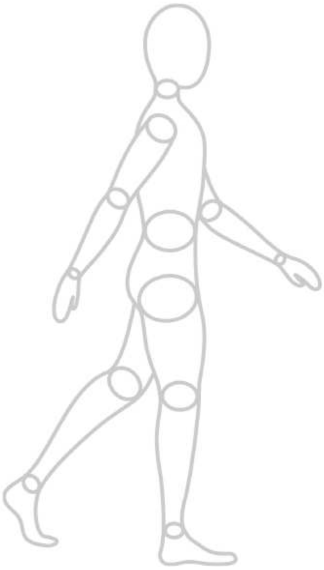
Chapter 8

VARUS-VALGUS MOTION AND FUNCTIONAL ABILITY IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE



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ABSTRACT

Objective. (i)To assess the relationship between knee varus-valgus motion and functional ability and (ii) to assess the impact of knee varus-valgus motion on the relationship between muscle strength and functional ability in patients with osteoarthritis of the knee.

Methods. Sixty-three patients with OA of the knee were tested. Varus-valgus motion was assessed by optoelectronic recording and 3D motion analysis. Functional ability was assessed by observation, using a 100-m walking test, a Get Up and Go test, and by the WOMAC-questionnaire. Muscle strength was measured by a computer-driven isokinetic dynamometer. Regression analyses were performed to assess the relationships between varus-valgus motion and functional ability, and to assess the impact of varus-valgus motion on the relationship between muscle strength and functional ability.

Results. In patients with high varus-valgus range of motion, muscle weakness was associated with a stronger reduction in functional ability (i.e. longer walking-time and GUG-time) than in patients with low varus-valgus range of motion. A pronounced varus position and a difference between the left and right knees in varus-valgus position were related with reduced functional ability.

Conclusions. (i) In knee OA patients with high varus-valgus range of motion, muscle weakness has a stronger impact on functional ability than in patients with low varus-valgus range of motion, and (ii) knee OA patients with more pronounced varus knees during walking show a stronger reduction in functional ability than patients with less pronounced varus knees or with valgus knees.

Keywords: Osteoarthritis, Knee, Disability, Kinematics, Muscle Strength

INTRODUCTION

In patients with osteoarthritis (OA) of the knee, limitations in daily activities such as walking, climbing stairs, and getting out of a chair are common (1,2,3). It has been found that patients with OA knee joints show reduced functional ability in the presence of varus-valgus laxity of the OA knee (4,5). Furthermore, malalignment of the knee predicted decline in functional ability (6). The terms varus and valgus refer to lateral and medial angulations of the tibia from the center of the knee in the frontal plane (7). Recently it has been found that a varus position of the knee during midstance may predict reduced functional ability (8). It has also been shown that patients with knee OA use greater magnitudes of muscle activities during walking (9,10), presumably to minimize high varus-valgus motion.

During normal walking there is low varus-valgus motion of the knee (7). High varus-valgus motion of the knee may causes difficulties in carrying out physical tasks in which the knee is pivotal and therefore may predict reduced functional ability. Thus, it is hypothesized that varus-valgus motion is associated with reduced functional ability.

The relationship between functional ability and muscle strength in patients with knee OA is well established (11). It is assumed that low varus-valgus motion results in efficient use of muscle strength during walking (12). On the other hand, high varus-valgus motion may result in inefficient use of muscle strength. This implies that muscle weakness would lead to more severe functional disability in patients with high varus-valgus motion than in patients with low varus-valgus motion.

The following two hypotheses were tested in this study: 1) high varus-valgus motion is associated with reduced functional ability, and 2) in patients with high varus-valgus motion, muscle weakness is associated with a more severe reduction of functional ability than in patients with low varus-valgus motion.

PATIENTS AND METHODS

Patients

Sixty-three patients diagnosed with OA of the knee were included in the study. Inclusion criteria were OA of the knee (uni- or bilateral) according to the clinical criteria of the American College of Rheumatology (13), and age between 40 and 85 years. Exclusion criteria were: poly-arthritis, presence of rheumatoid arthritis or other systemic inflammatory arthropathies, knee surgery within the last twelve months or a history of knee arthroplastic surgery, intra-articular corticosteroid injections into either knee within the previous three months, and/or inability to understand the Dutch language. All patients provided written informed consent. The study was approved by the human research ethics committee of the VU University Medical Center in Amsterdam.

Measures

Procedures. Patients visited the laboratory twice within the same week. During the first visit, patients completed a questionnaire, muscle strength was tested and two performance tests for functional ability were carried out. The second visit consisted of a 3-dimensional gait analysis. Patients were tested at a similar time of day, by the same examiner. This was always at the end of the afternoon for all patients.

Demographics. A series of demographic variables were obtained including age, gender, height, weight, and duration of complaints.

Gait analysis. An Optotrak motion analysis system (model 3020, Northern Digital Inc., Waterloo, Ontario, Canada) recorded the 3D position of light emitting diode markers in order to assess varus-valgus motion. 3D ground reaction force were synchroniously recorded using a 51 x 46.5 cm force plate (AMTI, Watertown, Massachusetts, USA). An open source Matlab software program BodyMech (www.bodymech.nl) was used to reconstruct the anatomical axis and, from that, 3D knee motion and loading data (14). Varus-valgus knee motion resulted from decomposing knee motion using a flexion-varus-exorotation sequence

To describe skeletal movement, body segments were considered as rigid bodies (lower leg, thigh, pelvis and trunk) with a local coordinate system defined to coincide with a set of anatomical axes (15). The limb segments were determined by anatomical landmarks: greater trochanter, medial and lateral femur condyl, medial tibia condyl, caput fibulae, lateral and medial malleolus, superior anterior and posterior iliac crest, acromion, spinal processus Th8 and xiphoid processus. A cluster of three surface infrared light emitting diodes (LEDs) were secured to 6 body segments (lower leg 2x, the thigh 2x , the sacrum and the spinal processus C7). The 3-dimensional position of each LED was sampled with a frequency of 50Hz. Using these LED positions, data collection of knee varus-valgus motion started when the foot reached the force plate (i.e. initial contact) and continued until the foot left the force plate. This data produced a vertical ground reaction force curve and a curve presenting the varus-valgus position in time.

The ground reaction force curve presents itself as a M shape curve, from which the loading response phase (i.e. from zero to the first peak) and midstance (i.e. the lowest point of the M shape in between two peaks) were determined. These two parts of the ground reaction force curve were used to determine (i) the knee varus-valgus range of motion (VV-ROM) and (ii) the varus-valgus position (VVP) (see Figure 1).

Figure 1. Ground reaction force curve of three walk trials and the average of the three trials. From initial floor contact till the end of the loading response phase (i.e. first peak in ground reaction force curve, solid line) the motion of the knee in valgus-varus direction was measured. In midstance the valgus-varus position of the knee was determined (dotted line).

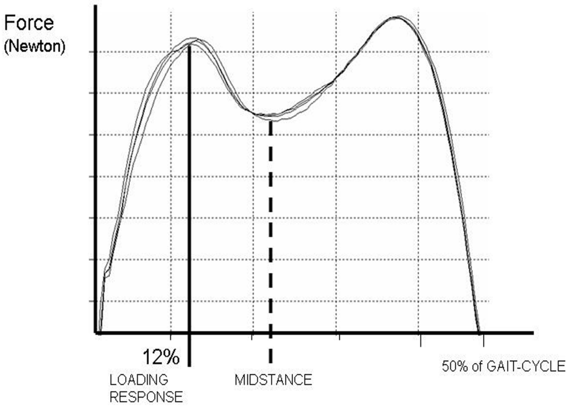


Figure 1

Varus-valgus range of motion of the knee was measured from initial floor contact to the instance in which maximum ground reaction force was recorded (i.e. loading response phase) (see Figure 1). The movement of the knee in varus and valgus direction was assessed. The difference between the peak excursion in varus direction and the peak excursion in valgus direction reflects VV-ROM (in degrees) (see Figure 2). The position of the knee was measured in midstance. Midstance is the instance in which the other foot has been lifted, the body weight has been aligned over the forefoot and the knee is extended. At the start of measurement, prior to walking, the patients were standing on the platform with body weight divided over both legs (bipedal stance). During this "rest" or anatomic posture, knee position was determined. The knee position at the lowest point of the M shape in between two peaks of the ground reaction curve was compared with the position of the knee at the beginning of the measurement to determine the midstance-VVP. Midstance-VVP was expressed in degrees (see Figure 3).

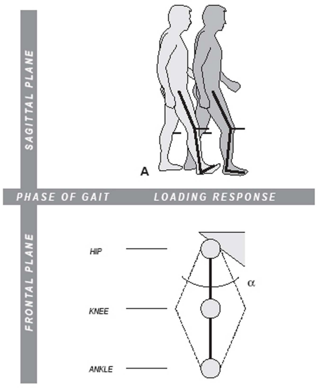


Figure 2. The loading response phase of the right leg (A). Varus-valgus range of motion (VV-ROM) is measured during the loading response phase of the gait-cycle. VV-ROM is the angle (a) between peak excursion in varus direction and peak excursion in valgus direction during the loading response phase.

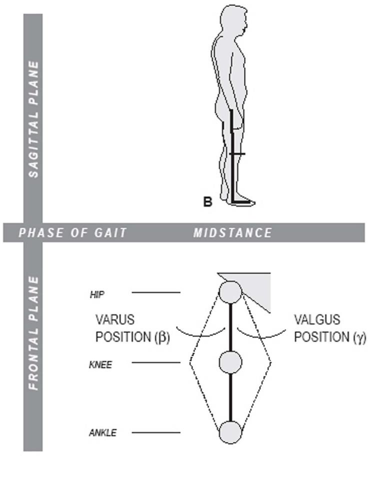


Figure 3. The midstance phase of the right leg (B). Varus-valgus position (VVP) is measured at midstance of the gait-cycle. Varus position is the angle (ß) between the varus excursion of the knee at midstance and the position of the knee at the start of measurement. Valgus position is the angle (γ) between the valgus excursion of the knee at midstance and the position of the knee at the start of measurement.

All subjects were instructed to walk at a self-selected normal speed along an 8 m walkway. They practiced until they could consistently and naturally make contact with the force plate. In order to achieve a natural gait pattern, subjects were not informed of the need to contact the force plate. The measurement of varus-valgus motion began with some steps before the force plate, to obtain a fluent walking pattern and stopped a few steps after leaving the force plate. Three acceptable trials were obtained for each knee and averaged to yield representative values of VV-ROM and midstance-VVP. The mean in degrees for VV-ROM and midstance-VVP of the right and left knees obtained from these three measurements was used for analysis.

Functional ability. Functional ability was assessed with both two standardized physical performance tests and a self-report questionnaire (WOMAC). As a performance-based measure of function a 100 m walking test and a Get Up and Go test were used (16). The 100 m walking test measured the time to walk a distance of 20 m 5 times (100 m) along a level and unobstructed corridor. Patients were instructed to walk the distance as fast as possible. On the command "go", patients walked along the corridor. They were instructed not to stop before crossing the finish line. A stopwatch was used to measure in seconds the time from the command "go" until subjects crossed the finish line. The examiner was standing at the finish line during the test. Patients who used canes while walking were permitted to use them during the test. All patients were wearing walking shoes.

The Get Up and Go (GUG) test was performed as described by Hurley et al. (17). To perform the test, subjects were seated on a standard height chair with armrests. On the command "go" subjects stood up without help of their arms and walked along a level, unobstructed corridor as fast as possible. A stopwatch was used to measure the length of time it took for the subject to stand and walk 15 meters. Patients who used canes while walking were permitted to use them during the test. All patients were wearing walking shoes. A longer time to complete the GUG test represents reduced functional ability. The intra class correlation coefficient (ICC) for the intratester reliability is 0.98 and the ICC for the intertester reliability is 0.98 (17).

The Dutch version of the Western Ontario and MacMasters Universities Osteoarthritis Index (WOMAC) was used to assess self-reported functional ability (18). The WOMAC is a disease specific measure of pain, stiffness, and physical function for individuals with OA of the knee. The WOMAC, with a possible range of 0-96, includes 5 items related to pain, 2 items related to stiffness, and 17 items related to physical function (PF). Each item is scored on a 5-point Likert scale. Reliability and validity of the WOMAC have been established (18). Higher scores on the WOMAC represent greater reduction in functional ability. The ICC for Dutch WOMAC physical functioning is 0.92 (18).

Muscle strength. Muscle strength was assessed for flexion and extension of the knee using an isokinetic dynamometer (EnKnee; Enraf-Nonius, Rotterdam, the Netherlands). Quadriceps and hamstrings strength were measured isokinetically at 60^0/second.

All patients were assessed according to a previously described device and protocol (19). The mean in Nm per kg body weight (Nm/kg) for quadriceps and hamstrings strength of the right and left maximum voluntary contraction obtained from three measurements was used for analysis. The mean of the right and left knee were averaged to obtain a measure for total muscle strength around the knee at the patient level (11,20).

Radiography and skeletal alignment. Radiographs of the knee were scored in a blinded fashion by an experienced radiologist using the grading scales proposed by Kellgren & Lawrence (K/L)(21,22). Weight-bearing, anteroposterior radiographs of the knee joints were obtained following the Buckland-Wright protocol (23). Skeletal alignment was assessed by a goniometer. In the frontal plane the angle between the thigh and shank was measured in degrees, with the axis of the arm of the goniometer at the transversal axis of the knee. The measurement was carried out in a non-weight-bearing position, with the knee extended.

Statistical analysis. Multilevel (linear mixed-model) analysis was applied for varus-valgus motion (VV-ROM and midstance-VVP) to analyse the dependency between left and right knees of the same patients (24). In this way two levels were distinguished: between-patients and between-knees within patients. Since functional ability (i.e. walking ability and WOMAC-PF score) was specific to patients, varus-valgus motion were averaged across right and left knees for analyses involving functional ability.

First, Pearson correlation coefficients were computed to establish the bivariate relationships between varus-valgus motion and functional ability. Second, a regression analysis was used to assess the relationship between varus-valgus motion, muscle strength and functional ability. An interaction variable between VV-ROM and muscle strength was added to the regression analysis, to assess the role of VV-ROM as a modifier of the relationship between muscle strength and functional ability. To adjust for the dependency of the left and right knees for VV-ROM, the mean of both knee measurements and the difference between both knee measurements were added to the regression analyses. This procedure controls for the independent contribution to the regression model of the left and right knee data of VV-ROM. When the difference between the two knees had a significant effect in regression analyses, the difference was included into the final model. The same regression analysis was performed with midstance-VVP, muscle strength and their interaction as independent variables. The independent contribution to the regression model of the left and right knee data of midstance-VVP was controlled by the same procedure as for VV-ROM. The variables VV-ROM, midstance-VVP and muscle strength were centered around the mean (25). Centering allows for a meaningful interpretation of main effects when interaction is present in the model. Other independent variables in the analyses comprised age, gender, duration of complaints, and current pain.

Results were considered statistically significant if p-values were < 0.05. All analyses were performed using SPSS version 14.0 software (Chicago, IL).

RESULTS

Characteristics of the study sample are listed in Table 1. Mean VV-ROM in the loading respons phase of a step was 3.24° ± 1.47°. In left knees, the VV-ROM was 3.49° ± 1.72° and in right knees 2.98° ± 1.74°, with a Pearson correlation coefficient of r = 0.44 (*P* < 0.001) between VV-ROM of the left and right knee. Mean midstance-VVP in the midstance phase of a step was 2.22° ± 1.65°. In left knees, the midstance-VVP was 3.02° ± 1.79° and in right knees 1.37° ± 2.72°, with no significant Pearson correlation coefficient (r = 0.05; *P* = 0.685) between midstance-VVP of the left and right knee. At midstance 105 knees showed a varus position, 19 a valgus position and 2 were neutral.

A linear mixed model analysis established variance in VV-ROM scores between-patients and between-knees within patients resulting in an ICC of 0.42. This means that 42% of the variance in VV-ROM score occurs between patients and 58% occurs between knees within patients. A linear mixed model analysis of midstance-VVP established an ICC of 0.19. This means that 19% of the variance in midstance-VVP score occurs between patients and 81% occurs between knees within patients.

No correlation was found (r = -0.019; P = 0.831) between the midstance-VVP and the skeletal alignment measured by goniometer.

Table 1. Characteristics of patients with knee osteoarthritis (N =63)

		Mean ± SD	**Range**	**n(%)**
Sex	Female			48(76%)
	Male			15(24%)
Age, years		60 ± 7.5	45-79	
Body mass index,kg/m^2		30.2 ±6.5	22.4 –56.6	
Duration of symptoms, years		5.7±7.6	1-47	
WOMAC-Pain score		11.2 ± 6.1	0-32	
WOMAC-Stiffness score		4.0 ± 1.9	0-8	
WOMAC-PF score		29.7 ± 14.1	4-56	
Walking time, seconds		97.5 ± 35.6	49.7-97.5	
GUG-time‡, seconds		13.6±7.0	6.9-43.0	
Varus-valgus range of motion (VV-ROM), degrees				
Left knee		3.49 ± 1.72	0.38 - 8.01	
Right knee		2.98 ±1.74	0.75 - 8.21	
Varus-valgus position (midstance-VVP), degrees				
Left knee		3.02 ± 1.79	-2.84 – 7.16	
Right knee		1.37 ± 2.72	-6.39 – 6.12	
Isokinetic quadriceps strength, Nm/kg				
Left knee		0.97 ± 0.61	0.08-2.78	
Right knee		1.02 ± 0.59	0.09-2.66	
Isokinetic hamstrings strength, Nm/kg				
Left knee		0.65 ± 0.34	0.04-1.54	
Right knee		0.69 ± 0.35	0.08-1.90	
Muscle strength averaged L/R and Ex/Fl		0.83 ± 0.45	0.08-1.98	
K&L grade*, no of knees				
Right (n=62)				
	Grade 0			0
	Grade 1			45 (71%)
	Grade 2			10(16%)
	Grade 3			6 (11%)
	Grade 4			1 (2%)
Left (n=63)				
	Grade 0			2 (3%)
	Grade 1			39(62%)
	Grade 2			9(14%)
	Grade 3			11(18%)
	Grade 4			2 (3%)

‡ GUG = Get Up and Go test

* K&L = Kellgren and Lawrence score of knee OA

Bivariate relationships between VV-ROM, midstance-VVP and functional ability.

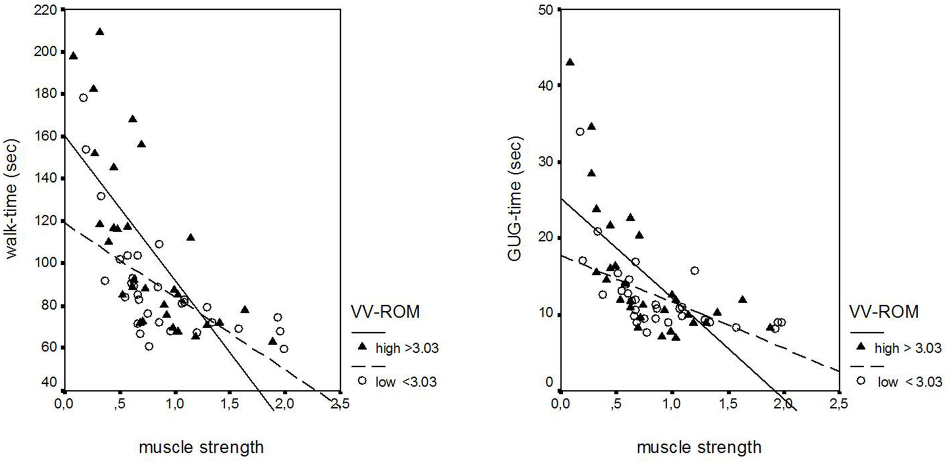
VV-ROM was not significantly correlated with reduced functional ability (walking-time r = .24; p=.060 and GUG-time r = 0.13; P = 0.332). However, a small correlation was found with WOMAC-PF (r = 0.26; P = 0.043). Midstance-VVP was correlated with reduced functional ability (walking-time r = 0.27; P = 0.034 and WOMAC r = 0.30; P = 0.017). However, no correlation was found with GUG-time (r = 0.18; P = 0.169).

Multivariate relationships between VV-ROM, muscle strength and functional ability.

To analyze the relationship between functional ability, VV-ROM and total muscle strength, a multiple regression model was constructed: Functional ability = b0 + b1*VV-ROM + b2*muscle strength + b3*VV-ROM*muscle strength (Table 2). The difference between the left and right data of the variable VV-ROM in the loading response phase did not add to the regression model. For that reason only the variable representing the mean score for VV-ROM at the patient level was used in the analyses of the data in the loading respons phase. The model explaining the total variation of walking-time in the loading respons phase was as follows (see Table 2): walking-time = 96.61 + 3.96*VV-ROM – 53.94*muscle strength - 14.21*VV-ROM * muscle strength (F = 19.04, P < 0.001, R2 = 0.50, N = 63). This means that 50% of the total variation of walking-time is explained by VV-ROM, muscle strength and their interaction. The interaction between VV-ROM and muscle strength (b= -14.21, P = 0.020) was significantly associated with walking-time. In the presence of high VV-ROM, muscle weakness was associated with an enhanced reduction of functional ability.

The model explaining the total variation of the GUG-time and the WOMAC-PF score are presented in Table 2. For the GUG-time the results show the same trend as the results obtained with walking-time (P = 0.067). This means that muscle weakness is associated with a higher GUG-time in the presence of an increased VV-ROM. Muscle weakness was associated with both GUG-time and WOMAC-PF score.

To visualize the interaction between VV-ROM and muscle strength in the loading response phase, VV-ROM was dichotomized into low VV-ROM and high VV-ROM using the median-split method (Figure 4).



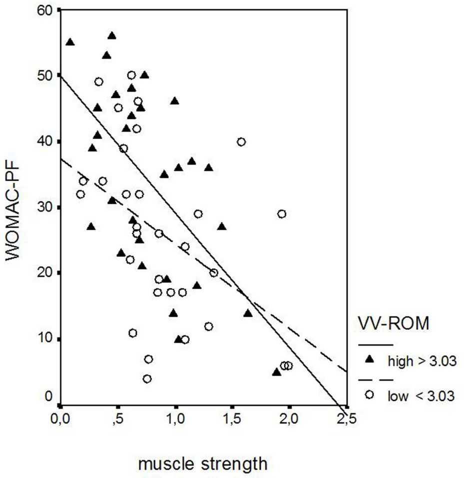


Figure 4.
The relationship between functional ability and muscle strength in a high VV-ROM (> 3.03°) group and a low VV-ROM (< 3.03°) group in the loading response phase of the gait-cycle.
A: walking-time vs. muscle strength. B: GUG-time vs. muscle strength C: WOMAC-PF vs. muscle strength.

Multivariate relationships between midstance-VVP, muscle strength and functional ability.

The difference between left and right knee midstance-VVP data contributed to the variance in walking-time and GUG-time (see Table 3), but not to the variance in the WOMAC-PF score. Therefore, the difference between left and right VVP data (in midstance) was added to the regression model. The main effect of midstance-VVP was significant for walking-time, GUG-time and WOMAC-PF score. This means that patients with an increased midstance-VVP (i.e., more varus position) have a stronger reduction in functional ability, than patients with low midstance-VVP (i.e., less varus or more valgus position). Thus, "bowing out" of the knee is related to reduced functional ability. The interaction between midstance-VVP and muscle strength was not significant and did not contribute to the variance in walking-time, GUG-time and the WOMAC-PF score.

Table 2. Results of the regression of functional ability (walking-time, GUG-time‡ and WOMAC-PF) on VV-ROM and total muscle strength

	Walking- time		GUG-time		WOMAC-PF	
Variables**	b* (SE)†	p-value	b* (SE)†	p-value	b* (SE)†	p-value
Intercept	96.61		13.46		29.62	
VV-ROM (degrees)	3.96 (2.28)	0.088	.25 (.49)	0.612	1.91 (1.04)	0.071
Muscle strength (Nm/kg)	-53.94 (7.63)	0.000	-9.97 (1.64)	0.000	-17.24 (3.47)	0.000
VV-ROM * muscle strength	-14.21 (5.94)	0.020	-2.39 (1.28)	0.067	-2.89 (2.70)	0.289
	R^2 = 0.50 F = 19.09 *P* <.001		R^2 = 0.40 F = 12.85 *P* <.001		R^2 = 0.35 F = 10.18 *P* < .001	

‡VV-ROM as the varus-valgus range of motion of the OA knee in the loading response phase of the gait-cycle
* b = unstandardized regression coefficient
** Variables centered around the mean
† SE = Standard Error
‡ GUG = Get Up and Go test

Table 3. Results of the regression of functional ability (walking-time, GUG-time‡ and WOMAC-PF) on midstance-VVP and total muscle strength

	Walking- time		GUG		WOMAC-PF	
Variables**	b* (SE)†	p-value	b* (SE)†	p-value	b* (SE)†	p-value
Intercept	86.93		11.33		30.90	
Midstance-VVP	7.40 (2.16)	0.001	1.03 (.47	.031	2.29 (1.01)	.028
Muscle strength	-52.17 (7.48)	0.000	-10.00 (1.61)	.000	-15.83 (3.51)	.000
Midstance-VVP * muscle strength	-5.74 (4.52)	0.210	-.36 (.97)	.716	-.1.30 (2.12)	.543
Midstance-VVP DIFF***	3.96 (1.53)	0.012	.87 (.33)	.011	-1.46 (.72)	.851
	R^2 = 0.54 F = 16.66 *P* < 0.001		R^2 = 0.45 F= 11.57 *P* < 0.001		R^2 = 0.36 F = 8.03 *P* < .001	

‡Midstance-VVP as the varus-valgus angle of the OA knee in midstance of the gait-cycle
* b = unstandardized regression coefficient
** Variables centered around the mean
*** Midstance-VVP diff = the difference between left and right midstance-VVP data
† SE = Standard Error
‡ GUG = Get Up and Go tes

All analyses were repeated in a more extensive model, with the demographic variables from Table 1 as controlling variables (age, gender, disease duration and current pain). The results of those analyses were consistent with the results reported here.

DISCUSSION

This study shows that varus-valgus motion of the knee is related to functional ability in patients with knee OA. It was found that in knee OA patients muscle weakness has a stronger impact on functional ability when the knee shows a high varus-valgus range of motion. It was also found that a pronounced varus position in midstance is associated with reduced functional ability. Finally, a left-right difference in midstance position of the knee is associated with a reduction in functional ability.

The results of the present study suggest that high VV-ROM is associated with inefficient use of muscle strength in the loading response phase. Patients with knee OA show greater magnitudes of muscle activities during walking (9,10). We presumed that low varus-valgus motion results in efficient use of muscle strength during walking. Low VV-ROM is a condition for functional ability. Conversely, in the presence of increased VV-ROM and muscle weakness patients are at risk of being disabled. Our results also suggest that a pronounced varus position is associated with reduced functional ability, independent from the influence of muscle strength. Therefore, in the presence of a pronounced varus position of the knee patients are at risk for developing reduced functional ability. These results are in agreement with the study of Chang et al. (8).

The results for VV-ROM are different from the results for midstance-VVP. The differences in findings between VV-ROM and midstance-VVP may be explained by the different phases of the gait cycle in which the data were collected. Forces at the knee are the highest in the first phase of the gait-cycle (i.e., loading-response phase) (26,27,28). During the loading-response phase, the knee is flexed (7). With the knee in flexion, forces at the knee are primarily absorbed by muscle actions (26,27,28). In midstance the knee is extended (30). With the knee in extension, forces at the knee are primarily absorbed by the passive restraint of the knee and not by high muscle action (7). The difference in knee position (i.e. flexed or extended) may explain the differences in findings between VV-ROM and midstance-VVP.

Midstance-VVP was used according to Chang et al (8). In that study midstance was chosen to assess the varus position (i.e. thrust) of the knee. In midstance full body weight is on 1 leg and at that moment of the gait-cycle the knee is most vulnerable to malalignment (8). Midstance-VVP was established relative to the patients' posture in rest, rather than relative to position of neutral alignment. This might explain the absence of a correlation between midstance-VVP and skeletal alignment.

It should be noted that the analysis showed a high variance in midstance-VVP between left and right knees within patients. To take into account the high variance between knees within patients, the difference between left and right midstance-VVP was included in regression analyses. This difference was significantly related to functional ability, indicating that walking ability is more limited in patients with pronounced asymmetric varus-valgus knees than in patients with symmetric knees. Varus knees and asymmetric knees may lead to a greater demand on compensating mechanisms in the knee joint stabilization process, which may ultimately lead to a stronger reduction in functional ability.

It has been stated that an adequate gait pattern contains little or no movement of the knee in the frontal plane due to sufficient passive restraint of the knee (7,12). The passive restraint of the knee is measured as the laxity of the knee joint. Knee joint varus-valgus laxity is measured statically in an unloaded situation (4,5), whereas varus-valgus motion was measured dynamically in a loaded situation. No relationship was found between joint laxity and varus-valgus motion (results not presented). Previously, we have found that joint laxity affects functional ability (19). Our present findings suggest that varus-valgus motion and joint laxity independently affect functional ability.

This study has strengths and limitations. We assessed functional ability with both a questionnaire and performance-measures. We controlled for the dependency of left and right knee data within patients by using multilevel analysis. A limitation of our study is the lack of measuring compensating mechanisms responsible for maintaining walking ability, such as muscle co-contractions (8), trunk movements (7, 34), movements of the hip and ankle (29), reduced walking speed (30-34) and the compensating movements of the knee in the sagittal (flexion-extension) and transversal (internal and external rotation) plane (35). These compensating mechanisms were not taken into consideration. Future research could examine the effect of different compensating mechanisms, particularly the effect of walking speed on varus-valgus motion of the OA knee in relation to functional ability.

Our results may have implications for exercise therapy directed toward increasing muscle strength to improve functional ability. The presence of high VV-ROM may influence the efficiency of the muscles in the loading response phase. Therefore, exercise therapy may entail specific exercises with the aim to reduce high VV-ROM of the OA knee. Specific treatments that address both muscle strength and the reduction of VV-ROM should be developed and tested because they may improve functional ability. To reduce the high varus position of the knee in midstance a different strategy should be considered. It is speculated that a change in varus position by a lateral wedged insole may influence the relationship with functional ability (36). Research on the effect of these strategies is warranted and requires further investigation.

In conclusion, in knee OA patients the (bivariate) relationship between varus-valgus motion and functional ability was absent or weak. In knee OA patients with high varus-valgus range of motion, muscle weakness has a stronger impact on functional ability than in patients with low varus-valgus range of motion. Furthermore, knee OA patients with more pronounced varus knees during walking show a stronger reduction in functional ability than patients with less pronounced varus or with valgus knees.

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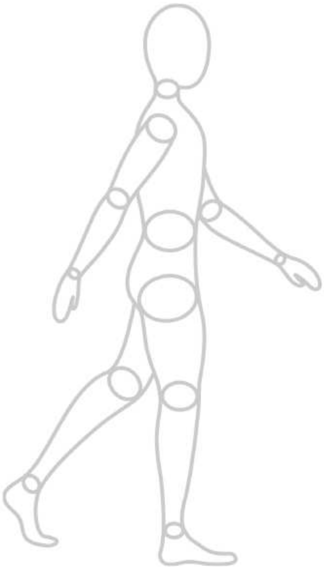
Chapter 9

KNEE VARUS-VALGUS MOTION DURING GAIT – A MEASURE OF JOINT STABILITY IN PATIENTS WITH OSTEOARTHRITIS?



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ABSTRACT

Objective. To determine the validity of varus-valgus motion as a measure of knee joint stability by establishing the relationship of varus-valgus motion with muscle strength, joint proprioception, joint laxity and skeletal alignment in patients with knee osteoarthritis (OA).

Methods. Sixty-three patients with OA of the knee were tested. Varus-valgus motion was determined with a video-based optoelectronic gait analysis system. Muscle strength was measured using a computer-driven isokinetic dynamometer. Proprioceptive acuity was assessed by establishing the joint motion detection threshold in the anterior-posterior direction. Laxity was assessed using a device which measures the passive angular deviation of the knee in the frontal plane. Alignment was assessed using a goniometer. Regression analyses were performed to assess the relationship between varus-valgus motion, muscle strength, joint proprioception, joint laxity and skeletal alignment.

Result. Varus-valgus motion was not related to muscle strength, joint proprioception, joint laxity and skeletal alignment.

Conclusions. Knee joint stability cannot be measured as varus-valgus motion. Rather, a number of independent factors seem to contribute to the process of stabilization of the knee joint.

Keywords: Osteoarthritis, Knee, Kinematics, Stability, Muscle Strength

INTRODUCTION

In patients with knee osteoarthritis (OA) there is an increasing attention for the role of biomechanical processes in daily physical functioning. In particular, stability of the knee joint has been a focus of research (1,2).

Stability of the knee is defined as the ability of the joint to maintain a position or to control movement under differing external loads. It is supposed that stability is provided by the active neuromuscular system (muscle strength and proprioception) and by passive restraint (ligaments and capsule) (3,4). It is hypothesized that muscle weakness, poor proprioception, laxity (i.e., inadequate passive restraint) and malalignment result in instability. However, so far no adequate measure of knee joint stability has been identified. A possible measure of stability of the knee is the varus-valgus motion during walking. In a normal gait pattern there is minimal varus-valgus motion (4). Therefore, the presence of excessive varus-valgus motion of the knee during walking might be a measure of instability of the joint.

The aim of the study was to determine the validity of varus-valgus motion as a measure of knee joint stability by establishing the relationship of varus-valgus motion with variables which determine stability of the knee, i.e. muscle strength, joint proprioception, joint laxity and skeletal alignment.

PATIENTS AND METHODS

Patients

Sixty-three patients diagnosed with OA of the knee were included in the study. Inclusion criteria were OA of the knee (uni- or bilateral) according to the clinical criteria of the American College of Rheumatology (5), and age between 40 and 85 years. Exclusion criteria were poly-arthritis, presence of rheumatoid arthritis or other systemic inflammatory arthropathies, knee surgery within the last 12 months or a history of knee arthroplastic surgery, intra-articular corticosteroid injections into either knee within the previous three months, and/or inability to understand the Dutch language. All patients provided written informed consent. The study was approved by the human research ethics committee of the VU University Medical Center in Amsterdam.

MEASURES

Procedures. Patients visited the laboratory twice within the same week. During the first visit, patients' muscle strength, joint proprioception, joint laxity and knee alignment were tested. The second visit consisted of a three-dimensional (3D) gait analysis.

Demographics. A series of demographic variables were obtained including age, gender, height, weight, and duration of complaints.

Gait analysis. An Optotrak motion analysis system (model 3020, Northern Digital Inc., Waterloo, Ontario, Canada) recorded the 3D position of light emitting diode markers in order to assess varus-valgus motion. 3D ground reaction force were synchroniously recorded using a 51 x 46.5 cm force plate (AMTI, Watertown, Massachusetts, USA). An open source Matlab software program BodyMech (www.bodymech.nl) was used to reconstruct the anatomical axes and, from that, 3D knee motion and loading data (6). Varus-valgus knee motion resulted from decomposing knee motion using a flexion-varus-exorotation sequence

To describe skeletal movement, body segments were considered as rigid bodies (lower leg, thigh, pelvis and trunk) with a local coordinate system defined to coincide with a set of anatomical axes. The limb segments were determined by anatomical landmarks: greater trochanter, medial and lateral femur condyl, medial tibia condyl, caput fibulae, lateral and medial malleolus, superior anterior and posterior iliac crest, acromion, spinal processus Th8 and xiphoid processus. A cluster of three surface infrared light emitting diodes (LEDs) were secured to 6 body segments (lower leg 2x, the thigh 2x , the sacrum and the spinal processus C7). The 3-dimensional position of each LED was sampled with a frequency of 50Hz. Using these LED positions, data collection of knee varus-valgus motion started when the foot reached the force plate (i.e. initial contact) and continued until the foot left the force plate. This data produced a vertical ground reaction force curve and a curve presenting the VVP in time.

The ground reaction force curve presents itself as a M shape curve, from which the loading response phase (i.e., from zero to the first peak) and midstance (i.e., the lowest point of the M shape in between two peaks) were determined. These two parts of the ground reaction force curve were used to determine (i) the knee varus-valgus range of motion (VV-ROM) (see Figure 1) and (ii) the varus-valgus position (VVP) (see Fig. 2).

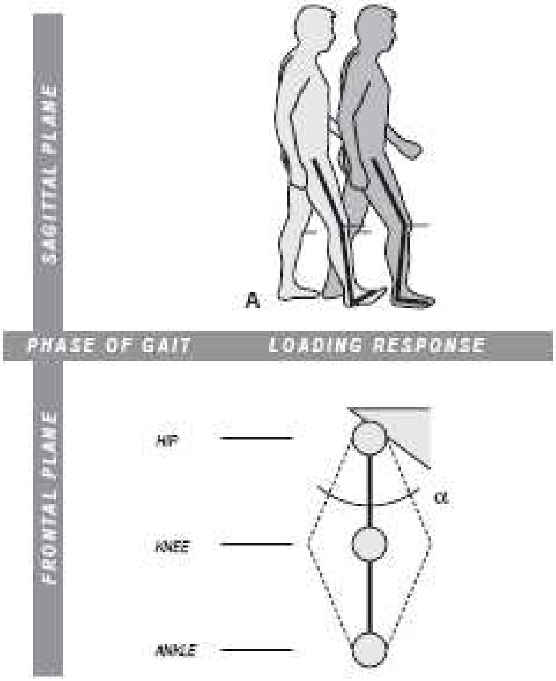

Figure 1. The loading response phase of the right leg (A). Varus-valgus range of motion (VV-ROM) is measured during the loading response phase of the gait-cycle. VV-ROM is the angle (α) between peak excursion in varus direction and peak excursion in valgus direction during the loading response phase.

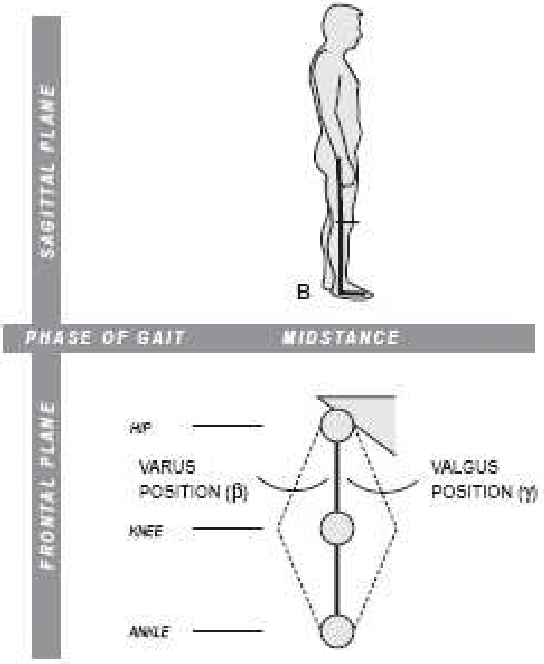

Figure 2. The midstance phase of the right leg (B). Varus-valgus position (VVP) is measured at midstance of the gait-cycle. Varus position is the angle (ß) between the varus excursion of the knee at midstance and the position of the knee at the start of measurement. Valgus position is the angle (γ) between the valgus excursion of the knee at midstance and the position of the knee at the start of measurement.

VV-ROM of the knee was measured from initial floor contact to the instance in which maximum ground reaction force was recorded (i.e., loading response phase). The movement of the knee in varus and valgus direction was assessed. The difference between the peak excursion in varus direction and the peak excursion in valgus direction reflects VV-ROM (in degrees). The position of the knee was measured in midstance. Midstance is the instance in which the other foot has been lifted, the body weight has been aligned over the forefoot and the knee is extended. The knee position in the varus or valgus direction was obtained by comparing the position of the knee in midstance with the position of the knee at the start of measurement (anatomical posture, prior to walking). Midstance-VVP was expressed in degrees.

All subjects were instructed to walk at a self-selected normal speed along an 8 m walkway. They practiced until they could consistently and naturally make contact with the force plate. In order to achieve a natural gait pattern, subjects were not informed of the need to contact the force plate. The measurement of varus-valgus motion began with some steps before the force plate, to obtain a fluent walking pattern, and stopped a few steps after leaving the force plate. Three acceptable trials were obtained for each knee and averaged to yield representative values of VV-ROM and midstance-VVP. The mean in degrees for VV-ROM and midstance-VVP of the right and left knees obtained from these three measurements was used for analysis.

The measurements of muscle strength, joint proprioception, joint laxity and skeletal alignment have been described in previous studies (7,8,9). Muscle strength was measured isokinetically. Joint proprioception was measured as the detection sense of joint movement. Joint laxity was measured as he total movement in the varus-valgus direction in an unloaded situation. Skeletal alignment was measured by goniometer in an unloaded situation and expressed as the varus-valgus position of the knee.

Radiography. Radiographs of the knee were scored in a blinded fashion by an experienced radiologist using the grading scales proposed by Kellgren & Lawrence (K&L). Weight-bearing, anteroposterior radiographs of the knee joints were obtained following the Buckland-Wright protocol (10).

Statistical analysis. All analyses were performed at the level of the knee. In a previous study the variance between patients and within patients (i.e., between knees) was calculated (9). It was found that of the total variance in

VV-ROM, 42% occurred between patients and 58% occurred between knees within patients. Likewise, the variance in midstance-VVP occurred in 19% between patients and in 81% between knees within patients. This meant that with regard to VV-ROM and VVP, left and right knees within patients are relatively independent of each other. Therefore, for the present study in which all variables were measured at the knee level, it was decided to analyze at the level of the knee.

Pearson correlations were calculated to determine the bivariate relationships between VV-ROM and midstance-VVP and muscle strength, joint proprioception, joint laxity and skeletal alignment, respectively. A positive correlation indicates that an increase in VV-ROM and midstance-VVP is associated with an increase in muscle strength, joint proprioception, joint laxity and skeletal alignment.

Regression analyses were used to determine predictors of knee VV-ROM and midstance-VVP. To reduce the number of predictors, a regression analysis was carried out with the predictors muscle strength, joint proprioception, joint laxity and skeletal alignment, using a backward selection method. A liberal level of significance of 0.05 was used, in order not to miss predictors that might turn out to be important in the final model.

Analyses were performed using SPSS for Windows 14.0 (SPSS Inc., Chicago, IL).

RESULTS

Characteristics of the study sample are listed in Table 1. In left knees, the VV-ROM was 3.49° ± 1.72° and in right knees 2.98° ± 1.74°. Midstance-VVP in left knees was 3.02 ° ± 1.79 ° and in right knees 1.37 ° ± 2.72 °.

Table 1. Characteristics of patients with knee osteoarthritis (N =63)

	Mean ± SD	Range	n(%)
Sex (Female)			48(76%)
Age, years	60 ± 7.5	45-79	
Body mass index,kg/m^2	30.2 ±6.5	22.4 –56.6	
Varus-valgus range of movement (VV-ROM), degrees			
Left knee	3.49 ± 1.72	0.38 - 8.01	
Right knee	2.98 ±1.74	0.75 - 8.21	
Varus-valgus position (midstance-VVP), degrees			
Left knee	3.02 ± 1.79	-2.84 – 7.16	
Right knee	1.37 ± 2.72	-6.39 – 6.12	
Isokinetic quadriceps strength, Nm/kg			
Left knee	0.97 ± 0.61	0.08-2.78	
Right knee	1.02 ± 0.59	0.09-2.66	
Isokinetic hamstrings strength, Nm/kg			
Left knee	0.65 ± 0.34	0.04-1.54	
Right knee	0.69 ± 0.35	0.08-1.90	
Proprioception, degrees			
Left knee	4.76 ± 3.44	0.90-19.43	
Right knee	5.14 ± 3.14	1.33-16.50	
Laxity, degrees			
Left knee	7.34 ± 2.96	2.40-15.0	
Right knee	7.81 ± 3.52	1.90-17.90	
Varus-valgus alignment , no of knees			
Left knee (n=63)			
Varus			9
Valgus			27
Neutral			27
Right knee (n=63)			
Varus			8
Valgus			29
Neutral			26
K&L grade*, no of knees			
Right knee (n=62)			
Grade 1			45 (71%)
Grade 2			10(16%)
Grade 3			6 (11%)
Grade 4			1 (2%)
Left knee (n=63)			
Grade 0			2 (3%)
Grade 1			39(62%)
Grade 2			9(14%)
Grade 3			11(18%)
Grade 4			2 (3%)

* K&L = Kellgren and Lawrence

Relationships between VV-ROM and muscle strength, joint proprioception, joint laxity and skeletal alignment.

VV-ROM was not correlated with muscle strength (*r* = -0.09, *P* = 0.299), joint proprioception (*r* = 0.01, *P* = 0.956), joint laxity (*r* = 0.07, *P* = 0.453) and skeletal alignment (*r* = 0.04, *P* = 0.635). Multivariate relationships between VV-ROM, muscle strength, joint proprioception, joint laxity and skeletal alignment showed no significant regression coefficients (Table 2).

Relationships between midstance-VVP and muscle strength, joint proprioception, joint laxity and skeletal alignment.

Midstance-VVP was not correlated with muscle strength (*r* = -0.11, *P* = 0.229), joint proprioception (*r* = -0.02, *P* = 0.818), joint laxity (*r* = 0.04, *P* = 0.705) and skeletal alignment (*r* = 0.11, *P* = 0.208). Multivariate relationships between midstance-VVP, muscle strength, joint proprioception, joint laxity and skeletal alignment showed no significant regression coefficients (Table 2).

Table 2. Results of the regression analysis of varus-valgus motion (VV-ROM‡ and Midstance-VVP) at the knee level on muscle strength, joint proprioception, joint laxity and skeletal alignment (N=126)

	VV-ROM		Midstance-VVP	
Variables	b* (SEE)†	p-value	b (SEE)	p-value
Intercept	3.51 (.73)		3.36 (1.02)	
Muscle strength (Nm/kg)	-.18 (.20)	0.368	-.39 (.27)	0.154
Joint proprioception (degrees)	-.01 (.05)	0.778	-.05 (.07)	0.513
Joint laxity (degrees)	.02 (.05)	0.756	-.02 (.07)	0.805
Skeletal alignment	.02 (.03)	0.598	.06 (.04)	0.171
	R2 = 0.01 F = 0.392 P = 0.814		R2 = 0.03 F = 0.951 P = 0.437	

‡ The varus-valgus range of motion in the loading response phase.
* b = unstandardized regression coefficient
† SEE = standard error of the estimate

All analyses were repeated in a more extensive multi-level model, which included at the patient-level controlling variables age, gender, body mass index (BMI) and severity of OA. The results of those analyses were consistent with the results reported here.

DISCUSSION

The results show that varus-valgus motion is not dependent on muscle strength, joint proprioception, joint laxity and skeletal alignment. This suggests that varus-valgus motion is not a valid measure of joint stability.

To our knowledge, this is the first study that has explored varus-valgus motion in different phases of the gait-cycle with the aim to operationalise knee joint stability. Within a biomechanical model of joint stability it was hypothesized that excessive varus-valgus motion measures knee joint instability. However, no relationship was found between varus-valgus motion and biomechanical variables responsible for joint stability, i.e., muscle strength, joint proprioception, joint laxity and skeletal alignment. When these variables were considered together in the same regression model no associations were found with varus-valgus motion. As a consequence, VV-ROM and midstance-VVP cannot be considered as adequate representations of stability.

Stability of the knee joint is dependent on the passive restraint system (ligaments and capsule) and the active neuromuscular system (muscle strength and proprioception). Passive restraint was assessed as joint laxity. The contribution of the active neuromuscular system was assessed through measures of muscle strength and proprioception. The present study shows that varus-valgus motion is not related to laxity, muscle strength or proprioception. Apparently, varus-valgus motion is an independent aspect of joint stability. Joint stability should be regarded a process, involving a number of independent factors. Laxity, muscle strength, proprioception and varus-valgus motion are to be seen as independent factors, which all contribute to stabilization of the knee joint.

A possible explanation for not finding relationships might be lack of statistical power. However, for a total of 126 knees, a correlation coefficient of 0.18 is already significant (11). For regression analyses it is generally accepted that at least 10 subjects should be studied per independent variable. In our study on 126 knees, four independent variables were included in regression analyses. Therefore, it is unlikely that lack of statistical power was the reason for our results.

This study has several limitations. Some patients had a BMI over 30 and this could have influenced the 3-dimensional position of each LED on the anatomical landmarks f the upper and lower leg. Another limitation is the lack of measurement of compensating mechanisms responsible for movement of the knee, such as trunk movements (12), movements of the hip and ankle (13) and reduced walking speed (14). Future research could examine the effect of different compensating mechanisms, particularly the effect of walking speed on varus-valgus motion of the OA knee.

Our results may have clinical implications. The results indicate that varus-valgus motion is not a good measure of joint stability of the knee in OA. Instead, the evaluation of joint stability should be based on several independent factors, i.e., muscle strength, laxity, proprioception, and varus-valgus motion. Furthermore, the improvement of muscle strength, proprioception accuracy or the restriction of varus-valgus motion during walking may improve joint stability in knee OA patients.

In conclusion, knee joint stability cannot be measured as varus-valgus motion. Rather, a number of independent factors seem to contribute to the process of stabilization of the knee joint.

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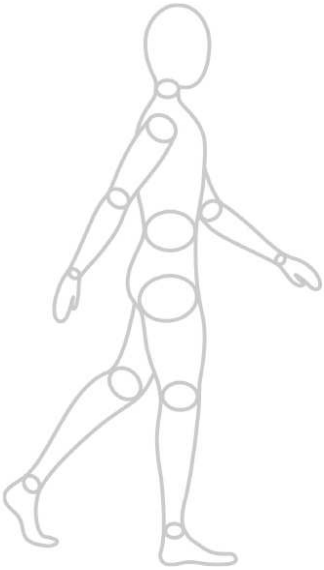
Chapter 10

GENERAL DISCUSSION



General Discussion

Osteoarthritis (OA) of the knee is characterized by a decline in functional ability (1,2). It is important to maintain or improve the performance of daily activities, such as walking, stair climbing and reclining, in knee OA patients (3-5).

Muscle strength is considered to be the strongest determinant of functional ability in knee OA (6-13). However, therapeutic interventions aimed at muscle strengthening have so far been only moderately effective on average, and their effectiveness has also varied considerably between patients (12). In Chapter 1 of this thesis, it was proposed that this variability may be related to the process of knee joint stabilization. Knee joint stability may affect the functional ability of knee OA patients in two ways. First, impaired knee joint stability may directly affect functional ability. Additionally, it was hypothesized that impairments in knee joint stability may affect the impact of muscle strength on functional ability Therefore, the overall research question addressed in this thesis was: Is knee joint stability a determinant of functional ability in patients with osteoarthritis of the knee?

Three factors involved in the process of knee joint stabilization were the focus of the studies described here. Firstly, knee joint laxity was studied, with the following research questions:

Is knee joint laxity of influence on the strength of the relationship between muscle strength and functional ability? (Chapter 2)

When measuring knee joint laxity in knee OA patients, what are the intra- and inter-rater reliability and the intra- and inter-rater agreement parameters? (Chapter 3)

Is knee joint laxity related to structural joint change (joint space narrowing and osteophyte formation) and joint malalignment in knee OA patients? (Chapter 4)

Is knee varus-valgus laxity higher in women than in men in knee OA patients? (Chapter 5)

Secondly, this thesis focused on the following questions in relation to proprioception:

Is knee joint proprioception related to functional ability and does poor proprioception aggravate the impact of muscle weakness on functional ability? (Chapter 6)

When measuring knee joint proprioception in knee OA patients and healthy subjects, what are the inter- and intra-rater reliability and the inter- and intra-rater agreement parameters? Additionally, what are the effects of variations in measurement procedure on measurement error? (Chapter 7)

Finally, varus-valgus motion of the knee joint was studied in an attempt to answer the following questions:

Is varus-valgus motion of the knee a valid measure of knee joint stability? (Chapter 8)

Is high varus-valgus motion associated with reduced functional ability in knee OA patients? Furthermore, in knee OA patients with high varus-valgus motion, is muscle weakness associated with a more severe reduction in functional ability than in knee OA patients with low varus-valgus motion? (Chapter 9)

We performed observational studies, in which a total number of 149 outpatients were assessed. Data collection took place at the Jan van Breemen Institute (JBI) in Amsterdam and at the VU University medical centre in Amsterdam, The Netherlands.

In this chapter, the main findings of our study are put into perspective and will be discussed. Implications for clinical practice, physiotherapy education and future research are given.

Knee joint laxity and functional ability

This thesis included a research question on the role of joint laxity as a determinant of functional ability in knee OA patients. It was found that there was only a weak direct relationship between laxity and functional ability. However, the relationship between muscle strength and functional ability was stronger in subjects with high knee joint laxity. Thus, knee joint laxity is an important determinant of functional ability by influencing the relationship between muscle strength and functional ability.

Knee joint proprioception and functional ability

A research question on the role of proprioception as a determinant of functional ability in knee OA patients was included in this thesis. It was found that the relationship between muscle strength and functional ability was affected by poor proprioception, although the direct relationship between knee joint proprioception and functional ability was weak. This means that functional ability is affected by poor proprioception, primarily through the impact of proprioception on the relationship between muscle strength and functional ability.

Knee joint varus-valgus motion during walking and functional ability

The varus-valgus motion of the knee was supposed to be a measure for stability of the knee in a loaded dynamic situation. However, varus-valgus motion was not related to muscle strength, joint proprioception, joint laxity and skeletal alignment. Therefore, the varus-valgus motion could not be interpreted as a measure of joint stability. Rather, a number of factors seem to contribute to the process of stabilization of the knee joint, including the varus-valgus motion.

The varus-valgus motion during walking has been proposed as a determinant of functional ability in knee OA. It was found that in knee OA patients with high varus-valgus motion, muscle weakness was associated with a stronger reduction in functional ability than in patients with low varus-valgus motion during walking. Additionally, it was found that a pronounced varus position of the knee and a difference between left and right knees in varus-valgus position were related to reduced functional ability. Thus, knee varus-valgus motion during walking showed to be a determinant of functional ability and was of influence on the relationship between muscle strength and functional ability.

Joint stability in knee OA

Several conclusions can be drawn from the presented studies concerning joint stability and functional ability. The first conclusion is that knee joint stability should be regarded as a process involving a number of separate factors, rather than as a singular entity. Joint stability is achieved through the interaction of the passive restraint system (ligaments, capsule) and the active neuromuscular system (muscle strength, proprioception)(14,15). Joint instability may be caused by the impairment of one independent factor or it may be multi-factorial, consisting of ligament and capsule laxity, and neuromuscular impairments including muscle weakness and proprioceptive deficits. Attempts to measure knee joint stability were presented in 2 studies (16,17). In both studies the perceived stability of the knee was measured by questionnaire (16). Both studies showed that a substantial part of knee OA patients report knee instability and that instability affects functional ability. Although joint stability is often mentioned in OA literature, no studies were found that measured observed joint stability. Our results support Fitzgerald et al (16), who suggested that knee instability experienced by knee OA patients is most likely a multi-factorial problem that may be the result of factors such as increased capsule-ligamentous laxity, structural damage to the knee, and altered lower muscular strength and neuromuscular control.

The second conclusion is that in knee OA patients with high joint laxity, poor joint proprioception and high varus-valgus motion during walking, the relationship between muscle strength and functional ability is stronger than in knee OA patients with low laxity, adequate proprioception and low varus-valgus motion during walking. These findings may be explained by compensatory mechanisms in the process of knee joint stabilization. Deficits in passive restraint or proprioception may be compensated for by increased muscle activity and co-contractions of antagonist muscles (18), preserving knee joint stability and ultimately functional ability. When muscle activity becomes a more dominant force in the process of knee joint stabilization, this would be reflected in a stronger relationship between available muscle strength and functional ability. This is in concordance with the findings of Chapters 2, 6 and 9.

Our conclusions are summarized in the model presented in Figure 1: the "knee joint stabilization model" (see Figure 1). As shown in Figure 1 the relationship between joint stability (i.e., joint laxity, joint proprioception and varus-valgus motion) and functional ability in knee OA patients indicates that a patient's functional ability will be reduced in the presence of poor joint stabilization of the knee joint.

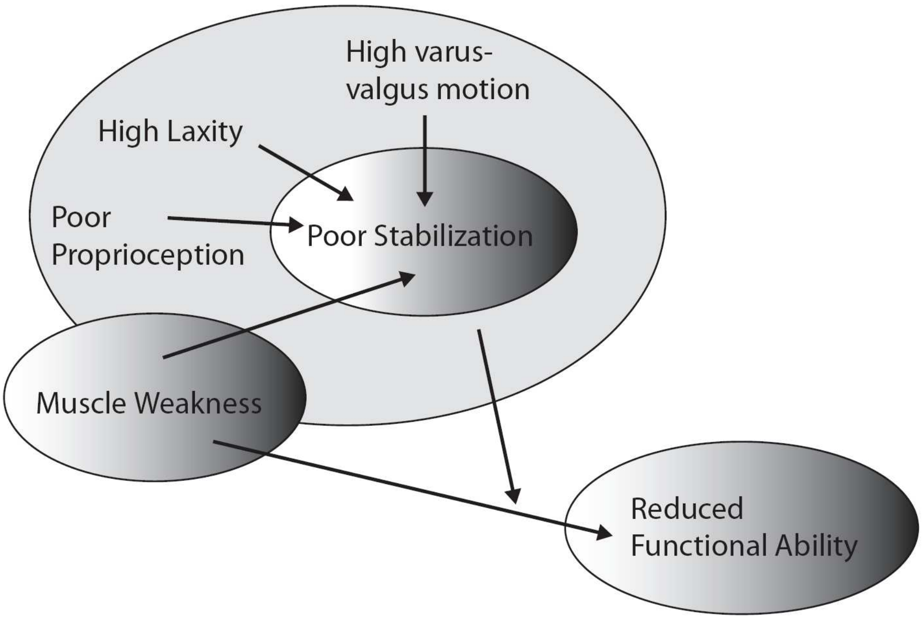


Figure 1. The "knee joint stabilization model": a model of the relationship between impaired factors of the stabilization process and reduced functional ability in patients with osteoarthritis of the knee.

Within this model it is summarized that relationships exist between factors of joint stability and functional ability. Interactions between factors of joint stability and muscle strength were found. Consequently, muscle actions can compensate for high laxity, poor proprioception, and high varus-valgus motion during walking as long as there is sufficient muscle strength available. However, when there is muscle weakness, the muscles will be unable to perform the dual tasks of stabilizing the joint and providing the joint movements necessary for the performance of physical activities, resulting in reduced functional ability.

Our findings concerning the impact of laxity on the relationship between muscle strength and functional ability are not in agreement with the conclusion presented by Sharma et al (19). In that study it was found that high laxity was associated with a weaker relationship between muscle strength and functional ability in knee OA patients. The difference in results may be explained by a different analytical approach. Whereas our study utilized regression analyses, Sharma et al used correlational analyses. The usage of an interaction term of muscle strength and laxity in regression analyses allows for one analysis, using data from all patients. Another benefit of regression analyses is that the interaction term provides an immediate insight into the statistical significance of the impact of laxity on the relationship between muscle strength and functional ability. Therefore, regression analyses are a more fitting approach to study this type of questions.

The aforementioned second conclusion considered also the relationship between poor proprioception and functional ability. This conclusion is partly in agreement with the conclusion of the study by Pai et al (20), in which the relationship between proprioception and functional ability was studied. The results showed a correlation between proprioception and perceived functional ability. However, no studies were found that examined the influence of proprioception on the relationship between muscle strength and functional ability. A comparison with other studies is also hampered by differences in measurement protocols, equipment and statistical analyses, particularly in the operationalization of proprioception. Some studies used joint motion sense as a measure of proprioception, whereas others used joint position sense.

No studies were found that related varus-valgus motion with functional ability and no studies were found that assessed the influence of varus-valgus motion on the relationship between muscle strength and functional ability. Therefore, the results of this study cannot be compared with other studies.

Above, it was hypothesized that available muscle strength can be utilized to compensate for impaired laxity or proprioception or varus-valgus motion. This would be achieved through increased muscle activity or co-contractions of antagonist muscles. A number of other compensatory mechanisms may also be available, and have been reported: this concerns trunk movements (21), movements of the hip and ankle (22), reduced walking speed (23-25) and the compensating movements of the knee in the sagittal (flexion-extension) and transversal (internal and external rotation) plane (26). It is to be expected that during the course of the disease compensating mechanisms will become increasingly important.

Limitations

It is useful to consider some limitations of the presented studies. One limitation of this thesis is that the studies were cross-sectional and causal conclusions are not allowed. In biomechanical studies it is supposed that joint laxity is the result of reduced cartilage volume. As the cartilage is worn away, the loss of cartilage and/or bone height results in laxity. The subchondral bone surfaces draw nearer to each other, reducing the distance between the compartment's ligament insertions and result in less tension in ligaments and capsule. However, it has been stated that at early stages of knee OA, laxity is unlikely to be a consequence of disease (27). If laxity was exclusively the local result of more advanced OA pathology, then uninvolved knees of OA patients as well as knees with mild OA should not be more lax than the knees of older control subjects (27) It has been hypothesized that excessive knee joint mobility can have various mechanical consequences and may result in more stress on either the tibiofemoral or patellafemoral compartments (27). This has been supported by Brandt et al. (28) who stated that cartilage degeneration is the result of joint instability due to ligamentous laxity and periarticular muscle weakness. This would mean that cartilage degeneration can be the result of changes in the environmental structures, such as capsule, and ligaments and the neuromuscular control mechanism (29). While knee joint laxity is associated with cartilage degeneration in the knee joint it is still unclear whether the observed laxity is a consequence or a cause of worsening OA. In the effort to better understand the etiology of knee OA it is essential to clarify the role of knee laxity in both the initial occurrence of the disease and its subsequent progression. Therefore, future research on the potential relationship between knee joint laxity and disease progression of knee OA is needed.

Secondly, our results are limited to patients with mild knee radiological osteoarthritis (ROA) (Kellgren&Lawrence 1-2), with a K&L grade 1 majority and extrapolation of the results to the severe group should be studied. However, it is a common observation that in knee OA patients the severity of the radiographic changes only plays a minor role in explaining reduced functional ability. Therefore, it is not be expected that OA severity strongly influenced the presented results.

The third limitation is the absence of criteria for adequate levels of joint laxity and joint proprioception in patients with knee OA. Consequently, we were not able to compare the results of our studies with generally accepted reference criteria. A cut-off point to separate low values and high values was established by the statistical median-split method. This means that a differentiation between high and low values is relative at the moment. It is recommended that further studies measure joint laxity and joint proprioception in large groups of healthy subjects to construct a databank with reference values for future research.

Assessment of joint stability

Reproducibility reflects the amount of error, both random and systematic, inherent in the measurement of knee joint stability factors (30-32). We found high reliability for the measurement of joint laxity and joint proprioception, respectively. However, measurement error was rather high in the measurement of joint laxity and joint proprioception. This means that the measurement of joint laxity and joint proprioception could adequately distinguish between patients, but that it would be difficult to establish changes in laxity or proprioception within patients. To make these measurements useful in clinical practice, it appears necessary to standardize the measurement protocol and to increase the number of measurement occasions (33). It is known that careful standardization of a measurement protocol reduces the magnitude of the variance component(s). If measurements are taken by more than one rater, both raters should be well-trained, using identical protocols. Our results showed that, in general, inter-rater reliability was less adequate than intra-rater reliability. For this reason we recommended measuring with one, well-trained rater. Measurement error can be reduced by using repeated measurements. In terms of clinical practicality this is a drawback, because it requires more measurements of an individual knee OA patient. However, an important advantage is that it results in a more precise value for laxity or proprioception and therefore a greater possibility to detect a change in laxity and proprioception. Therefore, it is recommended that in future studies the actual measurements are optimised by measurement repetition and by measurement standardization, both for research purposes and for patient assessment.

Since the measurement of small movements in the frontal plane is possible with an optoelectronic recording and 3D motion analysis system, this measurement suggests high precision (34). However, technical precision does not warrant error free application to the human body, since skin movement errors influence the accuracy. No information is available concerning the measurement error of this measurement in knee OA patients. Even in other patient groups no studies have been found concerning the reproducibility of this measurement system. Therefore, in future research the reproducibility of the measurement of knee joint motion by an optoelectronic recording and 3D motion analysis system in patients with knee OA should be established.

Implications for clinical practice

Knee joint stability is a challenge for clinicians that should be specifically addressed in rehabilitation programs for knee OA patients. There is cause for further optimization of exercise therapy, by both improving the content of therapy and by adequate selection of patients in whom improvement could be expected. Based on the presented findings, exercises which aim to improve the stability of the knee joint, through training of the neuromuscular and proprioceptive systems, attending to neutral alignment of the knee, and muscle strengthening are necessary. Exercises should focus on the training of daily activities relevant to the patient, e.g., walking, stair climbing or other transfers (35,36). Theoretically, this form of exercise therapy in combination with joint stability exercises and muscle strength exercises should be more effective than exercise therapy primarily focused on muscle strengthening.

It has been stated that muscle strengthening exercises increase the load on cartilage of the tibiafemoral joint in knee OA patients (17).The increased load may damage the cartilage and bone and therefore should not be carried out. Lewek et al. presented a study on co-contraction of antagonist muscles of the upper and lower leg in patients with knee osteoarthritis (OA) (17). Their main findings were that patients with osteoarthritis have higher levels of co-contraction than healthy controls, and that better knee stability correlated positively with higher co-contraction in patients with OA. The authors then suggested that this process of compensating for a lack of passive stabilization through increased active stabilization needed to be counteracted, due to the risk of increased disease progression (i.e., cartilage destruction). In our opinion, such an approach could be detrimental to the functioning of knee OA patients, because in this thesis it has been hypothesized to be a primary compensating mechanism to preserve functional ability in the absence of adequate knee joint stabilization (37).

Implications for physiotherapy education

Based on traditional textbooks, knee joint stability is presented as a clinical entity, and for a long time it has been considered as such when taught to physiotherapy students (38). However, no studies support the premise that knee joint stability is a single entity and the evidence for examining knee joint stability in physiotherapy practice is lacking. Modern physiotherapy education advocates Evidence Based Practice (EBP) (39). As such, if one were to follow these principles an assessment of knee joint stability would need to take into account all factors comprising joint stability. Therefore, physiotherapy students should not view stability as a separate entity. They need to develop their diagnostic skills to be able to examine all factors of the stabilization process.

To train physiotherapy students' skills, teachers need to be able to discern the reproducibility of all factors of knee joint stability (40,41). It was shown that reliability for the measurement of joint laxity and joint proprioception was adequate, but that the standard measurement error was rather high. To reduce measurement error, students need to develop skills to examine joint laxity and joint proprioception, both in a standardized way and through repeated measurements.

The improvement of functional ability from a knee OA patients' perspective is another aspect of the training skills that physiotherapy students need to develop (42). In this thesis the outcome measures were chosen according to the core set of outcome measures, as defined by the OMERACT (43). We assessed physical function by the Dutch version of the Western Ontario and MacMasters Universities Osteoarthritis Index (WOMAC) (44). However, another patient-centred measure of physical function in the clinical situation can be recommended. Specifically, the McMaster Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR) is a functional index that measures reduced functional ability indicated by patients in a baseline interview (45). The questionnaire may be used to encourage patients' active participation in the rehabilitation process. The MACTAR quantifies the relative importance of reduced functional abilities to the patient. This questionnaire may target patients' own needs, and could consequently be useful in increasing overall participation. Students may consider the WOMAC and the MACTAR questionnaire in the assessment of knee OA patients.

Implications for future research

Based on the findings in this thesis we may conclude that a relationship between knee stability and functional ability exists. Therefore, several considerations for future research can be made.

First, the research questions addressed in this thesis, have provided insight in the relationship between joint stability and functional ability. However, this information does not provide insight in the causal mechanisms through which joint instability leads to reduced functional ability. Therefore, there is a need for research that focuses on the basic mechanisms responsible for enhancing knee joint stabilization.

Second, future studies should focus on the measurement of compensation mechanisms. The measurement of trunk movement needs to be performed to answer the question whether the load upon the knee can be reduced by contra lateral trunk movement (21). To address knee stability patients could walk on different and forced walking speeds (23-25). Furthermore, the knee joint moves in dependency with the hip and ankle joints (27). Therefore, future studies should focus on the relationships between these three joints in maintaining functional ability. Finally, in our studies we focused on movements in the frontal plane (i.e., varus-valgus direction). Compensating movements of the knee in the sagital (flexion-extension) and transversal (internal-external rotation) planes were not taken into consideration (26). It has been stated that knee OA patients walk with an increased extension in the knee joint (27), although severe OA might result in a restriction of the extension movement (27). The compensation of frontal movements by sagital and transversal movements in knee OA patients is unknown. Therefore, in future research compensating mechanisms have to be studied in knee OA patients.

Third, our findings imply that patients with inadequacies in the joint stabilization process might benefit most from interventions specifically tailored to improve joint stability. Thus, there is a need for a high quality trial examining the effectiveness of exercise therapy aimed at improving knee joint stability in knee OA patients. Considering the results of our study, not only the patients' muscle strength seems to be essential in reducing functional ability, as muscle strengthening exercises would not be effective for every patient. Experimental research would be required to assess whether exercise therapy is more

successful when the aim is not only improving muscle strength, but also to improve other factors of the stabilization process.
Finally, concerning outcome measures, future research should focus on several aspects of the clinimetric features of the measurement of knee joint stability. Especially the clinical feasibility of the measurement of joint proprioception, joint laxity and varus-valgus motion during walking has to be evaluated. In our study the reproducibility of the measurement of joint laxity and joint proprioception was established. However, for longitudinal studies the responsiveness of these measurements has to be established. Finally, the reproducibility of the optoelectronic recording and 3D motion analysis system has to be established, especially for frontal knee motion.

In summary, joint stability should be regarded as a process, involving a number of independent factors. These factors, i.e., laxity, proprioception or varus-valgus motion during walking, influence functional ability and/or the relationship between muscle strength and functional ability in knee OA patients. This may indicate that in addition to the well-established aim of enhancing muscle strength, exercise therapy should aim at enhancing knee joint stability.

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Summary

Summary

The aim of this thesis was to study the relationship between knee joint stability and functional ability in knee osteoarthritis (OA) patients. It has been stated that joint stability might be crucial for functional ability in knee OA patients. However, the evidence for this statement is rather weak, since knee joint stability studies in knee OA are limited. Knee joint stability has been defined as the ability of the joint to maintain a position or to control movements under different external loading conditions. Stability of the knee is provided by the passive restraint system (ligaments, capsule) and the active neuromuscular system (muscle strength, proprioception). More specifically, the way in which patients stabilize their knee depends on (i) the muscle strength, (ii) the laxity of ligaments and capsule of the knee, (iii) the accuracy of proprioception, and (iv) the varus-valgus motion during walking.

The overall research question of this thesis was: is knee joint stability a determinant of functional ability in patients with osteoarthritis of the knee? Three factors involved in the process of knee joint stabilization were the focus of the studies described here. Firstly, knee joint laxity was studied, with the following research questions:

Is knee joint laxity of influence on the strength of the relationship between muscle strength and functional ability? (Chapter 2)

When measuring knee joint laxity in knee OA patients, what are the intra- and inter-rater reliability and the intra- and inter-rater agreement parameters? (Chapter 3)

Is knee joint laxity related to structural joint change (joint space narrowing and osteophyte formation) and joint malalignment in knee OA patients? (Chapter 4)

Is knee varus-valgus laxity higher in women than in men in knee OA patients? (Chapter 5)

Secondly, this thesis focussed on the following questions in relation to proprioception:

Is knee joint proprioception related to functional ability and does poor proprioception aggravate the impact of muscle weakness on functional ability? (Chapter 6)

When measuring knee joint proprioception in knee OA patients and healthy subjects, what are the inter- and intra-rater reliability and the inter- and intra-rater agreement parameters? Additionally, what are the effects of variations in measurement procedure on measurement error? (Chapter 7)

Finally, varus-valgus motion of the knee joint was studied, aiming to answer the following questions:
Is varus-valgus motion of the knee a valid measure of knee joint stability? (Chapter 8)
Is high varus-valgus motion associated with reduced functional ability in knee OA patients? Furthermore, in knee OA patients with high varus-valgus motion, is muscle weakness associated with a more severe reduction in functional ability than in knee OA patients with low varus-valgus motion? (Chapter 9)

Our first aim was to examine the influence of joint laxity on the relationship between muscle strength and functional ability (**Chapter 2**). Joint laxity has been defined as the displacement or rotation of the tibia with respect to the femur in the varus-valgus direction. Previous studies have shown that the relationship between varus-valgus laxity and functional ability is weak. In this thesis it was hypothesized that in knee OA patients with high knee joint laxity the relationship between muscle strength and functional ability is stronger than in knee OA patients with low knee joint laxity. This hypothesis was based on the assumption that in knee OA patients with high laxity, muscle activity has a dual role. Muscles around the knee compensate for the absence of stability due to impairments of the passive restraint system. The other role is that muscles influence directly functional ability. Taking on this dual role the importance of muscle strength increases for adequate functioning, which is reflected in a stronger relationship between muscle strength and functional ability. In our study it was shown that the interaction between muscle strength and laxity contributed to the variance in functional ability. Therefore, it was concluded that knee OA patients with high knee joint laxity and low muscle strength are most at risk of being disabled.

In **Chapter 3** the clinimetric characteristics of the measurement of joint laxity were described. From literature, a device was constructed to measure knee joint laxity. Movement in the frontal plane was assessed in an unloaded situation, with relaxed muscles around the knee. An external load was applied at the knee in the varus-valgus direction what resulted in a movement in the frontal plane. This measurement showed adequate reproducibility, where reproducibility consisted of reliability and agreement parameters. Although reliability was adequate, measurement error was rather high. Therefore, the measurement of laxity seems to be restricted to group assessment in research rather than for the assessment of individual patients in clinical practice. To reduce measurement error in the individual patient assessment, the number of measurements needs to be increased.

In **Chapter 4** we assessed the relationship between radiological OA (ROA) features of the knee and joint varus-valgus laxity in patients with OA of the knee. Joint Space Narrowing (JSN) and osteophytes were assessed for every compartment of the knee. The study showed that OA knees with a reduction in joint space were significantly more lax than knees without reduced joint space. There was no significant relationship between osteophyte formation and joint laxity. Malaligned knees were significantly more lax than aligned knees. It was concluded, that these results support the idea that biomechanical factors play a role in the degeneration of the OA knee joint.

In **Chapter 5** the difference in varus-valgus laxity between women and men was assessed. The results showed that women with knee OA have higher varus-valgus knee laxity than men with knee OA. It was concluded that gender is a potential source of bias when analyzing varus-valgus laxity data in knee OA.

In **Chapter 6** we examined the relationship between proprioception and functional ability and the influence of joint proprioception on the relationship between muscle strength and functional ability. Knee joint proprioception encompasses the sense of joint position and the sense of joint motion. In our study we focused on the sense of joint motion. Proprioception was measured as the threshold for detection of knee joint motion, expressed as the joint motion detection threshold (JMDT). It was found that poor proprioception (high JMDT) was related to a greater reduction in functional ability. The interaction between proprioception and muscle strength was significantly related to functional ability. This means that in the absence of adequate motor control through a lack of accurate proprioceptive input, muscle weakness has a greater effect on a patient's functional ability.

In **Chapter 7** we assessed whether the measurement of knee joint proprioception is reproducible in knee OA patients and healthy subjects. We measured joint motion sense in a joint motion detection task. The reproducibility of the knee joint proprioception measurement in both populations was good. An additional aim was to assess the effect of variations in the measurement procedure on measurement error. The original measurement and two variations in measurement showed comparable measurement errors for knee OA patients and for healthy subjects. It was concluded that in knee OA patients and healthy subjects the absolute measurement error was rather high. Therefore, this measurement has limited value in the assessment of individual patients in clinical practice, but can be recommended for scientific research in groups of patients. To reduce measurement error in the individual patient assessment, the number of measurement repetitions needs to be increased.

In **Chapter 8** it was studied whether knee varus-valgus motion during gait is a measure of joint stability in knee OA patients. For this purpose, we determined the validity of varus-valgus motion as a measure of knee joint stability by assessing the relationship of varus-valgus motion to muscle strength, joint proprioception, joint laxity and skeletal alignment in knee OA patients. However, it was found that varus-valgus motion was not related to muscle strength, joint proprioception, joint laxity or skeletal alignment. We concluded that joint stability is not an entity and should be regarded as a process, involving a number of factors.

In **Chapter 9** we assessed the relationship between varus-valgus motion and functional ability in knee OA patients. Additionally, we assessed the impact of varus-valgus motion on the relationship between muscle strength and functional ability in patients with osteoarthritis of the knee. It was hypothesized that high varus-valgus motion of the OA knee during walking may cause difficulties in carrying out physical tasks in which knee function is pivotal and therefore may predict reduced functional ability. This would imply that muscle weakness leads to more severe functional disability in patients with high varus-valgus motion than in patients with low varus-valgus motion. Our results showed that in patients with high varus-valgus range of movement in the loading response phase of the gait-cycle, muscle weakness was associated with a stronger reduction in functional ability than in patients with low varus-valgus motion. A pronounced varus position in midstance of the gait-cycle and a difference between the left and right knees in varus-valgus position in midstance were also related to reduced functional ability. Therefore, it was concluded that knee OA patients with high varus-valgus motion in the loading response phase and muscle weakness are more at risk of suffering a reduction in their functional ability. Furthermore, it was concluded that knee OA patients with more pronounced varus knees in midstance during walking show a stronger reduction in functional ability than patients with less pronounced varus knees or with valgus knees.

A general discussion of the results in this thesis was presented in **Chapter 10**. In this chapter the main results of the studies were discussed concerning the relationship between joint stability and functional ability in knee OA patients.

Critical issues concerning the relationship between knee joint stability and functional ability in knee OA patients were featured. The reproducibility of the measurement of knee joint laxity and the reproducibility of the measurement of knee joint proprioception were discussed. As were discussed some implications for the usefulness of these measurements for clinical practice. Further, it was recommended to measure knee joint laxity and knee joint proprioception in large groups of healthy subjects to construct databases with reference values for future research. Implications for clinical practice were discussed in the direction of optimization of exercise therapy, in particular in the improvement of knee joint stability. Implications for physiotherapy education, particularly the training of physiotherapy students from concepts of Evidence Based Practice were considered. Finally, some implications for future research were given. The main recommendation was to establish the effect of knee joint stability training as part of an exercise program in an experimental longitudinal study.

The overall conclusion in this thesis was that joint stability is related to functional ability in knee OA patients. It was also concluded that joint stability should be regarded as a process, involving a number of factors. These factors, i.e., laxity, proprioception and varus-valgus motion during walking, influence functional ability and/or the relationship between muscle strength and functional ability in knee OA patients. This may indicate that in addition to the well-established aim of enhancing muscle strength, exercise therapy could aim at enhancing knee joint stability: improved motor control might compensate for knee joint laxity, poor proprioception or varus-valgus motion during walking, which results in enhanced functional ability in knee OA patients.

Samenvatting

Samenvatting

Het doel van de in dit proefschrift beschreven studies was de relatie tussen de stabiliteit van het kniegewricht en het functioneren van patiënten met knieartrose te onderzoeken. De aanleiding was dat er gesteld is dat gewrichtsstabiliteit cruciaal kan zijn voor het functioneren van patiënten met knieartrose. Echter, het bewijs voor deze stelling is zwak, daar het aantal studies over gewrichtsstabiliteit gering is. Stabiliteit van het kniegewricht wordt gedefinieerd als het vermogen om een positie van de knie te handhaven of om bewegingen, beïnvloed door externe belastingen, te kunnen controleren. Stabiliteit van de knie wordt verzorgd door het passieve steunapparaat (ligamenten, kapsel) en het actieve neuromusculaire systeem (spierkracht, proprioceptie). Meer specifiek gesteld, de manier waarop patiënten hun knie stabiliseren hangt af van (i) de spierkracht, (ii) de laxiteit van de ligamenten en het kapsel, (iii) de nauwkeurigheid van de proprioceptie en (iv) de varus-valgus beweging van de knie tijdens het lopen.
De overkoepelende onderzoeksvraag van dit proefschrift luidt: Is de stabiliteit van het kniegewricht een determinant van het functioneren van patiënten met knieartrose? De focus in dit proefschrift ligt op drie factoren die betrokken zijn bij het proces van kniestabilisatie.

Ten eerste wordt de laxiteit van het kapselband apparaat van de knie bestudeerd aan de hand van de volgende onderzoeksvragen:
Is de laxiteit van het kniegewricht van invloed op de sterkte van de relatie tussen spierkracht en functioneren? (Hoofdstuk 2)
Wat zijn de intra- en interbeoordelaars betrouwbaarheidscoëfficiënten en de intra- en intermeetfouten bij het meten van knielaxiteit van patiënten met knieartrose? (Hoofdstuk 3)
Is er een verband tussen de laxiteit van het kniegewricht en structurele gewrichts- veranderingen (gewrichtsspleet vernauwing en osteofyteformatie) en scheefstand van het kniegewricht van patiënten met knieartrose? (Hoofdstuk 4)
Is de varus-valgus laxiteit bij vrouwelijke patiënten groter dan bij mannelijke patiënten met knieartrose? (Hoofdstuk 5)

Als tweede ligt de focus in dit proefschrift op de volgende vragen in relatie tot proprioceptie:
Is de proprioceptie van het kniegewricht gerelateerd aan functioneren en wordt de invloed van spierzwakte op het functioneren versterkt door niet-accurate proprioceptie? (Hoofdstuk 6)
Wat zijn de inter- en intrabeoordelaars betrouwbaarheidcoëfficiënten en inter- en intrameetfouten bij het meten van proprioceptie van het kniegewricht bij patiënten met knieartrose en bij gezonde proefpersonen. Additioneel, wat is het effect op meetfouten van variatie in de meetprocedure. (Hoofdstuk 7)
Tenslotte wordt de varus-valgus beweging tijdens het lopen bestudeerd om een antwoord te geven op de volgende vragen:
Is de varus-valgus beweging van de knie tijdens het lopen een valide meting van de stabiliteit van de knie? (Hoofdstuk 8)
Is een grote varus-valgus beweging van de knie tijdens het lopen gerelateerd aan verminderd functioneren van patiënten met knieartrose? En, is spierzwakte bij patiënten met een grote varus-valgus beweging geassocieerd met een grotere afname in functioneren dan bij patiënten met een geringe varus-valgus beweging? (Hoofdstuk 9)

Onze eerste studie was er op gericht te onderzoeken in hoeverre de laxiteit van het kniegewricht van invloed is op de relatie tussen spierkracht en functioneren (**Hoofdstuk 2**). De gewrichtslaxiteit wordt gedefinieerd als de verplaatsing of rotatie van de tibia ten opzichte van het femur in de varus-valgus richting. Uit eerdere studies blijkt dat de relatie tussen varus-valgus laxiteit en functioneren zwak is. In dit proefschrift wordt de veronderstelling getoetst dat bij patiënten met knieartrose en een grote gewrichtslaxiteit, de relatie tussen spierkracht en functioneren sterker is dan bij patiënten met een geringe laxiteit. Deze veronderstelling is gebaseerd op de gedachte dat spieractiviteit een dubbele rol heeft bij patiënten met een hoge laxiteit. De spieren rond het kniegewricht compenseren de afgenomen stabiliteit ten gevolge van een stoornis van het passieve systeem. Tevens beïnvloeden spieren direct het functioneren. Gezien deze dubbele rol van spierkracht neemt het belang toe voor adequaat functioneren.

In onze studie werd bevestigd dat de interactie tussen spierkracht en laxiteit bijdraagt aan de variantie in functioneren. Daarom werd geconcludeerd dat patiënten met knieartrose, bij wie het kniegewricht een grote laxiteit vertoont en bij wie de spierkracht laag is, meer risico lopen op beperkingen in functioneren.

In **Hoofdstuk 3** worden de klinimetrische eigenschappen beschreven van het meten van de laxiteit van het kniegewricht. Afgaande op gegevens in de literatuur werd een apparaat geconstrueerd om de laxiteit van het kniegewricht te meten. De beweging in het frontale vlak werd gemeten in een niet-belaste situatie met ontspannen spieren rond het gewricht. Een uitwendige belasting werd toegepast in de varus-valgus richting, hetgeen resulteerde in een beweging in het frontale vlak. Deze meting vertoonde een adequate reproduceerbaarheid. De reproduceerbaarheid bestond uit betrouwbaarheidscoëfficiënten en meetfouten. Hoewel de betrouwbaarheid adequaat was, bleek de meetfout tamelijk groot te zijn. Daarom lijkt de meting van de laxiteit van het kniegewricht wel geschikt te zijn voor het meten van groepen patiënten voor wetenschappelijke doeleinden, maar minder geschikt voor het meten van patiënten in de kliniek. Om de meetfout bij het meten van individuele patiënten te reduceren is het nodig het aantal metingen te herhalen.

In **Hoofdstuk 4** hebben we de relatie tussen röntgenologische afwijkingen bij knieartrose en de varus-valgus laxiteit van de knie van patiënten met artrose onderzocht. Gewrichtsspleetsvernauwing en osteofyten werden bepaald van ieder compartiment van de knie. De studie toonde dat artrotische knieën met in volume afgenomen gewrichtsspleten, significant een hogere laxiteit hadden dan knieën zonder gewrichtsspleetsvernauwing. Er was geen significante relatie tussen osteofytevorming en gewrichtslaxiteit. Knieën met een scheefstand vertoonden significant meer laxiteit dan rechte knieën. Geconcludeerd werd dat deze resultaten het idee ondersteunen dat biomechanische factoren een rol spelen in het degeneratieve proces dat optreedt bij knieën met artrose.

In **Hoofdstuk 5** wordt het onderzoek beschreven naar het verschil tussen mannen en vrouwen in varus-valgus laxiteit. De resultaten gaven aan dat het kniegewricht van vrouwen met knieartrose een grotere varus-valgus laxiteit vertoont dan bij mannen met knieartrose. Er werd geconcludeerd dat het geslacht van patiënten een potentiële bron van vertekening is bij het bestuderen van knieartrose.

Hoofdstuk 6 betreft onderzoek naar de relatie tussen proprioceptie en functioneren. Tevens werd de invloed van gewrichtsproprioceptie op de relatie tussen spierkracht en functioneren onderzocht. Proprioceptie van het kniegewricht omvat het gevoel van gewrichtspositie en het gevoel van gewrichtsbeweging. Onze studie was gericht op proprioceptie als gewrichtsbeweging. Proprioceptie werd gemeten als de drempel om gewrichtsbewegingen waar te nemen, uitgedrukt als de gewrichts-bewegings-waarnemings-drempel (DGBW). Er werd gevonden dat niet accurate proprioceptie (een hoge DGBW) gerelateerd was aan een grotere afname in functioneren. Dit betekent dat door de afwezigheid van een adequate motorische controle, als gevolg van een gebrek aan accurate proprioceptieve input, spierzwakte een groter effect heeft op het functioneren van de patiënt met knieartrose.

In **Hoofdstuk 7** is onderzocht of het meten van proprioceptie van het kniegewricht reproduceerbaar is bij patiënten met knieartrose en gezonde proefpersonen. Via mechanische weg werd de knie langzaam bewogen in de extensie richting. Patiënten en proefpersonen kregen de opdracht op een knop te drukken, zodra zij de beweging in de knie voelden. De reproduceerbaarheid van de meting was in beide populaties goed. Een toegevoegd doel was het bepalen van het effect van variaties in de meetprocedure op meetfouten. De originele meting en twee variaties in de meetprocedure vertoonden vergelijkbare meetfouten voor patiënten met knieartrose en voor gezonde proefpersonen. Er werd geconcludeerd dat de absolute meetfout tamelijk groot was bij patiënten met knieartrose en bij gezonde proefpersonen. Daarom heeft deze meting een beperkte waarde in het onderzoek van individuele patiënten in de klinische praktijk, maar kan worden aanbevolen als onderzoeksmethode voor wetenschappelijke doeleinden in groepen van patiënten. Om meetfouten te reduceren in individuele patiënten is het nodig het aantal metingen te herhalen.

Hoofdstuk 8 beschrijft een onderzoek naar de vraag of de varus-valgus beweging van de knie gedurende het lopen een maat is voor gewrichtsstabiliteit bij patiënten met knieartrose. Om de validiteit van de varus-valgus beweging als maat voor stabiliteit van het kniegewricht te bepalen hebben we de relatie onderzocht tussen enerzijds de varus-valgus beweging en anderzijds spierkracht, gewrichtsproprioceptie, gewrichtlaxiteit en de kniehoek bij patiënten met knieartrose. Er werd echter geen relatie gevonden tussen de varus-valgus beweging enerzijds en spierkracht, gewrichtsproprioceptie, gewrichtlaxiteit of de knie hoek anderzijds. We concludeerden dat gewrichtstabiliteit niet een entiteit is. Het stabiliseren van de knie moet beschouwd worden als een proces dat door een aantal factoren beïnvloed wordt.

In **Hoofdstuk 9** onderzochten we de relatie tussen de varus-valgus beweging en het functioneren van patiënten met knieartrose. We bepaalden tevens de invloed van de varus-valgus beweging op de relatie tussen spierkracht en functioneren van patiënten met knieartrose. Er werd verondersteld dat een grote varus-valgus beweging van de artrotische knie gedurende het lopen problemen kan veroorzaken bij het uitvoeren van fysieke taken, waarbij de kniefunctie van groot belang is. Dit kan betekenen dat spierzwakte bij patiënten met een grote varus-valgus beweging tot een grotere afname in het functioneren leidt, dan spierzwakte bij patiënten met een kleine varus-valgus beweging. Onze resultaten toonden aan dat bij patiënten met een grote varus-valgus beweging, spierzwakte meer geassocieerd was met een afname in het functioneren, dan bij patiënten met een kleine varus-valgus beweging. Een uitgesproken varus positie in de middenfase van de loopcyclus en een verschil tussen de linker- en rechterknieën in de varus-valgus positie in de middenfase waren ook gerelateerd aan een afname in het functioneren. Daarom werd er geconcludeerd dat patiënten met knieartrose, die een grote varus-valgus beweging in de eerste belastingfase van de loopcyclus hebben en die eveneens spierzwakte vertonen, een groter risico hebben op een afname in functioneren. Verder werd er geconcludeerd dat patiënten met knieartrose die gedurende het lopen uitgesproken varus knieën hebben in de middenstandsfase een sterkere afname vertonen in het functioneren dan patiënten met minder uitgesproken varus knieën of met valgus knieën.

In **Hoofdstuk 10** worden de belangrijkste resultaten besproken van de onderzoeken betreffende de relatie tussen gewrichtsstabiliteit en functioneren van patiënten met knieartrose. De bevindingen van de studies worden met elkaar in verband gebracht en er worden suggesties gedaan voor toepassing in de klinische praktijk, het fysiotherapie onderwijs en voor het toekomstig onderzoek.
De betekenis van de bevindingen voor de relatie tussen stabiliteit van het kniegewricht en functioneren van patiënten met knieartrose wordt toegelicht. De reproduceerbaarheid van het meten van de laxiteit van het kniegewricht en de reproduceerbaarheid van het meten van de proprioceptie van het kniegewricht worden besproken. Eveneens worden enige implicaties voor het gebruik van de metingen voor de klinische praktijk besproken. Verder wordt aanbevolen om de laxiteit van het kniegewricht en de proprioceptie van het kniegewricht in grote groepen van gezonde proefpersonen te meten, met het doel databanken op te zetten zodat referentiewaarden kunnen worden opgeslagen voor toekomstig onderzoek. Implicaties voor de klinische praktijk worden besproken. Het betreft het optimaliseren van oefentherapie, met als hoofddoel het verbeteren van de stabiliteit van het kniegewricht. Implicaties voor het fysiotherapie onderwijs worden besproken en met name de training van fysiotherapie studenten vanuit het concept van Evidence Based Practice. Tenslotte worden enige aanbevelingen gedaan voor toekomstig onderzoek. De belangrijkste aanbeveling is te onderzoeken wat het effect is van het trainen van de stabiliteit van het kniegewricht als onderdeel van een oefenprogramma in een longitudinale experimentele studie.

De belangrijkste conclusie in dit proefschrift is dat de stabiliteit van het kniegewricht gerelateerd is aan het functioneren van patiënten met knieartrose. Er wordt eveneens geconcludeerd dat het bereiken van stabiliteit van het gewricht beschouwd moet worden als een proces, dat door een aantal factoren beïnvloed wordt. Deze factoren (dwz. laxiteit, proprioceptie en varus-valgus beweging tijdens het lopen), beïnvloeden het functioneren en/of de relatie tussen spierkracht en functioneren van patiënten met knieartrose. Dit kan betekenen dat, naast het goed onderbouwde doel van spierkrachttoename, oefentherapie als toegevoegd doel de verbetering van de stabiliteit van het kniegewricht kan hebben. Immers, verbeterde motorische controle kan de laxiteit van het kniegewricht, niet accurate proprioceptie of de varus-valgus beweging gedurende het lopen compenseren. Dit resulteert in een verbetering van het functioneren van patiënten met knieartrose.

Dankwoord

Dankwoord

In dit proefschrift staan de begrippen stabiliteit en functioneren centraal. Of te wel, als er geen stabiliteit bestaat neemt het functioneren af. Met dit dankwoord probeer ik de mensen die ervoor hebben gezorg dat ik wetenschappelijk "stabiel" geworden ben, in het voetlicht te plaatsen. Zonder de medewerking, ondersteuning, het vertrouwen en de betrokkenheid van velen zou die nodige "stabiliteit" niet bereikt zijn waardoor het functioneel onmogelijk was geworden om dit proefschrift tot stand te brengen. Het zijn bijzonder veel mensen die me "overeind" hebben geholpen, teveel om ze allemaal te bedanken. Een aantal van hen wil ik in het bijzonder noemen.

Allereerst de patiënten en studenten die aan verschillende onderzoeken hebben deelgenomen. Zonder hen zou ik dit proefschrift niet gemaakt kunnen hebben.

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De leden van de leescommissie, bestaande uit prof.dr. Ben Dijkmans, prof.dr. Guus Lankhorst, prof.dr. Jaap van Dieën, prof.dr. ir. Riekie de Vet, prof.dr. Sita Bierma en dr. Leo Roorda, bedank ik voor het lezen en beoordelen van dit manuscript.

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List of publications

List of publications

1. Esch van der M, Heymans M and Dekker J. Factors contributing to possession and use of walking aids among persons with Rheumatoid Arthritis and Osteoarthritis. Arthritis Rheum 2003; 49:838-42.

2. M. van der Esch, G.G.M. Scholten-Peeters, M. Steultjens. Manuele Therapie in engere zin en Manuele Therapie in ruimere zin; een nuttig onderscheid? Jaarboek Fysiotherapie 2004.

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Curriculum Vitae

Curriculum vitae

Martin van der Esch was born on the 18th of July 1956 in Amsterdam, The Netherlands. After completing secondary school in 1974 he started studying Physiotherapy at the "Stichting Akademie voor Fysiotherapie Amsterdam (S.A.F.A.)". Following graduation in 1978, he began working as a physiotherapist in the Jan van Breemen Institute, a regional center for rheumatology and rehabilitation in Amsterdam. Additionally, in 1979, he commenced teaching clinical physiotherapy skills at the S.A.F.A., which became part of the "Hogeschool van Amsterdam" in 1999. Martin still works at both institutes today.

In 1982 he successfully completed a manual therapy specialisation at the "Stichting Opleiding Manuele Therapie (SOMT)" in Amersfoort, where he went on to teach manual therapy from 1984 until 1999.

In 2001 he successfully completed the Postgraduate Epidemiology Program at the 'EMGO institute' directed by prof.dr. L.M. Bouter of the VU University Medical Center (VUmc) in Amsterdam, and during its Summer Program of 2001 he followed a course in Regression Analysis at the University of Ohio in Columbus, USA.

In 2003 he became a member of the scientific paramedical board (Lectoraat Paramedische Zorg) at the Hogeschool van Amsterdam, directed by M. van Tulder and from 2005 by R.W.J.G. Ostelo.

In the Jan van Breemen Institute Martin has conducted several studies on osteoarthritis of the knee under supervision of prof.dr. J. Dekker, in collaboration with the Department of Rehabilitation at the VUmc in Amsterdam.