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Determinants of outcome prior to and after total hip and knee arthroplasty

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Chapter I

General introduction

Epidemiology of hip and knee osteoarthritis

Osteoarthritis (OA) is a whole joint disease that is characterized by local loss of cartilage, remodeling of adjacent bone and associated inflammation (1, 2). Currently, OA is among most common causes of disability in older adults worldwide (3, 4) and affects approximately 10-15% of all adults aged over 60 (5). Due to the aging population and the increasing number of people being overweight or obese, the numbers of persons suffering from OA are expected to rise (6, 7). Estimations for the year 2050 conclude that by then the amount of persons suffering from OA has increased to 130 million persons globally (8). Of those, the majority will suffer from OA in the knee, hand or hip (9). In the Netherlands, the expected numbers of people suffering from hip or knee OA by the year of 2040 are 560.000 and 800.000 persons, respectively (10).

Pathogenesis and risk factors of hip and knee OA

The aetiology and pathogenesis of OA are poorly understood. The occurrence of OA is considered to be multifactorial, with a number of risk factors. For both hip and knee OA, risk factors for their occurrence are ageing (11, 12), female sex (13), congenital or developmental deformities (such as hip dysplasia and knee malalignment) (6, 11, 12, 14, 15), previous joint injury (16), (repetitive) joint loading activities (mostly in the context of high-impact sports or employment) (2) and a genetic predisposition (17-20). Besides, additional risk factors for knee OA are obesity and increased joint laxity or instability (2, 21). The variation in risk factors suggests that OA is not a single joint disease, but a final common phenotype of different disorders (21).

Diagnosis of hip or knee OA

There are various sets of diagnostic criteria for the clinical diagnosis of either hip or knee OA (22-24). A confident diagnosis of OA is based on three symptoms and three signs by physical examination. Symptoms include joint pain (typically intermittent, worst during and after weight-bearing activities), brief stiffness (in the morning, after inactivity or particularly in the evening, generally resolving in minutes) and functional limitations (including limitations in daily activities such as stair climbing) (22-24). The three signs by physical examination are crepitus (a sensation of

crunching or cracking), restricted active and passive movement and bony enlargement (from joint effusion and/or bony swelling). In addition, to abovementioned signs by physical examination, some guidelines include bone margin tenderness and the lack of palpable warmth of the joint (2, 22-24). Radiographic imaging or blood tests are not needed to confirm the diagnosis of OA (22, 23), but could help confirm the diagnosis of OA and/or make alternative or additional diagnosis when the presentation is atypical (25).

In the diagnostic process a holistic approach is recommended (2). As such, the initial assessment should include the effect of osteoarthritis on different domains of a person's life (i.e. function, quality of life, occupation, mood, relationships and leisure activities) as well as patients' preferences and beliefs towards certain treatment options (2). In addition, patient knowledge of disease and treatment options should be ascertained as well as previous medical experiences and expectations towards treatment modalities (2). All of this information should be used to develop an appropriately tailored management plan informed by patient expectations, preferences and goals, and existing evidence.

Imaging in hip and knee OA

OA is characterized by several structural changes of the joint. Loss of cartilage (i.e. joint space narrowing), osteophyte formation, subchondral sclerosis and bony deformity are important features recognizable on radiographic images and defining radiographic signs of OA (26). Radiographic imaging may be used to determine disease severity and progression (22, 23, 27). However, discordance is observed between disease severity as measured by radiographic imaging and the severity of OA symptoms. At the age of 70, the large majority of people has structural evidence of OA on radiographic images in at least one joint (11, 28). However, not all of them report symptoms of OA (28-30). According to a systematic review, 15-81% of the persons with radiographic knee OA reported OA-related knee pain (29). Conversely, of the persons with symptomatic OA, 15-76% had signs of radiographic knee OA (28, 29). This implicates that the experienced pain cannot solely be explained by structural damage of the joint. For this reason, it is not recommended to

make the clinical diagnosis of hip or knee OA on radiographic imaging (31). As measured by magnetic resonance imaging (MRI), similar moderate associations were found between OA-related symptoms and structural evidence of OA (32).

Management of hip and knee osteoarthritis

Currently, there is no cure for OA. Therefore, treatment modalities are primarily aimed at reducing OA symptoms. Treatment of OA can be divided into conservative (which consists of non-pharmacological and pharmacological management) and surgical management. Conservative, non-pharmacological management includes education and self-management, weight loss, exercises to increase muscle strength and range of motion and the use of functional aids and mechanical assist devices (such as a walking aid or orthotics) (33, 34). Pharmacological management includes analgesics and anti-inflammatory agents such as paracetamol, Non-Steroidal Anti-Inflammatory Drugs (NSAID's) and tramadol or tramadol plus paracetamol (33, 34). Opiates are mainly discouraged due to the small gains weighted against the side-effects and risk of addiction and overdose (2). In addition, intra-articular corticosteroids are recommended and some guidelines consider duloxetine, a serotonin and norepinephrine reuptake inhibitor with antidepressant for pain reduction and improvement of function (2). International guidelines and expert-based opinions unanimously recommend a stepped care approach, combining conservative treatment modalities in the management of early OA (33). The evidence underpinning comprehensive management strategies is however scarce with few appropriately designed randomized controlled trials (RCTs) or well-designed studies including expert-based strategies (2, 33). Ultimately, when conservative treatments fail to provide adequate pain relief or functional improvement, surgical treatment could be considered (33). The most common surgical treatment option is total hip or knee arthroplasty (THA or TKA). Other surgical treatment options consist of arthroscopic debridement, subchondral bone stimulation, osteotomy (in case of malalignment), knee joint distraction (in case of knee OA) and unicompartmental joint arthroplasty (33). In addition, new treatment modalities for cartilage repair are developed such as nerve growth factor antibodies, injectable hydrogel and disease modifying

OA drugs (DMOADs), which are in development phase and not current practice yet (33, 35, 36).

Total Hip and Knee Arthroplasty: indications and outcomes

For hip and knee OA, over 30.000 THA and 25.000 TKA are performed in the Netherlands every year (37). In parallel with the rising prevalence of OA, the number of performed arthroplasties has increased over the past years and is expected to further expand (37). Still the indication criteria for THA and TKA are based on limited evidence and the diversity of disease severity at time of surgery is large (38-40). Recently, attempts have been made to define indication criteria to improve the timing of THA and TKA, but this research was not conclusive and more empirical research is needed (41). Selecting the right patient at the right time is of utmost importance to achieve optimal outcomes and to reduce health care cost. Until a few years ago, outcome of interventions were determined by the treating medical specialist, using surgeon-assessed outcomes and survival analyses of implants. According to these standards THA and TKA are considered very effective interventions (42-45). However, when judged by the patients, less optimistic results are seen (46-52). With the implementation of the concept of value-based-driven health care, where patient reported outcomes play a central part, the perspective of the patient has become more and more important in clinical practice.

Outcomes of THA and TKA: Patient perspective and the ICF model

To measure the perspective of patients in the clinical setting, several sets of patient-reported outcomes measures (PROMS) have been proposed for TKA and THA. A set that gained much attention is the set published by the Internal Consortium for Health Outcomes Measurements (ICHOM) on patient reported outcomes that should be included in joint registries (53). The set covers approximately all domains of the International Classification of Functioning, Disability and Health (ICF) model (54). The ICF model is recognized as an important framework and classification which contributes to a holistic approach and covers the typical spectrum of functional problems of patients with a specific health condition and environmental and personal factors that may have an impact on patient's health. Hence, the Outcome Measures in Rheumatology Clinical Trials

group (OMERACT) and the World Health Organization (WHO) recommend using various domains that are incorporated in the ICF model (54, 55). The ICF model assesses the functioning of the whole human being (physically, mentally and socially) on individual as well as society level including the interaction with contextual factors (i.e. environmental and personal factors) (figure 2). Body functions are physical functions of body systems (including psychological functions) at the level of the body or body parts. Body structures are anatomical parts of the body such as organs, limbs and their components. This domain contains all complaints and functional impairments directly derived from the body or body structure that is affected by the health condition (54). The activity domain comprises the physical activities people perform and the difficulties an individual may have in executing activities. Participation concerns involvement of people in all areas of life (functioning of a person as a member of society). An important component is occupational participation. Lastly, contextual factors include personal factors that influence how disability is experienced by the individual such as gender, age, lifestyle and the presence of comorbidities and environmental factors which comprise the physical, social and attitudinal environment in which people live and conduct their lives. This encompasses having a social network and the possibility of making social and occupational adaptations (54).

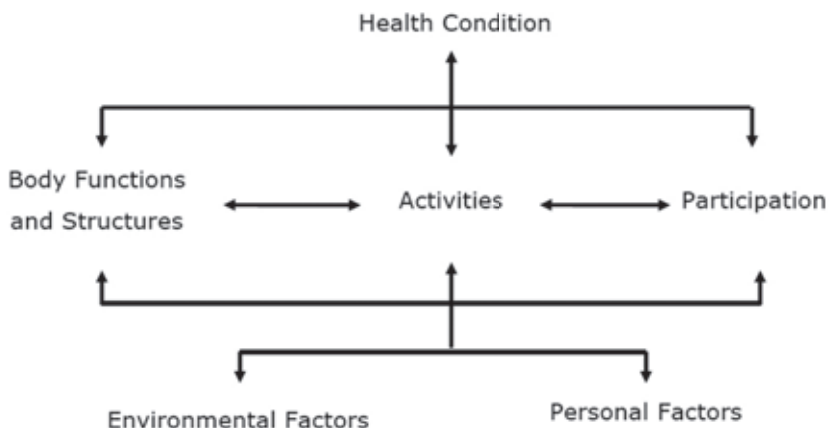


Figure 1. Bio-psycho-social model of the International Classification of Functioning, Disability and Health (ICF)

For OA, a specific ICF core set has been developed (56), which was modified for hip and knee OA by the Royal Dutch Society of Physical Therapy (57). With these core sets, the most important symptoms, health-associated problems and health-related domains of patients with hip and knee OA can be described. The current thesis focuses on a subset of factors within these domains namely pain, functional limitations and knee instability within the body functions and structures domain, and objectively measured physical activity within the activities domain and work participation within the participation domain. Thus, the focus of this thesis contributes to the holistic approach of patients with hip or knee OA undergoing total joint arthroplasty.

Body functions and structures

Pain and functional limitations

Pain and functional limitations are the most prominent and disabling symptoms of OA and among the main reasons for patients to undergo THA or TKA surgery (58). Yet, approximately 15-20% of the operated patients continues to experience persisting pain or functional limitations after surgery (46-52) resulting in 5300 THA and 4600 TKA patients with persisting pain, in the Netherlands alone (37). Persistent pain and associated disability have a substantial impact on quality of life as well as mortality, substantiating the urge to identify the patients with a risk of persistent postoperative pain, prior to surgery. Several studies focused on the preoperative prediction of postoperative pain and functional limitations after TKA and THA (59-62). These studies often included preoperative pain and radiographic OA severity as potential determinants, as they are important factors for orthopaedic surgeons to decide to perform surgery on (52, 63-65). Even though, no previous study investigated if radiographic OA severity modifies the effect of preoperative pain on postoperative outcome. Despite the previous attempts, it is currently still not possible to make reliable preoperative predictions on which patient is prone to have an unfavourable outcome. Therefore, the focus of research should probably shift towards the identification of patients with insufficient recovery shortly after surgery instead of prior to surgery, since these patients might still be influenced for the better. With early recognition of an unfavourable course, different

treatment strategies can be applied in order to prevent development of chronic pain.

Knee instability

Knee instability is considered an important, yet relatively underexposed factor in patients with knee OA (66). Knee instability is the sensation of buckling, shifting or giving way of the knee and is reported by 60-80% of the patients suffering from knee OA (66-68). However, the origin of the sense of instability in patients with knee OA has not yet been elucidated. Two causal hypotheses regarding knee stability are based on the presence of structural damage to the joint: (i) osteophyte formation, fibrosis of joint ligaments and capsular thickening increase the tightness of the joint and restriction of movement, resulting in a stiff and stable knee or (ii) more pronounced joint space narrowing leads to reduced stress on the ligaments and capsule of the knee, resulting in a less stable knee joint (69-71). Besides, the sense of knee instability was found to be associated with pain and activity limitations in patients with knee OA (72). A previous randomized controlled trial including selected patients demonstrated that, six months after TKA, 32% of the patients retained self-reported knee instability (72). Retained self-reported knee instability was associated with pain and activity limitations (72). In the long run and in clinical care, it is unknown whether retained knee instability associates with persistent pain and activity limitations after TKA.

Activities

The impact of OA on patients' functioning is usually measured in terms of limitations in specific daily activities or performance-based methods such as the 6-minute walk test (73). Less is known on how OA affects the amount of actual everyday physical activity. Physical activity is important to maintain health and was suggested to have (at least short term) beneficial effects on pain and function in patients with hip and knee OA (74, 75). Physical exercise is therefore included in treatment recommendations for hip or knee OA (76-79). However, from a patient's perspective, pain could be perceived as activity-related, leading to avoidance of physical activities (80). Indeed, several previous studies showed that perceived hip or knee related pain was associated with perceived physical activity (74, 81).

Whether this association also accounts for objectively measured physical activity, like accelerometers, in patients with an indication for THA or TKA (end-stage hip or knee OA) remains unknown. In addition, little is known on the association between patients' perception of quality of life (QoL) and the actual amount of objectively measured physical activity in this population.

Participation

Return to work

At time of THA or TKA, 15-45% of the patients is of working age (<65 years old) (82). These patients are dependent of their job to generate income, and thus consider return to work as one of the most important outcomes of surgery (83). The rates of patients who do not return to work postoperatively are substantial, and varying in the literature from 5-32%, (84). Overall, knowledge on determinants of partial or no return to work after total joint arthroplasties and potential differences between THA and TKA is scanty, especially information on prognostic factors after TKA (84, 85).

Outline of this thesis

In THA and TKA patients, knowledge of certain components of the ICF domains, specifically knee instability, physical activity and return to work and their association with pain and function prior to and after THA and TKA is limited. Therefore, the aims of this thesis are:

1. To investigate associations between radiographic OA severity, knee instability, pain and function prior to and after THA and/or TKA
3. To evaluate factors influencing physical activities in patients with end-stage hip or knee OA.
4. To identify determinants of return to work after THA or TKA.

In Chapters 2-5 the level of the body functions and structures domain of the ICF is addressed, with the main focus on pain and function. First, to gain more insight in the effect of radiographic evidence of OA and preoperative pain on postoperative pain and function, we investigated if radiographic OA severity modifies the effect of preoperative pain on postoperative pain and function (chapter 2). Second, to better predict postoperative outcome, it was investigated if preoperative pain and

function and their initial clinical improvement predicted one-year pain and function (Chapter 3). Furthermore, Chapters 4 and 5 are focused on knee instability, by determining the prevalence of self-reported knee instability before and/or one year after TKA and its associations with radiographic features of OA, pain, function and QoL. Chapter 6, the focus is on activities domain, with an exploration of the cross-sectional association between preoperative pain, function and QoL with objectively measured physical activity. Lastly, regarding participation, particularly return to work, is addressed in Chapters 7 and 8, by identifying determinants of return to work, including physical activity and patients' beliefs and expectations.

LOAS

Most of the research described in this thesis was performed using data from the Longitudinal Leiden Orthopedics Outcomes of Osteo-Arthritis study (LOAS), a multi-center, longitudinal prospective cohort study (Chapters 2-6, 8) (86). The LOAS study started in 2012 as, at that time, despite the availability of hip and knee registries and a considerable number of studies on the outcomes in terms of prosthesis survival, joint function and quality of life, knowledge on the impact of THA and TKA on societal participation (physical activity, sports, paid and unpaid work) and on health care usage, including rehabilitation was scarce. Moreover, at that time, available studies did not comprehensively include the role of personal factors on outcome. Therefore, the LOAS study was designed with the following aims: (1) to describe the midterm and long-term outcomes of THA and TKA in terms of health status as a whole, including the levels of body functions and structures, daily activities, participation in society and health care usage and (2) to determine which factors predict the outcomes of THA and TKA. Currently, the LOAS is still ongoing, with 7263 patients included by June 2019. Patients complete questionnaires preoperatively and 6, 12 and 24 months after surgery and every 2 years thereafter. Participating hospitals are the Leiden University Medical Centre, Leiden; Alrijne Hospital (former Diaconessenhuis and Rijnland Hospital), Leiden and Leiderdorp; Groene Hart Hospital, Gouda; Reinier de Graaf Hospital, Delft (participation from the start of the study up and until August 2013); LangeLand Hospital, Zoetermeer; Waterlandziekenhuis, Purmerend (participation from January 2015 up till December 2017). This thesis used data of patients recruited before June 2015.

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