

Muscle-tendon pain and outcome of hippreserving surgery in patients with hip dysplasia

Prospective investigations applying clinical examinations, ultrasonography, patient-reported outcome and measurement of physical activity

One-year follow-up study

PhD dissertation

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Health Aarhus University 2020

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Preface

The first draft of the work presented in this PhD dissertation started during my employment at the Department of Physiotherapy and Occupational Therapy at Aarhus University Hospital, Denmark. During this employment, I worked with physical rehabilitation of patients with hip dysplasia. Together with my excellent supervisors and invaluable colleagues, I identified a gap in knowledge related to the development of pain and use of outcome measures in hip dysplasia. My supervisors encouraged me to start working on this topic and with further invaluable support from the head of the Department of Physiotherapy at VIA University College, Denmark, I was enrolled as a PhD fellow at the Department of Clinical Medicine at Aarhus University, Denmark, in 2017.

I owe gratitude to a number of people who made this work possible. I owe Inger Mechlenburg a deep thanks for her ability to give inspiring professional and personal support and for continuously encouraging me to go further. Inger, you are truly a mentor. I have deep respect for you; and with you, the journey has been truly enriching. I also owe Kristian Thorborg a profound thanks for his ability always to ask spot-on questions, encouraging me to think deeper and explain my research more explicitly. Kristian, I admire your passion, energy and great knowledge. I also owe Kjeld Søballe a sincere thanks. Kjeld, we have been working together since 2008, and you have continuously supported and encouraged me to go one step further. I owe you deep gratitude for always believing in me. Inger, Kristian and Kjeld, I am grateful for your guidance throughout this journey.

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Julie Sandell Jacobsen, January 2020

List of papers

This PhD dissertation is based on the papers listed below.

- Jacobsen JS, Hölmich P, Thorborg K, Bolvig L, Jakobsen SS, Søballe K, Mechlenburg I. Muscle-tendon-related pain in 100 patients with hip dysplasia: prevalence and associations with self-reported hip disability and muscle strength. Journal of Hip Preserving Surgery 2018; 5(1): 39–46.
- Jacobsen JS, Bolvig L, Hölmich P, Thorborg K, Jakobsen SS, Søballe K, Mechlenburg I. Muscle-tendon-related abnormalities detected by ultrasonography are common in symptomatic hip dysplasia. Archives of Orthopaedic Trauma Surgery 2018; 138(8): 1059-1067.
- Jacobsen JS, Søballe K, Thorborg K, Bolvig L, Jakobsen SS, Hölmich P, Mechlenburg I. Patient-reported outcome and muscle-tendon pain after periacetabular osteotomy are related: 1-year follow-up study in 82 patients with hip dysplasia. Acta Orthopaedica 2019; 90(1): 40-5.
- Jacobsen JS, Thorborg K, Hölmich P, Bolvig L, Jakobsen SS, Søballe K,
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Abbreviations

	Physical function in daily living
ALanala	Tingsical function in daty invitig
Al angle	Tonnis acetabular index angle
CE angle	Centre-edge angle
CI	Confidence interval
COSMIN	COnsensus-based Standards for the selection of health
	Measurement INstrument
FABER	Flexion/Abduction/External Rotation test
FADIR	Flexion/Adduction/Internal Rotation
HAFAI	Horsens-Aarhus Femoro-Acetabular Impingement study
HAGOS	Copenhagen Hip and Groin Outcome Score
FAIS	Femoroacetabular impingement syndrome
HOOS	Hip disability and Osteoarthritis Outcome Score
HOS	Hip Outcome Score
ICF	International Classification of Functioning, Disability and
	Health
iHOT-12	International Hip Outcome Tool-12
iHOT-33	International Hip Outcome Tool-33
IQR	Interquartile range
KI	Konfidenseinterval (DK)
MRI	Magnetic resonance imaging
MIC	Minimally important change
NRS	Numerical rating scale
РА	Participation in physical activity
PAO	Periacetabular osteotomy
PRO	Patient-reported outcome
PROMs	Patient-reported outcome measures
SEM	Standard error of measurement
SD	Standard deviation
Sport/recreation	Physical function in sports and recreation
SQUASH	Short QUestionnaire to ASsess Health-enhancing physical
-	activity
QOL	Quality of life
-	

1. English summary

Hip dysplasia is considered a joint disease where pain presents secondary to intraarticular lesions. Yet, previous studies indicate that this understanding may be insufficient, and it has been suggested that extra-articular structures such as muscles and tendons may play a role in relation to the development of pain in hip dysplasia. However, muscle-tendon pain and structural abnormalities have not been investigated in patients with hip dysplasia, and there is a lack of studies reporting outcome of periacetabular osteotomy (PAO) with outcome measures considered relevant for the typical young and active patient.

A prospective case series study was conducted in 100 patients with hip dysplasia with follow-up 1 year after PAO. PAO outcome was investigated, applying the Copenhagen Hip and Groin Outcome Score (HAGOS), accelerometer-based measures of physical activity and standardised clinical examinations. Clinical examinations were used to identify muscle-tendon pain in specific anatomical regions (i.e. clinical entities). Moreover, prior to PAO, structural abnormalities in hip tendons were identified with standardised ultrasonographic examinations, while hip muscle strength was assessed with a handheld dynamometer.

Prior to PAO, the majority of patients experienced muscle-tendon pain, primarily affecting the iliopsoas (56%; CI 46 - 66) and hip abductors (42%; CI 32 - 52). Muscle-tendon pain was negatively associated with patient-reported outcome (PRO) and hip muscle strength, and abnormal ultrasonographic findings were identified in the corresponding painful structures. However, only weak to moderate correlations between abnormal ultrasonographic findings and clinically identified pain were found for the iliopsoas and hip abductors. One year after PAO, the proportion of patients with muscle-tendon pain had fallen by 39% points, while patients reported moderate to very high improvements across all subscales of the HAGOS. However, for patient-reported function in daily living and sport/recreation, about half of patients reported change scores lower than the minimally important change, indicating that these patients did not experience clinically relevant improvements after PAO. Moreover, despite considerable improvement in patient-reported physical activity, no changes in accelerometer-based physical activity were found.

Muscle-tendon pain and structural abnormalities were common in hip dysplasia; and 1 year after PAO, muscle-tendon pain decreased parallel with improvements in PRO. However, the level of daily physical activity did not change after PAO. Based on these results, hip dysplasia appears to be a joint disease that is associated with muscle-tendon pain and structural abnormalities in muscle-tendon tissue.

2. Danish summary

Hoftedysplasi anses som en ledsygdom, hvor smerte opstår sekundært til intraartikulære skader. Tidligere studier har dog indikeret, at denne forståelse kan være mangelfuld. Det er blevet antydet, at ekstraartikulære strukturer såsom muskler og sener kan spille en rolle i relation til smerteudvikling. Ingen studier har dog undersøgt muskelsenesmerter og strukturelle forandringer hos patienter med hoftedysplasi, og der er mangel på studier, som rapporterer resultater af periacetabulær osteotomi (PAO) med resultatmål, som vurderes relevante til den typiske unge, aktive patient.

Et prospektivt case-seriestudie blev gennemført på 100 patienter med hoftedysplasi med opfølgning 1 år efter PAO. Resultatet af PAO blev undersøgt med Copenhagen Hip and Groin Outcome Score (HAGOS), accelerometerbaserede metoder til at måle fysisk aktivitet og standardiserede kliniske undersøgelser. Sidstnævnte undersøgelser blev anvendt med henblik på at identificere muskelsenesmerte i specifikke anatomiske regioner (i.e. kliniske enheder). Strukturelle forandringer i hoftesener blev endvidere identificeret ved standardiseret ultralydsskanning, og muskelstyrke blev målt med et håndholdt dynamometer.

Størstedelen af patienterne oplevede muskelsenesmerter forud for PAO, hvor smerterne primært var relateret til iliopsoas (56%; KI 46 - 66) og hofteabduktorerne (42%; KI 32 - 52). Muskelsenesmerterne var negativt associeret med patientrapporteret resultat (PRO) og muskelstyrke. Samtidig blev strukturelle forandringer identificeret i de samme smertegivende strukturer ved ultralydsskanning. De strukturelle forandringer var dog kun svagt til moderat korreleret til klinisk identificeret smerte for iliopsoas og hofteabduktorerne. Andelen af patienter med muskelsenesmerte blev reduceret med 39% procentpoint 1 år efter PAO, og patienterne rapporterede moderate til meget store forbedringer for alle HAGOS subskalaer. På trods af dette rapporterede cirka halvdelen af patienterne ændringer i daglige aktiviteter, samt sports- og fritidsaktiviteter, der var lavere end mindste kliniske relevante ændring. Dette indikerer, at patienterne ikke oplevede en klinisk relevant forbedring i daglige aktiviteter og i sports- og fritidsaktiviteter efter PAO. På trods af betydelige forbedringer i patientrapporteret fysisk aktivitet var det derudover ikke muligt at påvise ændringer i accelerometer-baseret fysisk aktivitet.

Muskelsenesmerte og strukturelle forandringer var hyppige fund hos patienter med hoftedysplasi. Efter PAO blev muskelsenesmerterne mindre udtalte samtidig med, at der sås forbedringer i PRO. På den anden side ændrede mængden af daglig fysisk aktivitet sig ikke efter PAO. Disse resultater giver anledning til at forstå hofteledsdysplasi både som en ledsygdom og som en lidelse, der kan medføre muskelsenesmerte og strukturelle forandringer i muskelsenevævet.

3. Introduction

Hip dysplasia in the mature hip is worldwide one of the most common hip disorders (5-7). It can be asymptomatic (5,6), but is also related to pain, gait adaptations and early osteoarthritis and may require surgical correction (8-11). The stable dysplastic hip is seldom diagnosed and will only be discovered if pain presents (12). The aetiology of hip dysplasia is multifactorial, and many causative risk factors have been proposed, including gender (12), familial predisposition (12,13), breech presentation (12) and primiparity (5,12).

Historically, hip dysplasia is considered a joint disease and little attention is paid to extra-articular structures such as muscles and tendons. In this PhD dissertation, I will review the present knowledge and hopefully extend our knowledge by investigating muscle-tendon pain and structural abnormalities, and change in muscle-tendon pain after hip-preserving surgery.

Prevalence of hip dysplasia

Despite the fact that hip dysplasia is common, only few studies have investigated the prevalence of hip dysplasia in background populations with and without pain. In Danish citizens, radiological findings associated with hip dysplasia range from 3-13% with equal prevalences among men and women (5,6). Similarly, 2-20% of 19-year-old Norwegians have radiological findings associated with hip dysplasia with higher prevalences among women (4%) than among men (2%) (14). However, in background populations with hip symptoms, considerably higher prevalences have been reported (7,15), ranging from 8-32% with equal prevalences among men and women, and higher prevalences among subjects with hip osteoarthritis (7,15). Variations in prevalence are primarily due to differences in diagnostic criteria used (5,6,14), whereas environmental factors and ethnicity explain extreme variations in prevalence among African, Japanese and Saami people (12). Despite these findings among background populations, up to 80% of patients with hip dysplasia are women (16), indicating shortcomings in our current understanding of hip dysplasia. However, before considering this further, I will describe how we understand hip dysplasia today.

Pathology of hip dysplasia

Hip dysplasia is a pathological development of the hip joint that can cause pain (9,16,17). This development involves both the acetabulum and the femur (18). The dysplastic acetabulum is shallow and oblique with a reduced weight-bearing area (19) (Figure 1). This leads to lack of anterior, lateral and occasionally also posterior acetabular support to the femoral head (20). Hip dysplasia is also commonly accompanied by femoral deformities, covering cam deformity, increased anteversion

and insufficient head-neck offset (21). The incongruency between the acetabulum and the femur leads to increased pressure per unit of area and increased shear forces at the acetabular rim (10,22,23). Left untreated, hip dysplasia is associated with hypertrophy of the acetabular labrum and ligamentum teres (22). It has been proposed that these structures undergo hypertrophy secondary to the bony instability in order to keep the femoral head within the shallow and oblique acetabulum (22,24,25). In symptomatic hip dysplasia, the shear forces persist, and the supporting role of the acetabular labrum increases from 1-2% to 4-11% (26). This



Figure 1. Dysplastic hip joint with reduced coverage of the femoral head.

compensation can fail and result in labral and ligamentum teres lesions, cartilage delamination and accelerated development of hip osteoarthritis (5,6,8,11,27). Yet, only a case-control study and a retrospective cohort study have shown an increased risk of progression from no osteoarthritis to manifest osteoarthritis in patients with hip dysplasia (8,11). However, despite lack of prospective studies, several studies do indicate a relationship between hip dysplasia and hip osteoarthritis (5,6,8,11,27,28).

Cartilage and labral lesions are common in hip dysplasia (22,26), whereas ligamentum teres lesions are less common (22). The cartilage has no pain receptors, and labral lesions have therefore been suggested to cause pain when hip dysplasia becomes symptomatic (22). However, results of other studies suggest differently. The results of a systematic review on cross-sectional and case series studies showed a high prevalence of labral lesions in pain-free subjects (29), while results from a cohort study showed that pain level was not related to the degree of labral lesions in patients with dysplastic and borderline dysplastic hips (30). Consequently, pain may also derive from other structures than the acetabular labrum as explained in the below section on the clinical manifestation of hip dysplasia.

Clinical manifestation of hip dysplasia

Symptomatic hip dysplasia normally presents in young female patients from the age of 24-35 years (9,16,17). The clinical manifestation is longstanding activity-related pain and night pain (9,17,31), presenting bilaterally in 52% (18). In many cases, the pain is located to more than one anatomical region, most commonly the groin and the lateral hip region (9,31). The quality of the pain is sharp to dull with moderate to severe pain intensity (9,31). The pain often presents insidiously over a longer period of time (9) and causes symptoms that vary from fatigue to clear weakness of the hip

abductors (32). Therefore, many patients experience both delay and inaccurate diagnosis (9,33). Common impairments associated with hip dysplasia are gait adaptations (33,34), muscle strength deficits (35,36), pelvic instability (37), low patient-reported function and decline in patient-reported quality of life (33). Of these, impaired muscle strength and pelvic instability seem important and indicate that the muscle-tendon support to the hip joint could play a role in relation to the development of pain (38).

Muscle-tendon pain and structural abnormalities

The hip abductor muscles support the hip joint in the frontal plane (39,40) (Figure 2); and in hip dysplasia, the lack of bony support is associated with an increased role of these muscles (34,41,42). Using triaxial accelerometry in patients with unilateral affection, Maeyama et al. (41) reported increased magnitude of acceleration in dysplastic compared with contralateral healthy hips. The magnitude of acceleration was largest in the lateral direction (41) where the hip abductors are the primary active supporters. Likewise, higher medially directed joint reaction forces were



Figure 2. Gluteus medius & minimus muscles (primary hip abductors).

found among patients with hip dysplasia than among pain-free references due to lateralization of the hip joint centre (42). From a biomechanical perspective, lateralization of the hip joint centre requires higher force generation of the hip abductor muscles due to their reduced moment arms (42). This matches the results by Skalshøi et al. (34), who reported an increased hip abductor torque during the late stance phase of walking. Similarly, increased and earlier hip abductor activation has been reported in patients with chronic anterior hip pain (including hip dysplasia) during a step-down exercise (38). These observed

movement adaptations probably respond to a biomechanical necessity and are maybe consistent with a pain-protective behaviour as documented in subjects with low-back pain (43). These adaptations have short-time benefits, but long-time consequences may cause pain and structural abnormalities due to overuse (38). This could explain why Sucato et al. (35) and Sørensen et al. (36) found that patients with hip dysplasia had weaker hip abductors than pain-free references when maximal voluntary moments were measured in a isokinetic dynamometer. In other words, patients have sufficient capacity to generate the hip abductor moments necessary for walking (36), but their maximal voluntary capacity is impaired either due to weaker muscles, pain or both.

The iliopsoas muscle supports the hip joint in the sagittal plane, resting directly over the acetabular labrum (44) (Figure 3). In hip dysplasia, anterior acetabular support is

lacking (20), possibly causing compensatory loading of the iliopsoas as documented for the hip abductors (34,45); we speculate that this may also cause tendinopathy. These effects may be further aggravated by the close anatomical proximity of the iliopsoas and the acetabular labrum due to increased mechanical compression secondary to acetabular labrum lesions and hypertrophy. However, no studies have reported altered activation of the iliopsoas muscle or increased mechanical compression in patients with hip dysplasia. Still, gait adaptations in the sagittal plane

have been reported (33,34), showing that patients with hip dysplasia walk with smaller hip extension angles and reduced hip flexor moments in the late stance phase of walking (33,34). Reduced hip extension leads to a more vertical walking pattern with a smaller load on the anterior hip structures including the iliopsoas (34). This is probably consistent with a pain-protective behaviour. In line with what was mentioned above, patients with hip dysplasia also have weaker hip flexors than pain-free references (35,36), indicating lack of maximal voluntary capacity as described for the hip abductors. In summary, the iliopsoas muscle may be prone to pain and structural abnormalities due to altered muscle activation and mechanical compression and, among other factors, this may explain the



Figure 3. Iliopsoas muscle crossing the dysplastic hip joint.

documented gait adaptations and muscle weakness (33,35,36).

Muscle-tendon abnormalities have been documented in patients with hip dysplasia examined with hip arthroscopy (46) whereas knowledge of muscle-tendon pain in this population has apparently not been reported. Moreover, presence of muscletendon abnormalities were identified in small samples and only as secondary outcomes (46). Therefore, the plausible role of muscle-tendon pain and structural abnormalities in hip dysplasia remains uninvestigated. Among athletes with longstanding groin pain, different anatomical structures, also described as clinical entities, have been suggested to play a role in the development of pain (47,48). Clinical examinations (49,50), magnetic resonance imaging (MRI) (51) and ultrasonography (52) have been used to identify pain and structural abnormalities in specific clinical entities. In athletes, groin pain was most commonly related to the hip adductors (50-52), the iliopsoas (49,50), the symphyseal joint (51) and the inguinal region (49-51). The hip abductors were not examined and knowledge of pain in these muscles is therefore non-existent. Nevertheless, abductor-related pain was the most commonly self-reported painful anatomical region among young active patients following hip arthroplasty (53), indicating the relevance of these muscles among patients with a hip joint disease.

Muscle-tendon pain assessed with clinical examinations

Muscle-tendon pain can be assessed by standardised clinical examinations and by patient reports. Hölmich et al. (47,49,54) were the first to describe specific clinical entities as the origin of pain among athletes with groin pain. In 2015, the Doha agreement meeting on terminology and definitions of pain in athletes was published (48). Twenty-four international experts reached agreement on a classification system for groin pain. According to this system, athletic groin pain was divided into three major categories. The categories were defined clinical entities, hip-related groin pain and other causes of groin pain. The defined clinical entities for groin pain were: adductor-related, iliopsoas-related, inguinal-related and pubic-related pain (example, Figure 4) (48). To identify pain in these clinical entities, standardised pain-provocation tests, viz. anatomical palpation, resistance testing and stretching, were defined (48). A similar approach has been used in patients with lateral hip pain, where anatomical palpation and resistance testing among other criteria were used to identify pathology in the gluteal muscles (55).



Figure 4. Illustrating diagnostic criteria for iliopsoas-related pain: Palpatory pain of the muscle through the lower lateral part of the abdomen and/or just distal of the inguinal ligament and pain with passive stretching during modified Thomas' test (1).

Muscle-tendon pain recorded with patient reports

Muscle-tendon pain can also be assessed by pain drawings, where pain is identified in specific anatomical regions (53,56). Both advantages and disadvantages of patient reports as opposed to clinical examinations exist. The advantage of a patient report is the possibility to assess large populations (53,56). The disadvantage is that the reporting cannot be controlled by health professionals, introducing a risk of both under- and overestimation and low reproducibility. Therefore, in order to control potential risk of bias, a standardized clinical examination seems superior. However, the disadvantage of clinical examinations and patient reports is the possibility that pain presents as part of referred joint pain or chronic pain unrelated to any structural abnormalities (57).

Muscle-tendon abnormalities examined with ultrasonography

Muscle-tendon abnormalities can be visualised with ultrasonography and MRI (55,58,59). Ultrasonography is a diagnostic imaging technique where images are made by high-frequency sound waves, ultrasound. Ultrasonography has both advantages and disadvantages compared to MRI (58). The most important advantages are higher spatial resolution (60), quantification of structural

abnormalities, real-time scanning (59–61), rapid comparison to symptoms (59–61) and low costs (59,60). The higher spatial resolution with ultrasonography enables quantification of structural abnormalities; thus, the microanatomy of tendons, ligaments and muscles can be visualized (61). This makes it possible to detect minor structural abnormalities as seen in tendinopathy (60) where loss of a normal parallel hyperechoic fibrillar pattern indicate pathology. Moreover, ultrasonography can detect minor tears or calcifications in tendons, ligaments and muscles (60), which is considered difficult by MRI (55). However, MRI also outperforms ultrasonography in some respects; for example, gluteal tendon pathology has been confirmed by MRI in patients with lateral hip pain, where increased signal intensity and tendon thickening were diagnostic criteria (55). Despite many advantages of ultrasonography, limitations do exist. The most important disadvantages are the inability to assess intra-articular structures completely, operator dependence, a long learning curve and artefacts that may be misinterpreted as minor structural abnormalities (59,61). Therefore, using ultrasonography requires experience, a standardised protocol and only few examiners. Acknowledging these known limitations, hip ultrasonography is considered relevant to visualise potential muscle-tendon abnormalities in patients with hip dysplasia.

The above-mentioned known impairments related to hip muscles and tendons suggest that extra-articular structures may play a role in the development of pain in hip dysplasia. However, one must also consider if muscle-tendon pain change after treatment.

Treatment options today

Today, symptomatic and radiologically verified hip dysplasia are treated with hippreserving surgery. Hip-preserving surgery covers different procedures depending on geography, age and severity of hip dysplasia (32,62,63), and surgery may include



Figure 5. Correction of the hip joint with periacetabular osteotomy. Photo: Soballe.com

single, double, triple, spherical, chiari and PAO (32,63). PAO has become the most frequently performed procedure for surgical treatment of hip dysplasia in Western Europe and North America (64) and covers numerous approaches and modifications (32,65–68) (Table 1). PAO reorientates the acetabulum through three separate osteotomies (32), aiming to improve the coverage of the femoral head to a centre-edge (CE) angle of 30-40 degrees and a Tönnis acetabular (AI) angle of 0-10 degrees (32,67) (Figure 5). PAO is indicated in

skeletally mature patients with preserved articular cartilage and an active lifestyle (31,69). Patients should be healthy and <40 years of age because PAO is a highly

invasive procedure (69) and because poor outcome is associated with higher age (70). Moreover, adequate hip range of motion and hip joint congruency are also considered important as PAO reduces hip range of motion (69).

Smith-Petersen	Modified Smith-Petersen	Minimally invasive	Minimally invasive
Ganz et al. (1988) (62).	Leunig et al. (2001) (32).	Troelsen et al. (2008) (67).	Khan et al. (2016) (68).
Tensor fascia lata is	The ASIS is osteotomised	The inguinal	The abdominal
detached from the ilium.	with preservation of	ligament is cut at the	muscles and the soft
The capsule is freed from the attachment of the	muscle attachments.	attachment to the	tissue at the level of the ASIS are dissected
gluteus minimus.	The indirect head of the rectus femoris is	iliac spine.	off the bone.
The iliacus and sartorius muscles are elevated from the anterior iliac spine and from the iliac wing. The direct tendon of the rectus femoris is detached from the anterior inferior iliac spine, and fibres of the iliacus muscle are	tenotomised and the direct head is separated from the anterior inferior iliac spine.	The sartorius muscle is divided parallel with the direction of its fibres, and the deep fascia of the muscle is cut.	
dissected off the capsule.	The hip joint capsule is		
The hip joint capsule can	routinely opened.	The hip joint capsule	The hip joint capsule is
be opened.	T 11 (· · · · 15	is not opened.	not opened.
Length of incision: 15-20 cm.	Length of incision: 15 cm.	Length of incision: 7 cm.	Length of incision: 9 cm.
10 kg weight-bearing 3 th day after surgery.	day after surgery.	30 kg weight-bearing on the day of	Not described.
No active movement of reinserted muscles in 6 weeks.	no mp nexion in 6 weeks.	surgery.	
The iliginguinal and direct	antorior approach is not listo	d as these approaches ar	a loss fraguantly used

Table 1. Different PAO approaches and how they affect muscles and tendons around the hip joint

The ilioinguinal and direct anterior approach is not listed as these approaches are less frequently used nowadays. Abbreviation. PAO (periacetabular osteotomy), ASIS (anterior superior iliac spine).

Radiographic indications for PAO most commonly involve a CE angle <20-25 degrees and AI angle of >10 degrees (32,67,68). It has been anticipated (personal correspondence) that more than half of Danish patients are not candidates for PAO and receive no alternative treatment in the public sector. On the other hand, candidates for PAO receive an expensive and advanced surgical treatment including physical rehabilitation (67,71). After PAO, these patients can expect significant improvement in patient-reported pain, function, physical activity and quality of life (16,64,68,70,72–75). Furthermore, the hip joint remains preserved in 85% of patients after 10 years (73,76), in 60% after 20 years and in 29% after 30 years (64,72). Moreover, leg power also improves after PAO, indicating positive muscle adaptation secondary to acetabular correction (77). Nevertheless, surgery is not without risk, and complications have been reported after PAO procedures. Minor complications like haematoma, symptomatic hardware, wound infection and minor heterotopic ossification have been reported in 2-41% of cases (65,67,68,73,78–83). The lateral cutaneous nerve is affected in many cases (62,65,78,80,81) and is negatively associated with PRO (83). Major complications have been reported among 0-37% (65,67,68,73,78–83), including avascular necrosis, nerve dysfunction, major bleeding, fracture of the posterior column, major heterotopic ossification and delayed or non-union of the pubic, ischial or iliac bone (83). Despite complications and high costs, 196 Danes underwent hip-preserving surgery due to hip dysplasia in 2018 (84,85). On average, they were hospitalised for 2 days (84,85), and each joint-preserving procedure had a cost of 8,710 Euros (86). However, only about 40 Norwegians and 40 Swedes undergo PAO a year (personal correspondence) despite equal prevalences of hip dysplasia in Denmark and Norway (5,6,14). This indicates that hip dysplasia may be managed with other treatments than hip-preserving surgery.

Exercise therapy is an alternative to surgery and may be a relevant treatment option for those who are not candidates for surgery or do not wish to undergo surgery. The body of evidence to support exercise therapy to treat hip dysplasia is sparse in contrast to the numerous studies reporting outcome of surgery. In a prospective case series study, Kurado et al. (37) showed improved gait, hip abductor strength, patientreported pain and function 3 months after a hip abductor-strengthening program. Similarly, improvements in patient-reported and performance-based function were reported in a study examining the feasibility of 8 weeks of progressive resistance training in patients with hip dysplasia (87). Interestingly, the outcome of exercise therapy has been investigated in hip osteoarthritic patients with and without hip dysplasia for whom surgery was not recommended due to their level of pain, activity impediments, x-rays and in cases where patients did not want to undergo surgery (88). Despite absence of statistical significance, most outcome items had improved at 6 months of follow-up, suggesting a tendency towards general improvement (88). In line with this, Harris-Hayes et al. (89) showed a positive treatment effect of 6 weeks of movement-pattern training compared with wait-list in a feasibility study of 35 patients with chronic hip pain (including hip dysplasia). The positive effect was shown in relation to patient-reported symptoms and daily life. Moreover, in a case series study of 28 patients from the population described above, significant improvements in patient-reported and performance-based function were found after movement-pattern training (90). However, the long-time outcome of exercise therapy remains unknown. Even so, in patients with hip and knee osteoarthritis, exercise therapy is an established alternative to surgery and improves patient-reported and performance-based function (91-93). The low number of adverse effects of exercise therapy and the possibility to practice exercise almost anywhere at little cost (94–96) signify the role of exercise therapy for patients with hip dysplasia. Nevertheless, eligible patients have to be selected, and the effect of exercise therapy has to be

investigated with appropriate outcome measures as some patients probably require surgical correction. The degree of muscle-tendon pain or the level of physical activity could possibly be of relevance when choosing treatment.

How to measure outcome of treatment

Treatment can be evaluated with performance-based and PRO measures (PROMs). Performance-based measures include three-dimensional motion capture analyses, functional performance tests such as hop tests, single leg squats and muscle strength tests and accelerometer-based measures of physical activity (97,98). PROMs refer to self-administrated standardised questionnaires. These are well-established gold standards investigating the outcome of treatment, and they capture how patients feel and function in relation to health status and treatment without health professional interpretation (99). Traditionally, PROMs designed for older osteoarthritic patients have been used to investigate the outcome of treatment in patients with hip dysplasia (64,70,72,73,100). Preferably, PROMs designed for young and active patients should be the first-line choice in all patients with hip dysplasia. At present, the Hip Outcome Score (HOS), the International Hip Outcome Tool-12 (iHOT-12), the International Hip Outcome Tool-33 (iHOT-33) and the Copenhagen Hip and Groin Outcome Score (HAGOS) are recommended when assessing outcome of treatment in young to middle-aged patients with hip pain (101), and they all have adequate clinimetric quality for this population (101). Nevertheless, important differences between performance-based and PROMs of physical activity have been reported in previous studies (102,103) with no considerable change in level of daily physical activity despite considerable improvements in PROMs. This is not surprising since patientreported physical activity refers to self-perceived ability to complete a given task and may not reflect actual physical performance (104). Accelerometer-based measures of physical activity, on the other hand, deliver a neutral measure of actual physical performance (104). This is considered important as patients compared with references report reduced ability to participate in preferred physical activities (97) and report using less time on physical activities at higher intensity levels (105). However, no studies have investigated the actual level of physical activity in patient with hip dysplasia.

In summary, the traditional understanding of hip dysplasia as solely a joint disease seems insufficient. Hence, there is a need to extend our knowledge and consider if hip muscles and tendons could play a role in relation to the development of pain. We also ought to investigate the outcome of hip-preserving surgery with outcome measures considered relevant for the typical young, active patient.

4. Aim of the dissertation

The overall aim of this dissertation was to investigate muscle-tendon pain and structural abnormalities in hip dysplasia and outcome of hip-preserving surgery in a prospective study applying clinical tests, ultrasonography, PROs and measurement of physical activity. The aims of the four papers included in the dissertation are listed below.

- (1) The aim was to identify muscle-tendon pain in 100 patients with hip dysplasia in the following clinical entities: (i) iliopsoas, (ii) abductors, (iii) adductors, (iv) hamstrings and (v) rectus abdominis. Furthermore, the aim was to investigate if PRO and muscle strength were associated with muscle-tendon pain in patients with hip dysplasia.
- (2) The aim was to report abnormal ultrasonographic findings related to muscles and tendons in 100 patients with symptomatic hip dysplasia. Furthermore, the aim was to investigate correlations between abnormal ultrasonographic findings and clinically identified pain related to muscles and tendons.
- (3) The aim was to investigate changes in PRO, changes in muscle-tendon pain, and any association between them from before to 1 year after periacetabular osteotomy.
- (4) The aim was to investigate whether patients with hip dysplasia change physical activity profile from before to 1 year after periacetabular osteotomy, measured by accelerometer-based sensors and patientreported physical activity. Furthermore, the aim was to investigate association between change in accelerometer-based physical activity and change in patient-reported participation in preferred physical activities.

5. Design

This PhD dissertation is based on data collected from a prospective case series study in patients with hip dysplasia scheduled for hip-preserving surgery with 1-year follow-up. Throughout the dissertation, the case series study will be referred to as this study, and individual papers will be referred to as Paper 1-4 (1–4). This study was registered at ClinicalTrials.gov (ID: 20140401PAO) and conducted and reported in accordance with the WMA declaration of Helsinki and the STROBE statement.

6. Materials & methods

Ethical issues

Ethical aspects are important to consider when including patients in a study. This study was initiated at a time marked by a lack of studies investigating muscle-tendon pain and structural abnormalities in hip dysplasia and outcome of surgery with outcomes measures considered relevant for the typical young, active patient. Only few studies have reported outcome of the PAO with relevant PROMs (68,97), and abnormal findings in muscles and tendons have only been reported as secondary findings (46), and no studies have reported level of daily physical activity with accelerometer-based methods. Therefore, it was considered ethically right to invite patients to participate in this study. To impose as little burden on patients as possible, only outcome assessments that were absolutely essential to this study were collected. Moreover, economic compensation for transportation to the hospital was given. This study was notified to the Central Denmark Region Committee on Biomedical Research Ethics on 14 January 2014 (5/2014), who waived the request of approval since observational studies need no ethical approval in Denmark. The handling of personal data was authorised by the Danish Data Protection Agency (1-16-02-47-14), and all participating patients gave informed consent to participate by signing an informed written consent form.

Patients

Patients with bilateral and unilateral hip dysplasia were recruited consecutively from May 2014 to August 2015 from the Department of Orthopaedic Surgery at Aarhus University Hospital, Denmark (1–4). Patients were screened for initial eligibility by specialised orthopaedic surgeons. Eligible patients were given oral and written information about the mandatory procedures for participation. Patients agreeing to participate were hereafter contacted and enrolled if they fulfilled the inclusion and exclusion criteria. Criteria for inclusion were scheduled PAO due to symptomatic and radiologically verified hip dysplasia, applying Wiberg's centre-edge (CE) angle <25° (106). Patients were excluded if they had conditions and/or a history of previous surgical interventions affecting the function of their hip (Figure 6). Moreover, only patients <45 years of age, with a BMI <30, with normal hip range of motion and with non-arthritic hips were operated on.



Figure 6. Flowchart of the process of inclusion.

Patient characteristics

Patient characteristics were collected at a clinical examination before and 1 year after PAO by two experienced physiotherapists with 5-7 years of experience assessing patients with hip dysplasia (1-4). The examinations took place in a closed examination room at the Department of Physiotherapy and Occupational Therapy, Aarhus University Hospital. The physiotherapists randomly assessed patients with hip dysplasia with equal distribution between the two. Patient characteristics were recorded from standardised questions and/or medical records. The highest pain at rest was measured on a numerical rating scale (NRS) while the patient was lying down. Using anteroposterior radiographs, a single rater measured the following radiological angles: the CE angle (106), the AI angle (107) and the degree of osteoarthritis according to Tönnis' grading (107). Unilateral and bilateral affection and co-morbidities were recorded from medical records. Back pain intensity was recorded with the Oswestry Disability Index, section 1 (108). Hip-related pain was assessed by the Flexion/Adduction/Internal Rotation (FADIR) test and the Flexion/Abduction/External Rotation test (FABER) test (109,110). Occurrence of internal snapping hip was assessed using a standardised clinical test (111). Finally,

the springing palpation test for pain provocation over the lumbar spinous processes and the sacroiliac joints was used to assess whether springing palpation tests led to local pain in the back and/or in the hip and/or groin (112).

Hip-preserving surgery

Patients were surgically treated with the minimally invasive approach for PAO by two experienced orthopaedic surgeons (3,4). A 7 cm incision was made alongside the sartorius muscle, beginning at the anterior superior iliac spine. The sartorius muscle was cut parallel with its muscle fibres, and the medial part of the divided muscle was retracted medially together with the iliopsoas muscle. Osteotomies were hereafter performed. Patients were hospitalised for approximately 2 days. At the ward, they were given patient information and instructed in a rehabilitation programme including pain management, nutrition and mobilisation. Additionally, they were instructed in a home-based exercise programme involving unloaded hip exercises. Patients were allowed partial weight bearing the first 6-8 week with a maximum load of 30 kg. Additionally, patients were offered an individualised exercise programme, consisting of two weekly physiotherapist-supervised training sessions. The sessions started when full weight bearing was allowed and ended after 2-4 months.

Outcomes

Outcomes were collected at the two clinical examinations (1–4). The HAGOS was completed first, followed by ultrasonography, clinical examination of muscle-tendon pain and clinical assessment of hip muscle strength. Before ending the clinical examinations, patients were instructed to wear an accelerometer-based sensor the following 7 days.

Patient-reported outcome

The HAGOS was used to measure PRO in all patients (1–4). This questionnaire was developed to measure perceived and actual outcome in physically active, young-to-middle-aged patients with longstanding hip and/or groin pain (113). The HAGOS consists of six subscales measuring pain, symptoms, physical function in daily living (ADL), physical function in sports and recreation (sport/recreation), participation in physical activity (PA) and quality of life (QOL) during the past week. The individual subscales measure PRO from 0-4 through 37 individual items. The raw score can be transformed to a total score of 0-100 points, and 100 points indicate highest possible outcome. The HAGOS has been developed from the Hip disability and Osteoarthritis Outcome Score (HOOS) after translation and cross-cultural adaptation to Danish. Items from the HOOS were supplemented with three sports-specific items from the HOS to form the full HAGOS (113). The psychometric properties of the HAGOS have been evaluated in three prospective case series studies (113–115) in the following patients: (i) patients with hip and/or groin pain (n=101) (113), (ii) patients who had

undergone hip arthroscopic surgery 1-2 years previously (n=50) (114), (iii) healthy pain-free references (n=50) (114), and (iv) patients with femoroacetabular impingement syndrome (FAIS) scheduled for hip arthroscopy (n=502) (115). The test-retest reliability of the HAGOS is high. The interclass correlation coefficients range from 0.81 to 0.97 across all subscales, and the measurement error ranges from 1 to 5 points at the group level (113–115). Moreover, the HAGOS has adequate construct validity. The correlation coefficients range from 0.23 to 0.73 across all subscales when correlated to relevant constructs (113–115); with the HAGOS, relevant differences between patients and references can be detected (114). The responsiveness of the HAGOS, measured as effect size, range from 0.77 to 1.87 points across all subscales in patients with hip and/or groin pain and FAIS that reported improved condition (113,115). The interpretability of the HAGOS, measured as minimally important change (MIC), ranges from 9 to 13 points across all subscales in patients with FAIS who underwent hip arthroscopy 4 months earlier (115).

Methodological considerations

The HAGOS is not the only PROM developed to measure PRO in young-to-middleaged patients with hip pain. Evidence from recent systematic reviews (101,116), a Delphi study (117) and statements from an international agreement paper (118) also recommend the iHOT-12, iHOT-33 and HOS (101,116-118). Based on the COnsensusbased Standards for the selection of health Measurement INstrument (COSMIN) list, iHOT-12, iHOT-33, HOS and HAGOS are the most systematically investigated PROMs. However, the HOS and iHOT-33 are associated with the highest ratings of poor study methodology (46% in both studies), while the HAGOS and iHOT-12 are associated with the lowest ratings of poor study methodology (23% and 31%) (101). The responsiveness of the HAGOS and iHOT-12 is similar when comparing the HAGOS subscales pain, sport/recreation and PA with the total score of the iHOT-12 (116). Contrary to this, the HAGOS subscale symptoms and ADL are associated with poorer responsiveness, while the HAGOS subscale QOL is associated with higher responsiveness (116,119). Nevertheless, the six dimensions of the HAGOS provide precise and specific knowledge on PRO in specific domains, which cannot be obtained from the combined total score of the iHOT-12 (119). Furthermore, only the HAGOS measures PRO related to the hip and/or groin, and the HAGOS is therefore considered suitable for patients with hip dysplasia as the clinical manifestation of hip dysplasia is activity-related pain in the hip and groin.

Muscle-tendon pain

Muscle-tendon pain was examined in specific clinical entities as described above (47,48,54). In this study, standardised examinations consisting of five pain provocation tests covering palpation, resistance testing and passive muscle strength were used (1–3) (Table 2) (Supplementary files). The order of the tests was as follows: adductor-related pain, iliopsoas-related pain, rectus-abdominis-related pain,

abductor-related pain and hamstring-related pain. Unlike the defined clinical entities from the Doha classification system (48), we subsequently obtained information about abductor- and hamstring-related pain (1–3). These clinical entities were considered important in patients with hip dysplasia since patients have a hip abductor strength deficit (35,36) and hip abductors and extensors seem to be negatively affected by hip dysplasia in walking (33,34). Additionally, rectus-abdominis-related pain (47,54) was used instead of inguinal-related pain from the Doha classification system (48). Inguinal-related pain is less relevant in patients with hip dysplasia as the majority of patients are females who have a different inguinal canal anatomy than males. Muscle-tendon pain was reported in each of the five individual clinical entities and as the sum of painful clinical entities for each patient, ranging from 0-5. The outcome of each entity test was "yes" or "no" to the following question, "Did you feel known pain during the test?"

Clinical entities	Assessment			
Iliopsoas-related pain	Palpatory pain of the muscle through the lower lateral part of the abdomen and/or just distal of the inguinal ligament and pain with passive stretching during modified Thomas' test (47,48,54).			
Abductor-related pain	Palpatory pain at the insertion point at the greater trochanter and pain with side-lying abduction against resistance (55).			
Adductor-related pain	Palpatory pain at the muscle origin at the pubic bone and pain with adduction against resistance (47,48,54).			
Hamstring-related pain	Palpatory pain at the muscle origin at the tuber ischii and pain with extension against resistance.			
Rectus abdominis-related pain	Palpatory pain of the distal tendon and/or the insertion at the pubic bone, and pain at contraction against resistance (47,54).			
Similar table published in paper 1, Table 1 (1).				

Table 2. Standardised examination of muscle-tendon pain in individual clinical entities

The reliability of the standardised clinical examinations was investigated in a previous study, reporting acceptable intra- and inter-rater reliability with kappa coefficients ranging from 0.57 to 0.94 (54). The reliability was investigated in athletes with groin pain who are considered somewhat different from patients with hip dysplasia. Therefore, in this study, the inter-rater reliability of the standardised examinations was investigated since the examinations were carried out by two raters (A and B) for practical reasons (sick leave and holidays) (1).

Two physiotherapists examined 25 patients with hip dysplasia, surgically treated with PAO 6 weeks previously. The patients were examined on two occasions with 2 days between the first and the second examination, and patients were randomised according to whether rater A or B performed the first examination. The patients were instructed not to do physical training prior to the examinations.

Methodological considerations

Patients with hip dysplasia may show a higher day-to-day variation in pain than athletes with groin pain as physical activity one day affects both hip joint and muscle-tendon pain the following days. Moreover, examining patients with two raters could probably also increase the random variation in findings between patients. In this study, the inter-rater reliability was investigated with a period of two days between each examination in surgically treated patients (1). Optimally, the inter-rater reliability should have been examined the same day and in non-surgically treated patients. Nevertheless, the present procedure was chosen as the included patients already had two weekly scheduled training sessions at the hospital, enabling smooth inclusion into the investigation of inter-tester reliability.

Hip muscle strength

Hip muscle strength was assessed with a handheld dynamometer (Powertrack II commandor, JTECH Medical, Salt Lake City, Utah), using a standardised and reliable procedure (1). Two physiotherapists with experience in using the dynamometer performed the muscle strength tests at the baseline examination. The procedure included isometric strength test of the hip adductors and abductors in supine position, the hip flexors in sitting position and the hip extensors in prone position. These test positions were chosen as they were associated with small measurement variation (3-8%) (120) and considered comfortable for patients with a hip joint disorder. The order of the individual tests was random to avoid systematic bias. Resistance was applied 5 cm proximal to the lateral malleolus for hip adductor, hip abductor and hip extension tests, while resistance in hip flexion was applied 5 cm proximal to the proximal border of patella (Figure 7). Patients were instructed to stabilise themselves by holding on to the examination table.

In all tests, patients were informed about the procedure, and this was followed by a sub-maximal practice contraction and a maximal voluntary practice contraction. In all tests, patients performed a 5-s maximum voluntary contraction against the dynamometer, and the highest voluntary contraction out of four repeated measurements in each test was used in the analysis. When the last measurement was the highest recorded value, another measurement was performed until no higher values were measured. A 30-s pause between each measurement was included to avoid fatigue. The recorded strength values were body-size-normalised (lever arm and body mass) and reported as newton metres per kilogram of body weight. The muscle strength for the hip scheduled for PAO was used in the analyses. Two raters assessed patients, and therefore the inter-rater reliability was investigated using the same procedure as described for clinical examination of muscle-tendon pain with 2 days between test and re-test (1).



Figure 7. Muscle strength test of the right adductors (a), abductors (b) and extensors (c) and left flexors (d).

Methodological considerations

As described earlier, it would have been preferable to limit the muscle strength assessment to one rater and preferably a male rater since female raters seem to measure 4-13% lower hip strength values than their counterparts (121). In this study, both raters were females (1), and therefore systematic differences are not expected. However, it is possible that the patients' strength values will be related to the female raters' strength. However, in the chosen test positions, the body mass was behind the dynamometer to give extra support and stability; and in hip adduction, abduction and extension, patients had to resists the force from the rater using a long lever. The latter gave the rater advantage over the person being tested. Another approach to limit possible systematic differences would have been to use external belt fixation. This would have eliminated a possible negative effect of insufficient strength on the part of the rater as reported in a previous study (122).

Ultrasonographic findings

Abnormal ultrasonographic findings related to muscles and tendons were visualised with ultrasonography at the clinical examination scheduled before PAO (2). In ultrasonography, sound waves are generated in a high-resolution linear transducer, which transforms voltage into ultrasound via an array of piezo-electrical crystals (123). When ultrasound meets tissue, a sound reflection is generated, and this reflected sound energy is transformed back into voltage via the piezo-electrical crystals in the transducer (123). The reflected voltage signal includes information necessary to form a 2-dimensional grey-scale image (123). These grey-scale images



Figure 8. Illustrating ultrasonographic examination of the iliopsoas tendon (2).

display tissue of different densities, where high-density tissue (cortical bone) is displayed as bright grey-shades and lowdensity tissue (muscle) is displayed as dark grey-shades (123). In this study, a standardised protocol (Supplementary files) was used (2). The protocol was based on the review by Nestorova et al. (59) and included examination of the iliopsoas tendon, the

adductor longus tendon, the hamstring tendons, the pubic symphysis and the acetabular labrum (example, Figure 8). Moreover, a Noblus, Hitachi-Aloka Medical (Zug, Switzerland) ultrasound system and a multi-frequency linear transducer (5–18 MHz) (EUP-L64, Zug, Switzerland) were used in all examinations (2).

Abnormal ultrasonographic findings were defined as heterogeneous echogenicity with loss of normal fibrillar pattern, abnormal fluid intra- and/or extra-substantial and irregular bone configuration, enthesophytes and/or calcifications. These findings were recorded as normal or abnormal in the index limb by the two physiotherapists (example, Figure 9). Images and movie sequences of the anatomical structures were recorded in all patients and stored on an external disc. Additionally, valid image reading was optimised through a two-phase procedure (2).



Figure 9. Transverse image of a normal and homogeneous tendon with normal fibrillar pattern [a]. Transverse ultrasound image of a thickened heterogeneous tendon with loss of normal fibrillar pattern and diffuse margin appearance [b]. Iliopsoas tendon [1], iliopsoas muscle [2] and acetabular rim [3] (2).

The first phase comprised a pilot phase, where the standardised protocol was tested in ten subjects, including five patients and five pain-free references. Additionally, a radiologist specialised in musculoskeletal ultrasonography supervised the ultrasonographic examination in five of the ten pilot subjects. The second phase comprised data collection, using the approach by Branci et al. (51), where image findings were based on consensus by three radiologists. After the ultrasonographic examinations, stored images and movie sequences of the initial 50 patients were evaluated a second time by all raters (two physiotherapists and the specialised radiologist). Eighteen percent of the initial recordings gave rise to discussion between raters before reaching final consensus. In the last 50 patients, rating was performed solely by the two physiotherapists. In case of any doubts, they had the possibility to contact the specialised radiologist. This was done in five cases.

Two raters carried out the ultrasonographic examinations, and the intra- and interrater reliability were investigated (2). Stored images and movie sequences of 50 patients were rated twice by one rater with a period of median 10 days (7-13) between each evaluation, and the intra-rater reliability was based on these ratings. On a later occasion, the specialised radiologist evaluated images and movie sequences of the same 50 patients, and the inter-rater reliability was calculated based on the first and the third rating. In each of the three ratings, each rater recorded whether the individual structures were normal or abnormal.

Methodological considerations

Ultrasonography is associated with operator dependency, a long learning curve and artefacts that may be misinterpreted as minor structural abnormalities. Therefore, one rater would have been preferable. In this study, patients were examined by two raters, which may have increased the random variation in findings between patients (2). In order to reduce this variation and to ensure valid image reading, images and movie sequences of the initial 50 patients were evaluated a second time by all three raters. Optimally, images and movie sequences of all 100 patients should have been evaluated a second time by all raters. Unfortunately, this was not possible due to practical reasons. Moreover, to ensure valid imaging reading and to reduce variation, a standardised protocol was developed and used (Supplementary files). This protocol included a description of the procedure and illustrations of transducer placement, and the protocol was considered appropriate. Ideally, this protocol should have included images and/or movie sequences of normal and abnormal structures, and in case of doubts, these could have been used as a guideline.

Accelerometer-based physical activity

The level of daily physical activity was measured with commercially available triaxial accelerometer-based sensors (Gulf Coast Data Concepts, Mississippi, USA), using a validated procedure (4). The level of daily physical activity was measured



Figure 10. Accelerometer-based sensor taped between the lateral femoral condyle and the greater trochantor.

during seven consecutive days, including working and leisure days. Hypo-allergenic double-sided tape (3M, USA) was used to fasten the sensor to the patient's non-affected upper leg. The sensors were mounted halfway between the lateral femoral condyle and the greater trochantor (Figure 10) (124). Daily physical activity was measured during waking hours of minimum 8 hours per day, while physical activity at night and during swimming and showering activities was not measured. The sensor sampled data from -6 to 6g at 50 Hz. After 7 days of measurement, patients returned the sensors to the hospital by mail. The stored data were transferred to a computer, and the raw data were visually divided into separate days

using a customised MatLab-script, removing non-worn days (125). Hereafter, all data were calibrated manually by selecting a period of level walking of each day. The data were calibrated in order to adapt variations in height, morphology, sensor placement, walking pattern and speed. After calibration, the data of each day were run through a customised and validated algorithm (Figure 11) (125). This algorithm was based on a decision tree, and decisions were based on acceleration vectors (static versus dynamic), inclination of the accelerometer (sitting versus standing), by low-pass filters (sedentary versus upright dynamic events) and by consecutive peaks (shuffling versus walking) (125).



Figure 11. Illustration of algorithm, basing decisions on acceleration vectors, accelerometer inclination, low pass filters and consecutive peaks.

Based on these decisions, data could be divided into separate physical activities, including: resting, standing, cycling, level walking, walking on stairs and running (125). Additionally, the algorithm created an intensity variable based on the average data signal intensity in 10-second intervals grouped into four intensity levels (Table 3).

Intensity levels	Interpretation	Signal intensity, g		
1. Very low intensity	Sitting and standing	0.00-0.05		
2. Low intensity	Standing and shuffling	0.05-0.10		
3. Moderate intensity	Slow walking and normal walking	0.10-0.20		
4. High intensity	Brisk walking, running and jumping	>0.20		

Table 3. The intensity of accelerometer-based physical activity grouped in four intervals

Methodological considerations

The discriminative ability of the used algorithm was considered important as patients with hip dysplasia are relative young and may therefore experience impairments only in demanding sport and recreational activities. A limitation of the method is, however, that fitness training is not quantified. Fitness training includes many different activities (e.g. strength training, rowing, jumping and dancing). Consequently, the level of daily physical activity could be underestimated as many young patients do fitness training. Moreover, it is possible that patients do more physical activity when they are monitored than during normal days, resulting in an overestimation of the level of daily physical activity. Nevertheless, the possible effect on the results is considered small since possible overestimation will exist at all measured time points, and this will not cause bias.

Statistics

In the four papers included in this PhD dissertation (1–4), numerical data were presented as means (SD) if normally distributed, and otherwise as medians with interquartile ranges (IQR) or 95% confidence intervals (CI). Categorical data were presented as numbers and percent with CI. In all analyses, estimated results were considered statistically significant if $p \le 0.05$, and the STATA 14 (StataCorp, College Station, TX) software package was used for all data analyses.

Paper 1

The inter-rater reliability of the standardised clinical examinations was reported as percentage of agreement and Cohen's κ -coefficient, while inter-rater reliability if the hip muscle strength tests was reported as intraclass correlation coefficient (ICC) and standard error of measurement.

Simple and multivariable linear regression analyses were performed to investigate whether PRO and muscle strength were associated with muscle-tendon pain. In all regression analyses, the sum of painful clinical entities (i.e. muscle-tendon pain) was the independent variable, while each subscale of the HAGOS (symptoms, pain, ADL, sport/recreation, PA and QOL) and each hip muscle strength test (adduction,

abduction, extension and flexion) were the dependent variables. Crude and adjusted β -coefficients were estimated, and adjustments were made for age and sex.

In this study, we aimed to describe muscle-tendon pain and association with PRO and hip muscle strength. This means that a sample size calculation may be less relevant. Therefore, a convenience sample of 100 patients was considered appropriate to describe muscle-tendon pain before and 1 year after PAO. Nevertheless, to ensure that the sample size was large enough to investigate whether muscle-tendon pain was associated with PRO, a sample size calculation was performed. Given a minimal clinically relevant difference of 11.8 HAGOS ADL points (115), an estimated SD of 18.5 HAGOS ADL points (114), a significance level of 5% and a power of 80%, 80 patients were needed to detect changes between patients with and without muscle-tendon pain. Considering the risk of dropouts, the convenience sample of the 100 patients seemed appropriate.

Paper 2

The reliability of the ultrasound examination was reported as percentage of agreement and Cohen's κ -coefficient. For each anatomical structure, correlations between clinically identified muscle-tendon pain and abnormal ultrasonographic findings related to muscles and tendons were tested with Spearman's rank correlation coefficient.

Paper 3

Changes from before to 1 year after PAO were investigated with paired t-tests for PROs, while the McNemar's test was used to test changes in muscle-tendon pain. Additionally, estimated changes were supplemented with calculation of effect sizes. Cohen's d was calculated from the paired t-test as: d = t statistic/ $\sqrt{(n)}$ and Cohen's w was calculated from McNemar's test as: w = w statistics/ $\sqrt{(n)}$. Moreover, floor and ceiling effects were checked in all subscales of the HAGOS and considered present if >15% reported the lowest or highest outcome score. Furthermore, we reported the proportion of patient reporting a HAGOS chance score lower than the MIC according to Thomee et al. (115). Finally, simple and multivariable regression analyses were performed to investigate whether changes in PRO were associated with change in the sum of painful clinical entities from before to 1 year after PAO. Based on knowledge from previous studies, potential co-variates were identified using causal diagrams for observational research (126). The identified co-variates were pre- and postsurgical CE angles (continuous), age (continuous) and sex (nominal). Crude and adjusted β coefficients were estimated where the sum of painful clinical entities was the independent variable and each subscale of the HAGOS was a dependent variable.

Paper 4

Time in each physical activity (i.e. walking, cycling and running) and number of steps recorded at baseline were normalised to total accelerometer-based wear time recorded at baseline; time and steps recorded at 1-year follow-up were normalised to total accelerometer-based wear time recorded at 1-year follow-up. Changes in accelerometer-based physical activity and change in the HAGOS PA subscale were tested with paired t-tests if assumptions were met, and otherwise with the nonparametric Wilcoxon signed rank test. Estimated differences were supplemented with calculation of effect sizes. For parametric data, effect sizes were calculated as Cohen's d from the paired t-test; for non-parametric data, effect sizes were calculated from Wilcoxon signed rank test as: z = z statistic/ $\sqrt{(n)}$. Additionally, to investigate association between changes in accelerometer-based physical activity at four intensity levels (i.e. very low, low, moderate and high) and change in the HAGOS PA subscale from before to 1 year after PAO, simple linear regression analyses were performed. In the analyses, changes in accelerometer-based physical activity were the dependent variables; change in the HAGOS PA subscale was the independent variable.

Methodological considerations

In Paper 1, sex was included as a co-variate in the multivariable regression analyses. This was done because sex is associated with lesser improvement in PRO after PAO (16) and possibly also presurgical PRO, and furthermore because sex could be associated with muscle-tendon pain through the association between sex and morphology of the proximal femur and/or FAIS (127,128). Age was included as a co-variate in the multivariable regression analyses. This was done because age is associated with PRO of PAO (70), and therefore possibly also presurgical PRO, and because age and muscle-tendon pain could be associated via age-related changes of the muscle-tendon tissue (129). Nevertheless, age adjustments were indirectly done in all analyses as only patients with mature hips and patients under 45 years were included (criteria for the PAO). Therefore, age adjustments may not have been relevant.

In Paper 3, the post-surgical CE angle was treated as a co-variate in the multivariable regression analyses. This was done because the post-surgical CE angle is associated with outcome of PAO (64), and because the post-surgical CE angle could be associated with muscle-tendon pain; the latter because compromised joint stability has been suggested to increase in proportion to the severity of hip dysplasia (the CE angle) (41), thereby possibly increasing the risk of overuse injuries of hip muscles due to increased muscle force generation (34). Sex and age were considered relevant co-variates due to the above-mentioned associations described for Paper 1, and presurgical CE angle was considered a possible co-variate due to similar associations as reported for the postsurgical CE angle.

7. Results

In the study period, 100 consecutive patients fulfilled the in- and exclusion criteria and were included in this study (Figure 12) (1–4).



Figure 12. Flowchart of the study process. Abbreviations: HD (hip dysplasia), ADHD (attention deficit/hyperactivity disorder), MRSA (methicillin-resistant staphylococcus aureus).

One year after PAO, 18 patients were lost to follow-up, so 82 patients were available for analysis in Paper 3. In Paper 4, accelerometer-based physical activity data of five patients were missing, so 77 patients were available for analysis in that paper. The patients lost to follow-up did not differ from the analysed patients on any of the measured patient characteristics (data not shown).

Tuble 4. Characteristics of the included patients reported separately for the four papers						
	Paper 1 & 2	Paper 3	Paper 3	Paper 4	Paper 4	
	(n=100)	(n=82)	(n=82)	(n=77)	(n=77)	
Patient characteristics	Before PAO	Before PAO	After PAO	Before PAO	After PAO	
Age, years (SD)	30 (9)	30 (9)	31 (9)	30 (10)	32 (10)	
BMI, kg/m^2 (SD)	23 (3)	23 (3)	24 (3)	23 (3)	24 (3)	
Men (%)	17	11 (13)	-	9 (12)	-	
Pain, years (IQR)	3 (1 - 6)	3 (1 - 6)	-	3 (1 - 7)	-	
NRS pain (IQR)	3 (2 - 5)	3 (2 - 5)	0 (0 - 2)	2 (1 - 4)	0 (0 - 1)	
Bilateral affection (%)	89	74 (90)	-	69 (90)	-	
CE angle, degrees (SD)	17 (5)	17 (5)	30 (5)	17 (5)	30 (5)	
AI angle, degrees (SD)	14 (5)	14 (5)	3 (4)	14 (5)	3 (4)	
Osteoarthritis grade 0/1	97/3	79/3	77/5	74/3	72/5	
Pos. FADIR test (%)	83	70 (85)	55 (67)	66 (86)	52 (68)	
Pos. FABER test (%)	74	62 (76)	47 (57)	58 (75)	45 (58)	
Pos. i. snapping hip test (%)	30	25 (30)	16 (20)	23 (30)	15 (19)	
Back pain intensity (0-5)						
No (%)	31	26 (32)	31 (38)	26 (34)	31 (40)	
Very mild (%)	23	19 (23)	24 (29)	19 (25)	21 (27)	
Moderate (%)	26	20 (24)	16 (20)	18 (23)	14 (18)	
Fairly severe (%)	14	12 (15)	8 (10)	10 (13)	8 (10)	
Very severe (%)	5	4 (5)	2 (2)	3 (4)	2 (3)	
Worst imaginable (%)	1	1 (1)	0 (0)	1 (1)	0 (0)	
Missing (%)	-	-	1 (1)	-	1(1)	
Springing palpation test (SP)						
Hip pain (%)	12	10 (12)	2 (2)	10 (13)	2 (3)	
Back pain (%)	35	30 (37)	31 (38)	28 (36)	30 (39)	
No pain (%)	53	42 (51)	48 (59)	39 (51)	44 (57)	
Missing (%)	-	-	1 (1)	-	1 (1)	
Springing palpation test (SII)						
Hip pain (%)	18	17 (21)	3 (4)	14 (18)	3 (4)	
Back pain (%)	14	13 (16)	12 (15)	13 (17)	12 (16)	
No pain (%)	68	52 (63)	66 (80)	50 (65)	61 (79)	
Missing (%)	-	-	1 (1)	-	1 (1)	

Table 4.	Characteristics	of the included	patients re	ported set	naratelv	for the four	naners
1 abie 4.	Characteristics	of the included	patients re	poneu se	paratery	for the four	papers

Abbreviations: BMI (Body Mass Index), NRS (numerical rating scale), CE (centre-edge), AI (Tönnis' Acetabular Index), FADIR (flexion/adduction/internal rotation), FABER (flexion/abduction/external rotation). Pos. (positive), i. (internal), SP (spinous processes), SIJ (sacroiliac joints).

Patient characteristics

The characteristics of the included patients are reported separately for each paper in Table 4, whereas preferred physical activities of the patients are shown in Figure 13.


Figure 13. Distribution of preferred physical activities. Other covers different combat and self-defence sports, bicycling and hiking. Abbreviations: PAO (periacetabular osteotomy).

Paper I

The inter-rater reliability of the examination of muscle-tendon pain and assessment of hip muscle strength is reported in Table 5. The agreement between raters on recording each structure as painful or not as part of the standardised muscle-tendon pain examinations ranged from 64-100%.

% Agreement	Kappa coefficient	Interpreted agreement (130)
84	0.25	Fair
64	0.33	Fair
79	0.52	Moderate
80	0.60	Moderate
80	0.42	Moderate
80	0.53	Moderate
84	0.60	Moderate
88	0.36	Fair
80	0.17	Slight
100	-	-
80	0.55	Moderate
100	-	-
	% Agreement 84 64 79 80 80 80 80 84 88 88 80 100 80 100	% Agreement Kappa coefficient 84 0.25 64 0.33 79 0.52 80 0.60 80 0.42 80 0.53 84 0.60 80 0.53 84 0.60 85 0.36 84 0.60 85 0.36 86 0.36 87 0.55 100 -

Table 5. Inter-rater reliability on recording each structure as painful or not as part of the standardised muscle-tendon examinations (n=25)

^{*a*} Low prevalence, negatively affecting the kappa coefficient.

^b Not possible to calculate kappa coefficient as no tests were positive.

Abbreviation: LA (lower abdomen), DI (distal to inguinal band), DT (distal tendon), PT (pubic tubercle). Similar table published in Paper 1, Table 3 in Supplementary data.

The kappa coefficients ranged from 0.17-0.60, defined as slight to moderate agreement. Of note, in five tests the number of positive tests was low (0-4), making the k values questionable. For all muscle strength tests, the ICC values were >0.70 and the standard error of measurement (SEM) was 10-16% across all muscle strength tests (Table 6).

Hip strength	Rater A	Rater B	Mean diffe	rence	ICC (95% CI)	SEM	SEM% ^a
1 0					· · /		
	Mean (SD)	Mean (SD)	(95% CI)	p-value			
Flexion	1.1 (0.4)	1.1 (0.3)	0.0 (-0.1 - 0.1)	0.9	0.7 (0.5 - 0.9)	0.2	15.8
Abduction	1.2 (0.4)	1.2 (0.3)	0.0 (-0.0 - 0.1)	0.3	0.9 (0.8 - 1.0)	0.1	9.8
Adduction	1.0 (0.4)	0.9 (0.4)	0.1 (0.0 - 0.1)	0.008	0.9 (0.9 - 1.0)	0.1	10.2
Extension	1.7 (0.6)	1.6 (0.5)	0.1 (-0.1 - 0.2)	0.3	0.8 (0.6 - 0.9)	0.3	15.4
Abbreviations: ICC (intra-class correlation coefficient), SEM (standard error of measurement) in Nm/kg.							
^a SEM divided by the mean average value of rater A and B, multiplied by 100.							

Table 6. Inter-rater reliability of the hip muscle strength assessment reported in mean values in Nm/kg (n=25)

Similar table published in Paper 1, Table 4 in Supplementary data.

Muscle-tendon pain

The proportion of patients with muscle-tendon pain in the defined clinical entities was as follows: iliopsoas-related pain 56% (CI 46 - 66), abductor-related pain 42% (CI 32 - 52), adductor-related pain 14% (CI 8 - 22), hamstring-related pain 6% (CI 2 - 13) and rectus abdominis-related pain 4% (CI 1 - 10) (Figure 14).



Figure 14. Proportion with 95% CI (error bars) of patients with muscle-tendon pain in defined clinical entities; iliopsoas, abductor, adductor, hamstring, rectus abdominis-related pain. Abbreviation: Abd. (abdominis).

Among the patients, 26% reported no muscle-tendon pain (negative tests in all clinical entities). Opposite this, 38% reported muscle-tendon pain in one clinical entity, 27% reported pain in two clinical entities, 6% reported pain in three clinical entities and 3% reported pain in four clinical entities.

Association between patient-reported outcome and muscle-tendon pain

The analyses showed that there was a statistically significant inverse linear association between HAGOS scores and the sum of painful clinical entities (Table 8). In patients of same age and sex, a difference of one painful clinical entity was associated with a 3-8-point lower HAGOS score across all subscales.

	Crude		Adjusted	
Dependent variable	β Coefficient (95% CI)	p-value	β Coefficient (95% CI)	p-value
HAGOS Pain	-6.8 (-10.1 to -3.5)	< 0.001	-6.9 (-10.2 to -3.6)	< 0.001
HAGOS Symptoms	-6.3 (-9.5 to -3.0)	< 0.001	-6.3 (-9.6 to -3.1)	< 0.001
HAGOS ADL	-7.2 (-11.4 to -2.9)	0.001	-7.5 (-11.5 to -3.5)	< 0.001
HAGOS Sport/recreation	-7.1 (-11.0 to -3.2)	< 0.001	-7.4 (-11.2 to -3.6)	< 0.001
HAGOS Participation	-5.7 (-10.6 to -0.9)	0.02	-6.1 (-10.9 to -1.3)	0.01
HAGOS Quality of life	-3.2 (-6.0 to -0.4)	0.03	-3.4 (-6.1 to -0.6)	0.02
	1 C 1 .1 1		1	~ .

Table 8. Association between each HAGOS subscale and the sum of painful clinical entities (n=100)

Abbreviations: ADL (physical function in daily living), HAGOS (Copenhagen Hip and Groin Outcome Score). Adjustment were made for age and sex. Similar table published in Paper 1, Table 3.

Association between hip muscle strength and muscle-tendon pain

Similarly, a statistically significant inverse linear association was observed between isometric hip muscle strength and the sum of painful clinical entities (Table 9). In patients of same age and sex, a difference of one painful clinical entity was associated with 0.11-0.12 Nm/kg lower isometric hip muscle strength, corresponding to 9-11%.

Table 9. Associations between isometric hip muscle strength in four directions and the sum of painful clinical entities (n=100)

	Crude		Adjusted	
Hip muscle strength	β Coefficient (95% CI)	p-value	β Coefficient (95% CI)	p-value
Flexion	-0.12 (-0.23 to -0.02)	0.02	-0.11 (-0.21 to -0.01)	0.04
Abduction	-0.10 (-0.19 to -0.01)	0.02	-0.11 (-0.19 to -0.03)	0.01
Adduction	-0.12 (-0.21 to -0.03)	0.01	-0.12 (-0.20 to -0.03)	0.01
Extension	-0.14 (-0.28 to -0.01)	0.04	-0.12 (-0.25 to 0.01)	0.08
Adjustments were made for age and sex. Similar table published in Paper 1, Table 4.				

The mean isometric hip muscle strength ranged from 1.1 Nm/kg to 1.8 Nm/kg across all strength tests (Figure 15).





Paper 2

The intra- and inter-rater reliability of the standardised ultrasonographic examinations are reported in Tables 10 and 11. The reliability analyses tested whether the same rater and two raters agreed on recording the individual structures as abnormal or normal.

Table 10. Intra-rater reliab ultrasonographic examina	ility on recording each str tions (n=50)	ructure as abnormal or	r not as part of the standardised
Tissue	% Agreement	Kappa coefficient	Interpreted agreement (130)
Ilionsons tondon	80	0.64	Substantial

115500	70 Ingreement	Rappa coefficient	interpreted agreentein (150)		
Iliopsoas tendon	82	0.64	Substantial		
Glut. med./min. tendons	92	0.70	Substantial		
Adductor longus tendon	82	0.64	Substantial		
Hamstring tendons	84	0.60	Moderate		
Pubic symphysis	90	0.59	Moderate		
Acetabular labrum	76	0.51	Moderate		
Abbreviations: glut. med./min. (gluteus medius/minimus).					
Similar table published in Paper 2. Table 2 in Supplementary material.					

The agreement between the first and the second rating ranged from 76-92%, and the corresponding kappa coefficients ranged from 0.51-70, defined as moderate to substantial agreement. The agreement between rater B and the specialised radiologist ranged from 67-84% with kappa coefficients ranging from 0.19-46, defined as slight to moderate agreement.

Table 11. Inter-rater reliability on recording each structure as abnormal or not as part of the standardised ultrasonographic examinations (n=50)

Tissue	% Agreement	Kappa coefficient	Interpreted agreement	
Iliopsoas tendon	73	0.46	Moderate	
Glut. med./min. tendons	84	0.34	Fair	
Adductor longus tendon	64	0.29	Fair	
Hamstring tendons	74	0.42	Moderate	
Pubic symphysis	68	0.19	Slight	
Acetabular labrum	67	0.35	Fair	
Abbroviations: glut mod /min (glutous modius /minimus)				

Abbreviations: glut. med./min. (gluteus medius/minimus).

Similar published in Paper 2, Table 2 in Supplementary material.

Ultrasonographic findings

Abnormal ultrasonographic findings most commonly involved the iliopsoas tendon, the adductor longus tendon and the gluteal medius and minimus tendons, but abnormality of the acetabular labrum was also common (Table 12). Analyses investigating correlations between abnormal ultrasonographic findings and clinically identified pain in the iliopsoas and gluteus medius/minimus tendons proved statistically significant correlations (Table 13). However, no statistically significant correlations were found for the other anatomical structures.

	······································)		
Anatomical structure	Transducer placement	% abnormalities (95% CI)		
Iliopsoas tendon	Transverse scan with the femoral artery as medial landmark	50 (40 - 60)		
Glut. med./min. tendons	Longitudinal and transverse scan with the greater trochanter as landmark	27 (18 - 36)		
Adductor longus tendon	Longitudinal scan with the inferior ramus of the pubis as proximal landmark	31 (22 - 40)		
Hamstring tendons	Longitudinal and transverse scan with the ischial tuberosity as landmark	15 (8 - 22)		
Pubic symphysis	Transverse scan at the symphyseal cleft	9 (3 - 15)		
Acetabular labrum	Longitudinal scan parallel to the long axis of the femoral neck	55 (45 - 65)		
Abbreviations: glut. (gluteus), med. (medius), min (minimus). Similar table published in Paper 2, Table 4.				

Table 12. Proportion of patients with abnormal ultrasonographic findings (n=100)

Table 13. Correlations between abnormal structures identified with ultrasonography and clinically identified pain in five clinical entities (n=100)

Iliopsoas tendon US				Glut. med./min	. tendons US
Clinical entity	Rho	p-value	Clinical entity	Rho	p-value
Iliopsoas-related			Abductor-related	0.35	< 0.001
pain	0.24	0.02	pain		
	Adductor longu	s tendon US		Hamstring	g tendons US
Clinical entity	Rho	p-value	Clinical entity	Rho	p-value
Adductor-related			Hamstring-	0.04	0.69
pain	0.04	0.68	related pain		
	Pubic sy	mphysis US			
Clinical entity	Rho	p-value			
Rectus abdominis-					
related pain	0.11	0.26			
Abbreviations: glut. m	ed./min. (gluteus				
medius/minimus), US	6 (ultrasonography	⁷).			
Similar table published	d in Paper 2, Table				

Paper 3

Patient-reported outcome

All subscales of the HAGOS improved statistically significantly from before to 1 year after PAO (Figure 16) with effect sizes ranging from 0.66-1.37 (Table 14). However, a floor effect was present for the HAGOS PA subscale, before PAO (33%) and after PAO (22%). After PAO, a ceiling effect was present for the HAGOS ADL subscale (20%). Moreover, about half of patients experienced no clinically relevant improvements in ADL and sport/recreation after PAO, indicated by HAGOS change scores < MIC (115), and about half of patients reported a HAGOS sports/recreation score ≤70 points after PAO (Figure 17).



Figure 16. HAGOS mean scores in each subscale with 95% CI (error bars).

Abbreviations: ADL (physical function in daily living), PA (physical activity participation), rec (recreation), PAO (periacetabular osteotomy), HAGOS (Copenhagen Hip and Groin Outcome Score).

Table 14. Change in HAGOS subscales from before to 1 year after periacetabular osteotomy (n=82)

	Change score	Effect size MIC ¹ % abo		% above MIC
Outcome score	Mean (95% CI)	Cohen´s d		
HAGOS Pain	26 (22 - 30)	1.37	10	82
HAGOS Symptoms	19 (15 - 23)	0.99	10	73
HAGOS ADL	27 (22 - 31)	1.25	11	72
HAGOS Sport/recreation	25 (20 - 31)	1.02	13	61
HAGOS PA	21 (14 - 28)	0.66	17	48
HAGOS Quality of life	28 (22 - 33)	1.11	13	73

Abbreviations: HAGOS (Copenhagen Hip and Groin Outcome Score), ADL (physical function in daily living), PA (physical activity participation), MIC (minimally important change). ¹MIC reported by Thomee et al. (115) in patients with femoroacetabular impingement syndrome undergoing hip arthroscopy.



Figure 17. Distribution of patients reporting a HAGOS sport/recreation score within four defined intervals (n=82). Abbreviations: HAGOS (Copenhagen Hip and Groin Outcome Score), PAO (periacetabular osteotomy).

Muscle-tendon pain

Overall, hip muscle-tendon pain decreased statistically significantly 1 year after PAO, corresponding to an effect size of -2.46 (Table 15). In individual entities, only iliopsoas-related and abductor-related pain decreased statistically significantly, while no statistically significantly differences were found for the other clinical entities from before to 1 year after PAO.

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Painful clinical entities	Before PAO	After PAO	Change		Effect size
	% (95% CI)	% (95% CI)	% points (95% CI)	p-value	Cohen's w
Iliopsoas-related	54 (42 - 65)	22 (14 - 32)	-32 (-46 to -17)	< 0.001	-1.96
Abductor-related	37 (26 - 48)	15 (8 - 24)	-22 (-36 to -8)	0.002	-1.12
Adductor-related	12 (6 - 21)	7 (3 - 15)	-5 (-16 to 6)	0.5	-0.11
Hamstring-related	6 (2 - 14)	1 (0 - 7)	-5 (-12 to 2)	0.2	-0.29
Rectus-abdominis-related	4 (0 - 10)	0 (0 to 0)	-4 (-9 to 2)	0.3	-0.33
Patients with minimum 1 positive clinical entity	74 (64 to 83)	35 (25 - 47)	-39 (-54 to -24)	<0.001	-2.46
Abbreviations: PAO (periacetabular osteotomy). Similar table published in Paper 3, Table 3.					

Table 15. Change in muscle-tendon pain reported separately for each clinical entity and as the sum of painful clinical entities from before to 1 year after PAO (n=82)

Association between subscales of the HAGOS and muscle-tendon pain

Besides HAGOS PA, a statistically significant inverse linear association was observed between changes across all subscales of the HAGOS and change in the sum of painful clinical entities from before to 1 year after PAO (Table 16). In patients of same age, sex and pre- and postsurgical CE angle, a decrease of one painful clinical entity was associated with an increase of 5-8 HAGOS points across all subscales, besides HAGOS PA.

Table 16. Association between change in each subscale of the HAGOS and change in the sum of
painful clinical entities from before to 1 year after periacetabular osteotomy (n=82)

—				
	Crude		Adjusted*	
Outcomes	β Coefficient (95% CI)	p-value	β Coefficient (95% CI)	p-value
HAGOS Pain	-4.7 (-8.5 to -0.9)	0.02	-4.7 (-8.4 to -1.0)	0.01
HAGOS Symptoms	-4.8 (-8.6 to -1.0)	0.02	-4.7 (-8.6 to -0.9)	0.02
HAGOS ADL	-6.1 (-10 to -1.9)	0.005	-6.2 (-10 to -2.1)	0.004
HAGOS Sport/recreation	-5.9 (-11 to -1.0)	0.02	-6.0 (-11 to -0.9)	0.02
HAGOS PA	-1.2 (-7.9 to 5.5)	0.7	-1.2 (-7.9 to 5.6)	0.7
HAGOS Quality of life	-8.2 (-13 to -3.3)	0.001	-8.2 (-13 to -3.3)	0.001
*A divisted for pre- and postsu	rgical Centre-edge angles	age and sev	Abbreviations: HACOS	

*Adjusted for pre- and postsurgical Centre-edge angles, age and sex. Abbreviations: HAGOS (Copenhagen Hip and Groin Outcome Score), ADL (physical function in daily living), PA (preferred physical activity participation). Similar table published in Paper 3, Table 4.

Paper 4

Accelerometer-based physical activity

The accelerometer-based physical activity was measured during median 7 days (IQR 3-8); in six patients, physical activity was measured during less than 5 days. From

before to 1 year after PAO, changes ranged from -0.66% (CI -2.2 – 0.89) to 1.6% (CI - 0.89 – 4.0) across all intensity levels (from very low to high intensity) (Table 17). Furthermore, patients were sedentary in about 75% of their time, while only about 5% of their time was spent on activities at high intensity level (Figure 18). A general physical activity profile, measured before and 1 year after PAO, is reported in Table 18 in patients with full accelerometer-based data.

Outcomes	Change (95% CI)	p-value	Effect size
Change in percent of time			
Very low intensity	1.6 (-0.89 - 4.0)	0.2	0.14
Low intensity	-0.66 (-2.2 - 0.89)	0.4	-0.096
Moderate intensity	-0.40 (-1.1 - 0.31)	0.3	-0.13
High intensity	-0.32 (-0.77 - 0.13)	0.2	-0.16
Table values reported in Paper 4	Table 2		

Table 17. Change in accelerometer-based physical activity at four intensity levels from before to 1 year after surgery (n=77)



Figure 18. Percentage of time with 95% CI (error bars) at four intensity levels measured objectively before and 1 year after periacetabular osteotomy (n=77). Abbreviations: PAO (periacetabular osteotomy).

Patient-reported physical activity

Patient-reported participation in physical activities increased statistically significantly with 22 (CI 14 – 29) HAGOS PA points, corresponding to an effect size of 0.67 (Figure 19).

	Befo	ore (n=97)	1 year after	PAO (n=78)
Outcomes	Median	95% CI	Median	95% CI
Cadence as steps/min	99	98 - 100	100	98 - 102
Numbers of events/day				
Total steps	7404	6645 - 8418	7925	6637 - 8612
Steps (level)	6923	6192 - 7709	7322	6081 - 8217
Steps (up)	266	194 - 403	235	171 - 313
Steps (down)	155	134 - 183	146	123 - 169
Time in hours/day				
Total wear time	14	14 - 15	15	14 - 15
Time as percent				
Resting	64	61 - 68	63	59 - 66
Standing	23	22 - 27	26	23 - 27
Walking	11.2	9.9 - 12.5	11.0	9.3 - 12.5
Cycling	0.15	0.063 - 0.33	0.084	0.046 - 0.18
Running	0.011	0.0042 - 0.020	0.0078	0.0040 - 0.025
Abbreviations: PAO (periace	etabular osteoto	mv). Similar table r	ublished in pa	per 4. Table 3.

Table 18. General phys	ical activity profile measured with accelerometer-based sensors
before and 1 year after	periacetabular osteotomy



Figure 19. Mean values with 95% CI (error bars) measured with the Copenhagen Hip and Groin Outcome Score using the subscale participation in physical activity (0-100 points). Abbreviations: PAO (periacetabular osteotomy).

Association between accelerometer-based and patients-reported physical activity

Change in accelerometer-based physical activity was not statistically significantly associated with change in the HAGOS PA subscale as illustrated in Figure 20. The associations correspond to a percentage change in physical activity of only 0.022% for a change in 10 HAGOS PA points, covering very low, low, moderate and high intensity from before to 1 year after PAO (Table 19).

Table 19. Association between change in accelerometer-based physical activity and change in the HAGOS PA subscale from before to 1 year after periacetabular osteotomy (n=77)

	, <u>,</u>	
Outcomes	β Coefficient (95% CI)	p-value
Very low intensity	-0.00011 (-0.00087 -0.00065)	0.8
Low intensity	-0.000022 (-0.00050 - 0.00046)	0.9
Moderate intensity	0.000044 (-0.00018 - 0.00027)	0.7
High intensity	0.000072 (-0.000066 - 0.00021)	0.3
Abbreviations: HAGOS (Coper	nhagen Hip and Groin Outcome Score), PA	(preferred physical
activity participation).		



Figure 20. The prediction of change in accelerometer-based physical activity at high intensity as a linear function of change in the HAGOS PA subscale from before to 1 year after periacetabular osteotomy. Abbreviations: HAGOS (Copenhagen Hip and Groin Outcome Score), PA (physical activity). Similar figure published in Paper 4, Figure 2.

8. Discussion

Key findings

The overall aim of this PhD dissertation was to investigate muscle-tendon pain and structural abnormalities and outcome of hip-preserving surgery in patients with hip dysplasia. The overall results showed that muscle-tendon pain and structural abnormalities were common in hip dysplasia, and that muscle-tendon pain was negatively related to PRO and isometric hip muscle strength. Moreover, PRO improved after surgery; however, accelerometer-based physical activity did not change from before to 1 year after hip-preserving surgery.

Prior to PAO, muscle-tendon pain and abnormal ultrasonographic findings were common and primarily affected the iliopsoas and hip abductor muscles. The subscales of the HAGOS were negatively related to muscle-tendon pain and hip muscle strength. One year after PAO, patients reported medium to very high improvements across all subscales of the HAGOS, and improvements were related to decreased muscle-tendon pain. Nevertheless, about one-third of patients still experienced muscle-tendon pain 1 year after PAO, while about half of patients experienced no clinically relevant improvements in ADL and sport/recreation after PAO, indicated by HAGOS change scores < MIC for each subscale (115); and they reported a HAGOS sports/recreation score ≤70 points after PAO. Noteworthy, the HAGOS PA score was not related to change in muscle-tendon pain despite statistically significant improvements, and the improvement in the HAGOS PA did not manifest itself in any change in accelerometer-based physical activity either at low-intensity or high-intensity levels.

Comparison with the existing literature

Study results will be compared to the existing literature and the body of evidence will be evaluated in accordance with the Method Guidelines for Cochrane Musculoskeletal Group Systematic Reviews and Metaanalyses (131).

Muscle-tendon pain in the hip and groin

Hip dysplasia has been described as a cause of increased micro-instability of the hip joint. Especially the iliopsoas, gluteal muscles and hip adductors are considered important dynamic stabilisers in the dysplastic hip joint (132,133). Even so, Papers 1-3 are the first papers systematically reporting muscle-tendon pain and structural abnormalities in hip dysplasia. Clinically identified muscle-tendon pain has been described in five studies (47,49,50,55,134), and these studies are tabulated in Table 20. Among athletes, adductor-related pain was the most common painful clinical entity followed by iliopsoas- and abdominal/inguinal-related pain (47,49,50). This fit well with the primary sports of the athletes, comprising kicking and change of directions which involve high tensile and compressive loads to the adductors (50). However, the combined body of evidence to support this relationship is low. Adductor-related pain was less common in our patients (1,3), which makes good sense, as the patients' preferred sports were far more heterogeneous (4).

				-		
Study	Design	Population	Methods	Results		
Hölmich (2007) (47)	Cross- sectional study	207 athletes (196 males) with longstanding groin pain, age 26 (16–48).	Pain examined with the clinical entity approach (palpation, testing against resistance, flexibility, and/or cough impulse).	119 (58%) patients had adductor-related pain and 73 (35%) iliopsoas- related pain.		
Woodley et al. (2008) (55)	Cross- sectional study	40 patients (3 males) with lateral hip pain, age 54 (33–78).	Clinical examinations (palpation GT, FABER test, Ober´s test and resisted hip abduction).	36 (90%) patients reported pain in gluteal muscles and tendons, where GT palpation identified 32/40 symptomatic hips.		
Hölmich et al. (2014) (49)	Cohort study	998 sub-elite male soccer players during a 10-month season, age 25 (SD 5).	Pain examined with the clinical entity approach (palpation, testing against resistance, flexibility, and/or cough impulse).	30 (51%) patients had adductor-related pain, 11 (19%) abdominal- related pain, and 18 (30%) iliopsoas-related pain.		
Adib et al. (2018) (134)	Case series	252 patients (94 males, 37%) undergoing hip arthroscopy, age 22 (10–57).	Clinical examination (pain with resisted hip flexion in seated position OR pain during psoas stretch test).	60 (24%) patients had post-operative iliopsoas tendinopathy.		
Taylor et al. (2018) (50)	Cross- sectional study	100 athletes (98 males) with acute (n=31) and gradual onset (n=68) of groin pain, age 28 (15–52).	Clinical examinations, using Doha Agreements (palpation, testing against resistance, stretching, and/or Valsalva/cough.	61% patients had adductor-related pain, 40% inguinal-related pain and 31% iliopsoas-related pain.		
Abbreviations: GT (greater trochantor), FABER (flexion/abduction/external rotation).						

In patients with lateral hip pain, pain in gluteal muscles and tendons has been reported in 90% of the patients (55). This result is only supported by one low-quality study and the evidence is therefore considered very low. Nevertheless, gluteal pathology has also been identified with MRI and ultrasonography in patients with lateral hip pain (55,135), suggesting that gluteal pathology could be a possible extraarticular source of pain in patients with lateral hip pain. Iliopsoas tendinopathy has been found in 24% of patients undergoing hip arthroscopy due to labral lesions (134). Again, the evidence to support iliopsoas tendinopathy rests on a single case series study, and the evidence is therefore considered very low. In patients with lateral hip pain, hip abductor deficit and increased hip adduction during walking were associated with lateral hip pain (136,137), where iliopsoas tendinopathy in patients with labral lesions might be explained by the anatomical proximity of the acetabular labrum and the iliopsoas tendon (44). In this study (1,3), pain in the gluteal and iliopsoas muscles and tendons was also frequent in patients with hip dysplasia, and similar mechanisms as those described above may be evident. Coexisting intraarticular pathology has been reported in the above-mentioned study populations. In athletes with long-standing adductor-related groin pain, radiological signs of FAIS were found in 94% (138). Hip osteoarthritis was found in 20% of patients with lateral hip pain (55), while 92% of patients undergoing hip arthroscopy presented with bone morphology, either hip dysplasia or FAIS (134). The above-mentioned results support our findings since our patients all had an intra-articular joint disease and coexisting muscle-tendon pain (1,3).

Noteworthy, about 20% of our patients reported severe and worst imaginable back pain, and this pain did not improve considerably after PAO. Moreover, when applying the springing palpation test to the spine and sacrum, we found that 10-15% of the patients reported known hip pain. However, this pain improved after PAO and affected 3-4% of the patients after PAO. These findings indicate a possible relationship between hip dysplasia and back pain. However, the role of back pain in hip dysplasia needs to be assessed further in future prospective studies.

Abnormal ultrasonographic findings in the hip and groin

Abnormal ultrasonographic findings have been reported in two studies (52,135) (Table 21). In patients with longstanding groin pain, muscle-tendon abnormalities were most commonly located to the tendons of the hamstrings, the hip adductors, the rectus femoris and the gluteal muscles (52). In most cases (28/36), abnormal ultrasonographic findings were located to the painful anatomical regions. However, the body of evidence to support muscle-tendon abnormalities in these patients is very low. Abnormal findings have also been reported among patients with lateral hip pain, most commonly located to the gluteal tendons and the iliotibial band. Noteworthy, only 8% of the patients had isolated trochanteric bursitis. Again, studies are lacking, and evidence to support findings in these patients is considered very low (131).

Patient-reported outcome after PAO

Several studies have shown clinically relevant improvements in PRO after PAO, using both generic and disease-specific PROMs. In Paper 3, outcome 1 year after PAO was investigated with the HAGOS; and as mentioned before, HAGOS was originally developed from the HOOS (139) and three items from the HOS (140). The HAGOS, HOOS and HOS report outcome in individual subscales, covering body function and structure, activity and participation according to the International Classification of Functioning, Disability and Health (ICF) (113). In patients with hip

Study	Design	Population	Methods	Results
Kälebo et al. (1992) (52)	Cross- sectional study	36 patients (28 males) with longstanding groin pain, age 27 (14–57).	Ultrasonographic examinations of the tendons of the hamstrings, adductors, rectus femoris, gluteal muscles and rectus abdominis muscles.	Abnormal findings primarily involving the hamstring tendons followed by the tendons of the adductors, rectus femoris, gluteal muscles and rectus abdominis muscles.
Long et al. (2013) (135)	Cross- sectional study	877 patients (275 males) with lateral hip pain, age 54 (15- 87).	Ultrasonographic examinations. Retrospective review of gluteal tendon abnormalities, iliotibial band abnormalities and trochanteric bursitis.	438 (50%) patients had gluteal tendinopathy, 250 (29%) thickened iliotibial band, 177 (20%) trochanteric bursitis and only 70 (8%) isolated bursitis.

Table 21. Studies reporting abnormal ultrasonographic findings in hip and/or groin disorders

dysplasia, PRO after PAO using either the HAGOS, HOOS or HOS are reported in seven studies (Table 22). HAGOS was used as PROM in the studies by Jacobsen et al. (97) and Mechlenburg et al. (77), reporting HAGOS change scores similar to those reported in Paper 3. However, both the pre- and postsurgical HAGOS scores are higher in these studies than reported in this study (3), indicating that the patients may experience more pain and disability. In the previous studies (77,97), 32 and 41 patients were included over a period of 10 and 15 months, respectively. Compared to these study populations, this study included 100 patients over a period of 16 months (1-4). These differences could indicate that patients included in the previous studies represent a more selective study population than the patients in this study. In this study (3), outcomes were collected at two time points, while outcomes were collected at three time points in the previous studies (77,97). This may explain why patients with lower PRO may have been harder to recruit in the two previous studies. Moreover, one inclusion criterion also differed between this study (1-4) and the study by Mechlenburg et al. (77). In the latter study, only patients living less than 70 km away from the hospital were included (i.e. patients living close to a large Danish city), while all Danish patients with hip dysplasia - scheduled for PAO in Aarhus were invited to participate in this study (1-4). In five studies, PRO after PAO was investigated with either the HOOS (16,141-143) or the HOS (144). Comparing the pre- and postsurgical HOOS and/or HOS scores with the postsurgical HAGOS scores reported in this study (3), we found that the HOOS and/or HOS scores were generally higher, which makes sense since the HAGOS covers more demanding physical, sport and recreational tasks (113). However, the body of evidence to support the above-mentioned findings is considered low as the majority of the studies are case series studies.

Study	Patients	Follo	PROM	Res	Effect size	
		w-up		Mean pre PAO	Mean post PAO	
Jacobsen et al. (2014) (97) <i>Case series</i>	29 patients. Age 34 (18-53).	1 yr.	HAGOS	Pain ¹ : 50 (20-95) Sym ¹ : 50 (21-96) ADL ¹ : 60 (5-100) Sp/rec ¹ : 38 (3-91) PA ¹ : 25 (0-100) QOL ¹ : 40 (0-80)	Pain ¹ : 78 (20-100) Sym ¹ : 71 (25-93) ADL ¹ : 90 (30-100) Sp/rec ¹ : 63 (6-100) PA ¹ : 50 (0-100) QOL ¹ : 65 (10-100)	NC
Mechlenburg et al. (2018) (77) <i>Case series</i>	41 patients. Age 29 (SD 9).	1 yr.	HAGOS	Pain ² : 57 (46-68) Sym ² : 53 (43-67) ADL ² : 62 (53-78) Sp/rec ² : 43 (32-66) PA ² : 12 (0-38) QOL ² : 35 (26-45)	Pain ² : 75 (65-92) Sym ² : 72 (61-86) ADL ² : 90 (70-95) Sp/rec ² : 67 (50-88) PA ² : 37 (13-76) QOL ² : 57 (40-80)	NC
Bogunovic et al. (2014) (141) <i>Case series</i>	36 patients. Age 25 (15-45). Pre UCLA score ≥7.	1.5-5 yr.	HOOS	Pain: 61 Sym: 64 ADL: 73 Sp/rec: 48 QOL: 38	Pain: 86 Sym: 85 ADL: 94 Sp/rec: 80 QOL: 71	NC
Clohisy et al. (2017) (16) <i>Case series</i>	950 patients. Age 25 (10-54).	3 (2- 5) yr.	HOOS	Pain: 56 Sym: 59 ADL: 68 Sp/rec: 46 QOL: 35	Pain: 84 Sym: 79 ADL: 90 Sp/rec: 77 QOL: 70	Pain: 1.3 Sym: 1.0 ADL: 1.0 Sp/rec: 1.0 QOL: 1.3
Maeckelbergh et al. (2018) (142) <i>Case series</i>	42 patients. Age 27 (14-50).	3 (1- 5) yr.	HOOS	Pain ³ : 41 (0-93) Sym ³ : 39 (5-80) ADL ³ : 53 (0-99) Sp/rec ³ : 28 (0-81) QOL ³ : 34 (0-81)	Pain ³ : 84 (48-100) Sym ³ : 79 (40-100) ADL ³ : 89 (57-100) Sp/rec ³ : 74 (19-100) QOL ³ : 73 (31-100)	NC
Boje and Caspersen et al. (2019) (143) <i>Case series</i>	321 patients. Age 31 (22-39).	1 yr.	HOOS	Pain: 53 (SD 18) Sym: 52 (SD 20) ADL: 64 (SD 20) Sp/rec: 43 (SD 23) QOL: 33 (SD 16)	Pain: 78 (SD 20) Sym: 71 (SD 22) ADL: 84 (SD 18) Sp/rec: 69 (SD 25) QOL: 59 (SD 25)	Pain: 1.1 Sym: 0.8 ADL: 1.0 Sp/rec: 0.9 QOL: 1.0
Ricciardi et al. (2017) (144)	<i>Mild HD</i> n=27. Age 25 (15-43).	1 yr.	HOS	<i>Mild HD</i> ADL: 72 (SD 13) Sport: 53 (SD 21)	<i>Mild HD</i> ADL 93 (SD 8) Sport 82 (SD 19)	<i>Mild HD</i> ADL: 1.4 Sport: 1.0
Cohort study	<i>Severe HD</i> n=50. Age 23 (12-41).			<i>Severe HD</i> ADL: 72 (SD 14) Sport: 53 (SD 20)	<i>Severe HD</i> ADL: 92 (SD 12) Sport: 85 (SD 20)	<i>Severe HD</i> ADL: 1.1 Sport: 1.1

Table 22.	Studies	reporting	patient	-reported	outcome	of the	PAO
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Abbreviations: PAO (periacetabular osteotomy), PROM (patient-reported outcome measure), HAGOS (Copenhagen Hip and Groin Outcome Score), sym (symptoms), ADL (physical function in daily living), sp/rec (sport/recreation), QOL (quality of life), PA (participation in preferred physical activities), HOOS (Hip Osteoarthritis Outcome Score), UCLA (University of California Los Angeles activity score), HOS (Hip Outcome Score), HD (hip dysplasia). ¹Median (range), ²Median (interquartile range), ³Mean (range), NC (not calculated), SD of chance score was not reported or could not be calculated (e.g. no reported standard error or 95% CI).

Noteworthy, in this study (3), 20% of patients reported the highest possible outcome for the HAGOS ADL subscale after PAO, indicating a ceiling effect of this subscale. In line with this finding, Boje and Caspersen et al. (143) reported a ceiling effect for the HOOS ADL subscale. This suggest the presence of some limitations of the HAGOS ADL subscale despite the fact that the HAGOS was developed to measure PRO in young and active subjects. Similarly, 33% of our patients reported the lowest possible outcome for the HAGOS PA subscale before PAO, and 22% reported the lowest outcome 1 year after PAO, indicating a considerable floor effect for the HAGOS PA subscale (3). Floor and ceiling effects for the HAGOS ADL and PA subscales have also been reported in patients with hip and/or groin pain, in patient undergoing hip arthroscopy and in patients with FAIS (101,114,115). This suggests that certain limitations should be considered when measuring PRO with the HAGOS PA and ADL subscales.

The iHOT-12 and iHOT-33 are also recommended as PROMs in young-to-middleaged patients with hip pain (101,116–118). However, the iHOT-12 and iHOT-33 report outcome in one composite score. The latter is opposed to the HAGOS, making comparison more difficult. However, Ricciardi et al. (144) reported outcome of the PAO using the iHOT-33 in 77 patients grouped as having mild or severe hip dysplasia. Patients improved from 35 and 36 point before PAO to 79 and 78 points 1 year after PAO, corresponding to effect sizes of 1.8 and 1.4, respectively. These effect sizes are higher than the effect sizes reported in this study (3). However, the effect size for the HAGOS pain subscale was 1.4 (3), which is similar to the results reported in the study using the iHOT-33 in patients with severe hip dysplasia.

Accelerometer-based physical activity

Contrary to the large improvements in all subscales of the HAGOS (3), no changes in accelerometer-based physical activity were found after PAO in this study (4). Changes in accelerometer- and pedometer-based physical activity have been reported in patients with hip dysplasia, hip osteoarthritis and FAIS (77,103,145–150) (Table 23). Clinically relevant improvements were reported in three studies (149,151,152) measuring changes in daily steps, daily strides and accelerometer-based physical activity from before to after hip or knee arthroplasty. However, in one study (151), physical activity was measured during 2 days, which raises questions concerning the validity of the results since physical activity should be measured over at least 3 days to represent daily physical activity (153). Moreover, in another study, 40% of patients were lost to follow-up, and these patients had other characteristics than the patients who completed the follow-up (152). Their baseline PRO were higher, and they took more steps than patients completing the follow-up (152). This suggests that the observed changes could have been overestimated. Of note, in the Horsens-Aarhus Femoro-Acetabular Impingement (HAFAI) study (103), minor changes in resting and standing were reported after hip arthroscopy.

Study	Design	Population	Follow-	Outcomes	Results
De Groot et al. (2008) (151)	Case series	80 patients scheduled for THA or TKA. Age 62 (SD 11).	0.5 yr.	2 days daily PA with 3 accelerometer- based activity sensors. PRO by WOMAC, HHS, KSS and SF-36 PASIPD.	%PA improved for total group by 0.7%, p=0.03. STS improved for total group, p<0.001). PRO improved, p<0.001.
Vissers et al. (2011) (145)	Case series	30 patients scheduled for THA. Age 60 (SD 13). 30 references. Age 60 (SD 13).	0.5 yr.	Daily PA by 3 accelerometer- based activity sensors.	No changes in overall PA, in %walking, walking periods or chair rises. References did more overall PA, %walking and walking bouts, p<0.05.
Fujita et al. (2013) (152)	Case series	38 patients scheduled for THA. Age 61 (43- 82). 38 references. Age 62 (41-83).	1 yr.	7 days PA with a pedometers. PRO by SF-8 and OHS.	Steps/day improved, 4,632 (SD 2,246) to 6,163 (SD 2,410), p<0.001. Time in light/moderate PA increased (p<0.01). At 12 mo., references did more vigorous PA than patients (p=0.003). PRO improved, p<0.001.
Lin et al. (2013) (146)	Case series	12 adult females scheduled for THA. Age 58 (SD 4).	0.5 yr.	7 days PA with RT3 accelerometer. PRO with HHS.	No changes in PA. HHS improved, p=0.03.
Harding et al. (2014) (147)	Case series	44 patients scheduled for THA (n=19) or TKA (n=25). Age 69 (SD 8).	0.5 yr.	7 days PA with ActiGraph GT1M accelerometer. PRO with NRS, OHS, SF-12 and UCLA score.	No changes in daily PA, 149 (SD 133) versus 161 (SD 86) cpm, p=0.12. PRO improved, p<0.01.
Jeldi et al. (2017) (148)	Case series	30 patients scheduled for THA. Age 67 (50- 82).	1 yr.	6 days PA by activPAL3. PRO with HHS, OHS.	No change in daily PA. PRO improved (p<0.01).
Höll et al. (2018) (149)	Case series	46 patients scheduled for THA. Age 63 (SD 11).	0.25 yr.	7 days daily strides by a Stepwatch activity monitor PRO by HHS and WOMAC.	Strides/day and strides/hour improved by 18 and 15% (p<0.05). PRO improved (p<0.01).

Table 23. Accelerometer-based physical activity after surgery in subjects with hip and/or groin pain

Mechlenburg et al. (2018) (77)	Case series	23 patients with HD undergoing PAO. Age 29 (SD 9).	1 yr.	5 days PA by 3D accelerometers. PRO with HAGOS.	No changes in sitting, standing, walking and running time or STS transfers or cadence from 4 mo. to 12 mo. after PAO. Less cycling at 12 mo. compared to 4 mo., p=0.04.
Kierkegaard et al. 2019 (103)	Case series	60 patients with FAIS scheduled for hip arthroscopy. Age 36 (SD 9). 30 references. Age 36 (SD 9).	1 yr.	5 days PA by a tri-axial accelerometer. PRO with HAGOS.	No change in overall PA. Patients rested less (p=0.01) and stood more (p=0.02) after surgery. References were bicycling and running more (p<0.01). All HAGOS subscales improved (p<0.001).
Birch et al. 2020 (150)	Case series	37 patients scheduled for THA Age 75 (70 – 82). 29 age-matched references.	1 yr.	7 days PA by a tri-axial accelerometer. PRO with OHS.	No change in time, frequency or intensity of PA after THA. 12 mo. after THA, no differences in walking, standing, sitting or cycling between references and patients. At 12 mo., patients did fewer sit-to-stand transfers per hour than references, 0.2 (95%CI - 0.8 - 0.4).

Abbreviations: THA (total hip arthroplasty), TKA (total knee arthroplasty), PAO (periacetabular osteotomy), PA (physical activity), PRO (patient-reported outcome), WOMAC (Western Ontario and McMaster Universities Arthritis Index), HHS (Harris Hip Score), KSS (Knee Society Score), SF (Short Form health survey), PASIPD (Physical Activity Scale for Individuals with Physical Disabilities), STS (sitto-stand), OHS (Oxford Hip Score), NRS (numeric rating scale), UCLA (University of California-Los Angeles activity score), cpm (counts per minute), HD (hip dysplasia), FAIS (femoroacetabular impingement syndrome).

These changes are believed to be small and considered less clinically relevant. Therefore, only Höll et al. (149) seem to show valid improvements in daily strides 3 months after surgery in patients undergoing hip arthroplasty (149). Hence, a low level of evidence supports that no changes and/or only minor changes in accelerometer-based physical activity can be expected after hip surgery. This is supported by a systematic review from 2017, concluding "There is no statistically significant difference in physical activity levels before and up to one year after unilateral primary total hip replacement" (102). Contrary to this, large improvements can be expected if physical activity is patient-reported.

Noteworthy, in four studies (103,145,150,152), accelerometer-based physical activity was compared between patients and pain-free references. Across studies in patients

undergoing arthroplasty (145,150,152), references performed more overall physical activity, walked more, performed more sit-to-stand transfers per hour and performed more vigorous accelerometer-based physical activity than patients at 12month follow-up. In the HAFAI study (103), references ran and bicycled more than patients undergoing hip arthroscopy at 12-month follow-up. In summary, the above findings indicate that patients do not reach the references level of daily physical activity. However, the references from the HAFAI study were volunteers responding to an advertisements at Aarhus University and Aarhus University Hospital (103). These volunteers may share different characteristics than the rest of the healthy Danish population. They might volunteer because they are more health conscious and therefore more active, which may lead to overestimation of the differences between patients and references. However, Vissers et al. (145) and Birch et al. (150) found that references did more overall physical activity and did more sit-to-stand transfers per hour than patients. The references were included via an existing database (145) and via the Danish Central Person Register (CPR) (150), which is probably less impacted by healthy volunteer bias than the references in the HAFAI study (103). Hence, differences between patients and references probably do exist.

Interestingly, if the physical activity profile of our patients is compared to the physical activity profile of the references from the HAFAI study, we see that our patients also did more resting and less running 1 year after PAO (4,103). This comparison indicates that patients with FAIS and patients with hip dysplasia have a similar level of physical activity 1 year after surgery. This is supported by Harris-Hayes et al. (21), reporting no differences in daily strides between patients with hip dysplasia and FAIS.

Possible mechanism and explanations

Muscle-tendon pain and structural abnormalities in hip dysplasia

The causal relationship between hip dysplasia and muscle-tendon pathology is difficult to investigate and remains unanswered by our papers (1–3). However, the findings indicate a possible mechanism. In hip dysplasia, the acetabular weightbearing area is reduced with reduced acetabular coverage of the femoral head (154). The reduced weight bearing area allows more anterior, superior and lateral migration of the femoral head, and patients with dysplastic hips therefore have to rely more on extra-articular structures (i.e. acetabular labrum, ligaments and muscles) (133). An example of this has recently been reported, showing an association between the degree of acetabular coverage and the length of the acetabular labrum (25). However, in another study, it was demonstrated that the level of pain was not related to the degree of labral lesions (30), which suggests that other structures may also compensate and cause pain.

Reduced acetabular coverage in hip dysplasia has been associated with an increased role of the hip abductors (34,41,42). In hip dysplasia, the hip joint centre lateralizes secondary to the dysplastic acetabular coverage. This leads to reduced moment arms of the hip abductors (42), which implies that they have to generate higher medially directed forces to stabilise the femoral head in the socket (34,42). Hence, the hip abductors are prone to pain and structural abnormalities secondary to compensatory loading. Likewise, the iliopsoas muscle-tendon unit is located directly anterior to the hip joint (44). With reduced anterior acetabular coverage, the iliopsoas may therefore also be prone to pain and structural abnormalities secondary to compensatory loading, as shown for the hip abductors. Moreover, the iliopsoas muscle/tendon unit may also be prone to pain and structural abnormalities due to increased mechanical compression secondary to labral lesions and hypertrophy, which may explain why patients with hip dysplasia walk with reduced hip extension and a lower hip flexor moment (33).

Interestingly, after PAO, the hip joint centre is translated medially, which improves the anterior and lateral acetabular coverage of the femoral head (155) and the biomechanical conditions. Hypothetically, the PAO should reduce compensatory loading of the hip abductors and iliopsoas, leading to decreased muscle-tendon pain after PAO. The latter was confirmed in Paper 3, showing significant decreases of muscle-tendon pain in the iliopsoas and hip abductors. Additionally, the results of Paper 3 showed an association between improved PRO and decreased muscletendon pain, indicating a relationship between hip dysplasia, muscle-tendon pain and PRO.

The results of Papers 1-3 do not answer any questions about causality. However, the results do suggest that reduced acetabular coverage in hip dysplasia is related to pain and structural abnormalities primarily involving the iliopsoas and hip abductors. However, it remains unanswered if acetabular coverage is responsible for pain and structural abnormalities in hip dysplasia. The opposite pathway, where muscle-tendon pain and abnormalities cause bony morphology, seems unlikely and further support that acetabular coverage may partially be responsible for muscle-tendon pain in hip dysplasia.

Association between patient-reported outcome and muscle-tendon pain

In Paper 1 and 3, statistically significant associations between muscle-tendon pain and HAGOS subscales were reported. Before PAO, a difference of one painful clinical entity was associated with a 3-8 points lower HAGOS score across all subscales (1). Similarly, 1 year after PAO, a decrease of one painful clinical entity was associated with an increase of 5-8 HAGOS points across all subscales (3). These associations are considered clinically relevant for patients as regression coefficients were in line with the MIC of the HAGOS (113,115), indicating that the severity of pain is associated with PRO. This is supported by Terwee et al. (156), who reported that PROMs are more influenced by pain than performance-based measures of physical function. In patients with hip dysplasia, Boje and Caspersen et al. (143) proved statistically significant associations between changes in HOOS subscales and changes in the level of pain measured from before to 2 year after PAO. In line with this finding, Dierckman et al. (157) investigated associations between PROMs and VAS (0-10) in patients with FAIS. The results of the study showed that one unit difference in preoperative VAS was associated with 1 point lower score in PROMs. The results of the above-mentioned studies support our findings and indicate that PRO is related to severity and/or level of pain. Performance-based function such as accelerometer-based physical activity, on the other hand, covers a different aspect of physical function, which is also considered relevant.

Accelerometer-based physical activity

Patients with hip dysplasia experienced reduced pain and increased physical capacity after PAO (3), but the level of daily physical activity remained unchanged (4). Similar results have been reported in patients with hip osteoarthritis (77,145-149,158), where the level of physical activity was so low that it was considered a threat to patients' health (147). Therefore, measuring physical activity with accelerometer-based measures is important, as patient-reported methods would never recognize the actual, low level of daily physical activity in patients with hip osteoarthritis. However, in patients with hip dysplasia, the level of physical activity was within the levels recommended for healthy populations for both steps and cadence (4), indicating a level of physical activity from which patients may gain health benefits. Therefore, spending time and resources on motivating patients to increase their level of physical activity may not be relevant. On the other hand, hip dysplasia is a leading precursor of hip osteoarthritis (8,11), and the estimated prevalence of hip dysplasia in patients with hip osteoarthritis is 20-40% (159). Consequently, many patients with hip dysplasia will most likely adjust their physical activity to a low level over time; in older age, this could be a threat to their health. Minor differences in resting and running time seem to exist between patients with hip dysplasia and pain-free references when comparing our patients' physical activity profiles with those of pain-free references reported in the HAFAI study (4,103). This could indicate early adjustments in the patients' level of physical activity. Hence, patients with hip dysplasia should be encouraged to increase and/or preserve their level of physical activity. However, changing a lifestyle behaviour such as physical activity to boost health is difficult (160) and is influenced by perceptions and beliefs (160,161). Harding et al. (160) explored this matter 6 months after hip and knee arthroplasty, showing that patients recognised the importance of being physically active, but remained physically inactive due to other barriers than pain (147). Barriers to physical activity in patients with osteoarthritis are multifactorial and include: not perceiving a sedentary behaviour as harmful,

adjusting physical activity to a low level over time, perceiving physical activity as harmful or non-effective and finding other barriers than pain to physical activity (160,161). Similar barriers probably exist in patients with hip dysplasia. Therefore, health professionals should be aware of these barriers and try to facilitate daily physical activity by explicitly describing the physical and social gains of physical activity. Moreover, health professionals may engage in social policy to create facilitating environments where patients can engage in physical activity with people with similar physical capacities and age (161).

Key points - what this study adds

- 1. Muscle-tendon pain and structural abnormalities are common in hip dysplasia, primarily involving the iliopsoas and hip abductor muscles (1,2).
- 2. Muscle-tendon pain is negatively associated with patient-reported outcome (1).
- 3. 1 year after PAO, patients experience medium to very large patient-reported improvements which is associated with decreased muscle-tendon pain (3).
- 4. The level of daily physical activity does not change 1 year after surgery despite increased physical capacity (4).

Methodological limitations

Papers 1-4 are based on data from a prospective case series study, and some limitations do exist. The internal validity will be discussed systematically with regard to study design, measurement error, selection bias, information bias and confounding. The external validity will be discussed under the subheading generalisability.

Study design

Cohort and case series studies are often mislabelled and distinction between the two can be difficult (162). This study was labelled a case series study. Patients with hip dysplasia were sampled and observations were made before and after all patients underwent PAO. In cohort studies, patients have to be sampled based on a specific *a priori* exposure (e.g. muscle-tendon pain); and occurrence of outcome (e.g. HAGOS or muscle strength) has to be assessed over a specific period and risk should be compared between exposure groups (162). However, categorising muscle-tendon pain into exposure groups was not considered relevant in this study. Instead, the aim was to investigate if extra-articular structures such as muscles and tendons could be sources of pain and if structural abnormalities could be identified, and to investigate the outcome of PAO.

However, case series studies are associated with inherited biases, the most serious of which is the lack of pain-free reference groups. The lack of references implies lack of knowledge of muscle-tendon pain, structural abnormalities and physical activity in pain-free references. In Papers 1 and 3, we examined if muscle-tendon pain could be a source of known pain, implying a history of pain. References categorising themselves as pain-free do not have known pain. Thus, the lack of pain-free references most likely had no impact on these results. On the other hand, the lack of pain-free references in Paper 2 may be considered a weakness of the study. The results of Paper 2 showed a weak-to-moderate correlation between pain and abnormal ultrasonographic findings in the iliopsoas tendon and the gluteus medius/minimus tendons, whereas pain and structural abnormalities were not correlated for the other investigated structures. Abnormal ultrasonographic findings have been detected among pain-free subjects (51,163). Consequently, structural abnormalities can present due to previous injuries and/or excessive use, and this may not be related to present symptoms. Therefore, estimates of structural abnormalities in hip dysplasia may have been overestimated as abnormalities unrelated to the present symptoms may have been recorded. Similarly, pain-free references were lacking in Paper 4. However, the patients' physical activity profile was similar to that of the pain-free references included in the HAFAI study (103) and in two other previous studies (21,164), implying that the patients followed current health recommendations regarding regular physical activity. However, compared to the references included in the HAFAI study (103), patients in this study seemed to rest more and run less (4). As mentioned before, this could indicate early adjustment in the patients' level of physical activity, which may be an important indicator. Consequently, the lack of pain-free references may blur minor deviations from normality that may be important. However, this has no impact on the estimated changes of the accelerometer-based and patient-reported physical activity and the estimated associated between them.

Another limitation in Papers 3 and 4 was that no attempt was made to monitor physical rehabilitation after PAO. However, the aims of the papers were to investigate muscle-tendon pain and abnormalities and outcome of PAO in a setting comparable with usual practice. Therefore, physical rehabilitation was not monitored. Even so, all patients were instructed in a home-based exercise programme and offered an individualised exercise programme, ending 2-4 months after PAO. We therefore do not know if the changes in the measured outcomes exist due to surgery or time or are the result of intensive physical rehabilitation. This should be investigated in future studies, optimally comparing the effect of different rehabilitation approaches.

Finally, Papers 1-4 are based on data from one study population, and one may argue that this is tantamount to salami slicing. However, reporting all data in one paper

was considered inappropriate as the contents was too comprehensive for one paper. Hence, *a priori*, separate aims and methods were defined and described for each paper, and the original publication has been cited in all papers to ensure transparency. On the other hand, data from each paper will to some extent be interdependent, and per chance it is likely that drawing a sample from another study population would provide other results. However, in this case, it was considered ethical, economic and time-wise appropriate to disturb only one group of patients rather than collecting data from different patient samples. Bearing this in mind, dividing data in Papers 1-4 is not considered salami slicing.

Measurement error

The analysis of inter-rater reliability for the isometric hip muscle strength assessments showed measurement errors at group level of 10-16% (1). To our knowledge, no consensus about acceptable cut-off values has been reported, but cut-off values of 10% of variance have been suggested (165). Moreover, it has been recommended only to use strength assessment tools associated with limits of agreement < 15% in order to be able to detect small but clinically relevant changes in strength (166). Thus, in Paper 1, the measurement errors were a little higher than the suggested cut-off levels, indicating that measurement error might blur clinically relevant findings. However, Papers 1-4 included a large study population. Hence, measurement error has less impact on the results since the overall variation reduces with increasing sample size. Still, in one regression analysis (1), the association between isometric hip extension and the sum of painful clinical entities failed to reach statistical significance. This can probably be explained by the large measurement error (15%) for this assessment, blurring the underlying association.

Selection bias

In the study period, 138 consecutive patients were assessed for eligibility (1), approximately 100 patients per year. According to the Danish National Patient Register (DNPR), this number corresponds to the number of PAOs performed a year at Aarhus University Hospital (84). This indicates that all eligible patients were identified and that they most likely represent the target population. Among them, 19 patients declined to participate, and perchance these patients may share different characteristics than those of the included patients, which would introduce selection bias. However, patients declined to participate either due to time and/or transport (n=9) or due to lack of interest (n=7); they did not differ in age, gender or severity of hip dysplasia. Hence, the risk of selection bias in this context is considered low. However, the risk of selection bias. In Papers 3 and 4, data on 18% and 23%, respectively, were lost to follow-up due to different reasons (3,4). These numbers are considered high, which may lead to selection bias. However, patients lost to follow-up due to different reasons (3,4).

up did not share different patient characteristics than the analysed patients, and therefore the risk of selection bias due to missing data is considered low.

Information bias

In Papers 1-3, pain and/or structural abnormalities were identified in specific clinical entities with standardised clinical and ultrasonographic examinations. Patients were examined by experienced physiotherapists and they were aware of the study aims and were therefore not blinded. Possibly, they could have been prone to overestimation of pain and/or abnormal ultrasonographic findings (too many false positive). Nevertheless, for the standardised clinical examinations, patients had to confirm known pain when performing two separate tests, which reduces the risk of rater-depended overestimation (1). However, the analyses of inter-rater reliability of standardised clinical and ultrasonographic examinations revealed only slight to moderate agreement (1,2). In five clinical entity tests and in one ultrasonographic examination, kappa values were considered questionable due to a low prevalence of pain and/or structural abnormalities. For the other tests, the agreement was fair to moderate, indicating some risk of non-differential misclassification which could blur the calculated estimates. For the estimated associations between the HAGOS scores and the sum of painful clinical entities, overestimation of muscle-tendon pain and/or non-differential misclassification would most likely underestimate the associations since patients with muscle-tendon pain could have been diluted by false positives, indicating low risk of misclassification bias for these analyses.

In Paper 4, all activity data were calibrated manually by choosing a period of level walking of each day. This procedure may introduce non-differentiated misclassification as by mistake the researcher may choose cycling instead of level walking (the raw data signal looks similar). Again, this will not affect the results but may increase overall variation. Moreover, fitness training was not quantified with the accelerometer-based algorithm (4), and since most patients reported fitness training as their primary preferred physical activity, the level of daily physical activity may have been underestimated.

Confounding

In Papers 1 and 3, estimated associations between the sum of painful clinical entities and HAGOS scores and hip muscle strength may be explained by unknown confounding. To be a confounder for the above-mentioned associations, a co-variate has to be associated with both the exposure (sum of painful clinical entities) and the outcome (HAGOS and hip muscle strength). As described in the method section in Paper 1, associations were adjusted for sex and age as they were considered possible association confounders. Moreover, estimated associations - reported in Paper 3 were also adjusted for pre- and postsurgical CE angles. Adjusted analyses were associated with slightly narrower 95% CI, indicating the relevance of adjusting (1–3). Nevertheless, unknown confounding may also be relevant and may also explain reported associations and/or correlations in the individual papers (1–4). Overweight has been reported as an independent predictor of PRO after PAO (16). Therefore, the impact of overweight on outcome of treatment should be investigated in future studies.

Key points - important limitations	
Study design	No pain-free references, implying that structural abnormalities may also be common among pain-free references.
	No pain-free references, implying that minor deviations from normality in the level of daily physical activity may not be detected.
Measurement error	The analyses of inter-rater reliability show fair to moderate agreement of the clinical and ultrasonographic examinations, implying that relevant changes or associations may be blurred due to measurement error.

Generalisability

The external validity is considered high and a strength of the papers included in this dissertation. All patients were included consecutively during a study period of 16 months, and the flow of identified eligible patients (Figure 12) was similar to the general flow of patients at Aarhus University Hospital (84), indicating that most patient were identified. The study population hereby represents the target population, which - in other words - represents the general population of Danish patients with hip dysplasia scheduled for PAO. As a result, patients were heterogeneous, including patients on sick leave, young physically active students, employed middle-aged patients living alone and/or with families, patients with low and high income jobs and patients represented the target population, and future studies may investigate if separate analyses of some subgroups may be relevant.

9. Conclusion

Muscle-tendon pain and abnormal ultrasonographic findings were common in hip dysplasia, primarily involving the iliopsoas and the hip abductor muscles (1,2), and pain was negatively associated with PRO (1).

After hip-preserving surgery, patients with hip dysplasia experienced medium to very large improvements in PRO, which was associated with decreased muscle-tendon pain (3). Consequently, the understanding of hip dysplasia as solely a joint disease should be reconsidered since muscle-tendon pain seems to play an important role in relation to PRO before and after PAO (1,3).

Patients with hip dysplasia did not change their physical activity profile 1 year after hip-preserving surgery when activity was measured with accelerometer-based sensors. This is interesting as patient-reported physical activity indicated that patients' ability to participate in physical activities increased, suggesting that this increased self-reported participatory capacity was not manifested as increased accelerometer-based physical activity.

10. Perspectives and future research

The severity of pain seems important and most likely describes how patients with hip dysplasia experience their physical well-being. Therefore, improving muscletendon pain through specific interventions - focusing on reducing muscle-tendon pain - seems relevant for patients with hip dysplasia. As stated previously, no studies have investigated the effect of exercise therapy in patients with hip dysplasia, nor have any studies investigated the effect of PAO. However, in a newly registered randomised controlled trial (RCT), the authors aim to investigate if PAO - followed by 4 months of usual care and 8 months of progressive resistance training - is superior to 12 months of progressive resistance training in terms of self-reported pain measured with the HAGOS (ClinicalTrials.gov ID: NCT03941171). The progressive resistance training will focus on exercises in machines that strengthen the hip abductors, flexors and extensors. Potentially, these exercises will have a positive impact on muscle-tendon pain, as exercises are performed slowly including an eccentric emphasis with a relatively heavy load. Similar interventions have been found to be effective in reducing pain in relation to Achilles (167) and patellar tendinopathy (168). In a few years, the efficacy of PAO followed by progressive resistance training compared with progressive resistance training will be reported, and knowledge on expected effects, complications and risk factors will be obtained. This is considered highly relevant. In a case series study on 321 patients with hip dysplasia, treatment satisfaction was investigated 2 years after PAO (143). Although improvements exceeded the MIC measured with the HOOS, 36% of patients were not satisfied with their outcome in relation to patient-reported pain, symptoms, daily life, physical function and quality of life. However, 84% of patients would have undergone PAO again if they knew their result in advance, whereas 16% would not. These findings raise the question whether the unsatisfied patients share other characteristics than the satisfied patients, and, if so, whether knowledge of these characteristics be used in advance when planning treatment. This is considered relevant to investigate because it would provide relevant data on which patients should undergo surgery and which patients should not. Possibly, such data can be provided from the ongoing RCT (ClinicalTrials.gov ID: NCT03941171); if this is not the case, this issue should certainly be investigated in future studies.

Nevertheless, as stated previously, not all patients are offered surgical treatment. Patients with a BMI above 25, age above 45 years, manifest osteoarthritis, reduced hip range of motion and low level of pain are not candidates for PAO (69,169,170). In Denmark, these patients – and patients who do not want to undergo surgery – receive no other any treatment in the public sector. The consequence is that they find themselves left with no treatment options despite similar levels of pain, physical function and risk of osteoarthritis as candidates for surgery. Worldwide, osteoarthritis is the leading cause of pain and low physical function, and osteoarthritis is associated with an inactive lifestyle, threatening patients' overall health (147). The prevalence of hip dysplasia in hip osteoarthritic populations is 20-40% (159), indicating that patients with hip dysplasia may develop osteoarthritis later in life. It is likely that the dysplastic patients of today, who are left with no treatment option, may be at high risk of poor health later in life. Possibly, they will adjust their level of daily physical activity to their pain and over time develop an inactive lifestyle. Therefore, to improve physical function and muscle-tendon pain and to preserve an active lifestyle, an alternative treatment option should be developed, and the effect of this treatment should be investigated and proved in a RCT. As stated previously, exercise treatment could be an alternative for patients who are not candidates for surgery. Currently, co-authors and I work on designing a relevant treatment option for these patients. We will investigate the feasibility of progressive exercise therapy in a feasibility study starting in 2020; based on that study, a RCT will be designed and the effectiveness and cost-effectiveness of progressive exercise therapy will be tested against usual practice. Hopefully, this RCT will be running in late 2020, and the first results will be published in 2024. To our knowledge, such an RCT study will be the first study investigating short- and long-term effectiveness of exercise therapy for patients who are not candidates for PAO. We will investigate patient-reported and performance-based function, costs of interventions and muscle-tendon pain. Hence, valuable knowledge will be provided to health professionals, patients and health policy makers by highlighting the benefits, adverse events and cost of such exercise therapy. Moreover, the intervention will be simple and home-based, allowing implementation at large scale if the results show that the intervention is effective and/or cost-effective. Nevertheless, this RCT will not fully describe how the intervention should be implemented, nor will it investigate if specific characteristics lead to poor outcome. Likewise, the RCT will not investigate if other treatment options are more effective. Such questions should be addressed in future studies.

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12. Appendix

Paper 1

Muscle-tendon-related pain in 100 patients with hip dysplasia: prevalence and associations with self-reported hip disability and muscle strength

Muscle-tendon-related pain in 100 patients with hip dysplasia: prevalence and associations with selfreported hip disability and muscle strength Julie Sandell Jacobsen^{1,2*}, Per Hölmich³, Kristian Thorborg³, Lars Bolvig⁴, Stig Storgaard Jakobsen⁵, Kjeld Søballe⁵ and Inger Mechlenburg⁶

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ABSTRACT

The primary aim was to identify muscle-tendon-related pain in 100 patients with hip dysplasia. The secondary aim was to test whether muscle-tendon-related pain is associated with self-reported hip disability and muscle strength in patient with hip dysplasia. One hundred patients (17 men) with a mean age of 29 years (SD 9) were included. Clinical entity approach was carried out to identify muscle-tendon-related pain. Associations between muscle-tendon-related pain and self-reported hip disability and muscle strength were tested with multiple regression analysis, including adjustments for age and gender. Self-reported hip disability was recorded with the Copenhagen Hip and Groin Outcome Score (HAGOS), and muscle strength was assessed with a handheld dynamometer. Iliopsoas- and abductor-related pain were most prevalent with prevalences of 56% (CI 46; 66) and 42% (CI 32; 52), respectively. Adductor-, hamstrings- and rectus abdominis-related pain were less common. There was a significant inverse linear association between muscle-tendon-related pain and self-reported hip disability ranging from -3.35 to -7.51 HAGOS points in the adjusted analysis (P < 0.05). Besides the association between muscle-tendon-related pain and hip extension a significant inverse linear association between muscletendon-related pain and muscle strength was found ranging from -0.11 to -0.12 Nm/kg in the adjusted analysis (P < 0.05). Muscle-tendon-related pain exists in about half of patients with hip dysplasia with a high prevalence of muscle-tendon-related pain in the iliopsoas and the hip abductors and affects patients' self-reported hip disability and muscle strength negatively.

INTRODUCTION

Symptomatic hip dysplasia normally presents in early life [1] and left untreated, hip dysplasia may lead to development of early osteoarthritis [2, 3]. The aetiology of hip osteoarthritis in hip dysplasia is unknown and often described as multifactorial [2]. However, the lack of acetabular support to the femoral head [4] and the compromised passive stability of the hip joint lead to an increased mechanical pressure on the acetabular labrum and cartilage [2],

and intra-articular injury has been reported as one important predisposing factor to development of osteoarthritis [2]. Labrum injury or degeneration is present in 49– 83% of patients with hip dysplasia [2, 5], and causes pain at the groin and/or lateral to the hip [5, 6]. Moreover, the shallow acetabulum and the reduced weight bearing are associated with increased load on the muscles acting close to the hip joint [7, 8], and muscle-tendon-related pain may potentially coexist with intra-articular pathology.

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The acetabular labrum functions as an important anterior stabilizer to the dysplastic hip [9], and the location of the iliopsoas muscle close to the capsule–labral complex enables the muscle to work as an anterior stabilizer to the hip joint [10]. The gluteus medius and minimus muscles work together with the iliopsoas muscle as important lateral stabilizers to maintain a level led pelvis during ambulation [11]. The stabilizing role of the iliopsoas and gluteus medius and minimus muscles may be increased in hip dysplasia due to the morphology of the hip joint [7, 10], and potentially higher load on the muscles may lead to overuse-related pain in the muscles and tendons.

Muscle-tendon-related pain is present in hip dysplasia [6, 12], and abnormality of the iliopsoas muscle identified as internal snapping hip has been verified in 18% using hip arthroscopy [12]. In patients with femoroacetabular impingement muscle-tendon-related pain frequently coexist with the morphology of the hip joint [13], and in sportsactive subjects with long-standing groin pain, muscle-tendon-related pain has been identified with the clinical entity approach [14, 15]. In patients with hip dysplasia, however, no previous studies have systematically examined the presence of muscle-tendon-related pain in a consecutive cohort scheduled for periacetabular osteotomy.

The primary aim was to identify muscle-tendon-related pain in 100 patients with hip dysplasia in the following clinical entities: (i) iliopsoas, (ii) abductors, (iii) adductors, (iv) hamstrings, and (v) rectus abdominis. The secondary aim was to test if muscle-tendon-related pain is associated with self-reported hip disability and muscle strength in patient with hip dysplasia.

MATERIALS AND METHODS

This study complies with the Helsinki Declaration and was notified to the Danish Committee on Biomedical and Research Ethics at 14 January 2014 (5/2014). The Danish Data Protection Agency gave permission for the handling of personal data (1-16-02-47-14), and the study was registered at ClinicalTrials.gov (20140401PAO).

Subjects

In a consecutive sample, patients with bilateral or unilateral hip dysplasia were invited to participate from May 2014 to August 2015 from the Department of Orthopedics at Aarhus University Hospital in Denmark. Inclusion criteria were Wiberg's center-edge (CE) angle $<25^{\circ}$ [16], groin pain for at least 3 months and scheduled periacetabular osteotomy (PAO) [17]. Patients were excluded based on the following criteria: (i) Calvé Perthes and epiphysiolysis, (ii) Surgery due to herniated disc and spondylodesis, (iii) Previous joint preservation procedure or arthroplasty of

the hip, knee or ankle, (iv) Neurological, rheumatological or medical conditions affecting the function of the hip joint, (v) Tenotomy of the iliopsoas tendon or z-plastic of the iliotibial band and (vi) Steroid-injection in the iliopsoas tendon and/or bursa trochanterica within the last 6 weeks.

Study design

All outcomes measures were collected prior to PAO during a clinical examination. The clinical examination was completed by two experienced physical therapists (CMS and JSJ) with 5 and 7 years of experience assessing patients with hip dysplasia, respectively. The patients were randomly assessed by the two physical therapists with approximately equal distribution between the two (60:40). The examination included recording of self-reported hip disability, examination of muscle-tendon-related pain in clinical entities and hip muscle strength tests.

Self-reported hip disability

The Copenhagen Hip and Groin Outcome Score (HAGOS) questionnaire was completed by all patients prior to the clinical examinations [18]. HAGOS has shown to be a valid, reliable and responsive measure of hip disability and associated problems in young to middle-aged physically active patients with longstanding hip and/or groin pain including patients undergoing hip arthroscopy [18, 19]. HAGOS consists of six separate subscales rating hip disability from 0 to 100 points, where zero points indicates the lowest outcome [18]. The six subscales measure pain, symptoms, physical function in daily living (ADL), physical function in sports and recreation, participation in physical activity and quality of life [18].

Muscle-tendon-related pain

A standardized clinical entity approach was carried out to identify muscle-tendon-related pain in clinical entities assessed in the limb scheduled for PAO [14, 15, 20]. The standardized entity approach includes a number of pain provocation tests covered by anatomic palpation, resistance testing and passive muscle stretch (Table I). The approach includes five entities, and the entities were tested in the following order: adduction-related pain, iliopsoas-related pain, rectus abdominis-related pain, abductor-related pain and hamstring-related pain. Rectus abdominis-related pain is in the Doha consensus covered by the term inguinalrelated pain [20]. Inguinal-related pain is less relevant among patients with hip dysplasia as many of these patients are women in which the inguinal canal anatomy is somewhat different from males, and therefore rectusabdominis-related pain was the focus in the present study.

Clinical entities	Diagnostic criteria
Iliopsoas-related pain	Palpatory pain of the muscle through the lower lateral part of the abdomen and/or just dis- tal of the inguinal ligament and pain with passive stretching during modified Thomas' test [14, 20, 21]
Abductor-related pain	Palpatory pain at the insertion point at the greater trochanter and pain with side-lying ab- duction against resistance
Adductor-related pain	Palpatory pain at the muscle origin at the pubic bone and pain with adduction against resistance [14, 20]
Hamstring-related pain	Palpatory pain at the muscle origin at the tuber ischii and pain with extension against resistance
Rectus abdominis-related pain	Palpatory pain of the distal tendon and/or the insertion at the pubic bone, and pain at con- traction against resistance [14, 20]

Table I. Diagnostic criteria for each individual entity

Muscle strength

Isometric muscle strength tests were performed using a reliable dynamometer technique [22]. Muscle strength was tested with a handheld dynamometer (powertrack II comandor, JTECH Medical, Salt Lake City, Utah). Isometric hip adduction, abduction, flexion and extension strength were measured in the limb scheduled for PAO, and the order of the individual tests was randomized before each session to avoid systematic bias. The examiner applied resistance 5 cm proximal to the proximal edge of the lateral malleolus for hip abduction, adduction and extension. Resistance in hip flexion was performed 5 cm proximal to the proximal border of patella. In all the isometric tests, the patients exerted 5-s Maximal Voluntary Isometric Contraction (MVIC) against the dynamometer. The highest value of four repeated measurements for each test was used in the analysis. To avoid fatigue, patients rested for 30 s between each measurement. All strength values were weight-adjusted and reported as Newton meters per kilogram of the bodyweight.

Baseline characteristics

Baseline characteristics were registered using standardized questions. Pain was measured on a numeric rating scale (NRS) in rest while sitting and lying. The center-edge (CE) angle [16], Tönnis' acetabular index (AI) angle [23] and Tönnis' osteoarthritis grade [23] were measured by a single rater (SSJ) using anteroposterior radiographs, whereas hospital charts was used to record unilateral or bilateral hip involvement and other pathologies.

Inter-rater reliability of the test battery

Two different testers assessed muscle-tendon-related pain and muscle strength and the inter-rater reliability of these

measures was investigated. Twenty-five patients were tested 6 weeks after PAO by two physiotherapists, rater A and B (CMS and JSJ), with a 2-day period between a first and second test. Each patient was randomized to whether rater A or B performed the initial testing.

Sample size

Since it was not possible to calculate the sample size based on the prevalence of muscle-tendon-related pain, we chose to calculate it based on the secondary outcome of the study. The sample size calculation was based on the HAGOS ADL subscore with an estimated difference of 11.8 points and an estimated standard deviation of 18.5 points between patients with and without muscle-tendonrelated pain. The estimated difference was based on the Minimal Important Change of 11.8 points reported in a cohort study on patients with femoroacetabular impingement scheduled for hip arthroscopy [19], and the standard deviation was based on the standard deviation of the HAGOS ADL subscore of 18.5 points reported in a cohort study on patients with intra-articular hip lesions undergoing hip arthroscopy [24]. Based on a significance level of 5% and a power of 80%, 80 patients were needed, and considering the risk of dropouts, we included 100 patients.

Statistics

Normal distribution was checked with histograms and probability plots. Multiple linear regression analyses were performed with muscle-tendon-related pain as the independent variable (i.e. the sum of positive clinical entities for each patient) and each HAGOS subscale as the dependent variable (pain, symptoms, ADL, physical function in sports and recreation, participation in physical activity



Fig. 1. Flowchart of the study process. One hundred consecutive patients with unilateral and bilateral symptoms were included from the Division of Hip Surgery, Department of Orthopedics, Aarhus University Hospital in Denmark from May 2014 to August 2015. Abbreviations: HD, hip dysplasia; ADHD, attention deficit/hyperactivity disorder; MRSA, methicillin-resistant *Staphylococcus aureus*.

and quality of life). Crude and adjusted β -coefficients were estimated, and adjustments were made for age and gender. Likewise, multiple linear regression analyses were performed with muscle-tendon-related pain as the independent variable (i.e. the sum of positive clinical entities for each patient) and strength of each muscle group as the dependent variable (i.e. flexion, abduction, adduction and extension). Crude and adjusted β -coefficients were estimated, and adjustments were made for age and gender. The assumptions (independent observations, linear association, constant variance of residuals, normally distribution of residuals) for the multiple and linear regression analyses were met. The significance level was 0.05 and STATA 14 (StataCorp, College Station, TX) software package was used for data analysis.

RESULTS

A consecutive sample of 135 patients was assessed for eligibility and out of those, 100 patients were included in this study (Fig. 1). Baseline characteristics of the included patients are reported in Table II.

The inter-rater reliability of the standardized clinical entity approach is reported in Supplementary Appendix Table S1 and the inter-rater reliability of the muscle strength test is reported in Supplementary Appendix Table S2. Agreement between rater A and rater B ranged from 64% to 100% with kappa-coefficients ranging from 0.17 to 0.60. The ICC was >0.70 for all muscle strength

Table II. Baseline characteristics in 100 consecutive patients with hip dysplasia

Outcomes	Patients (SD)
Men	17
Bilateral symptoms	89
Osteoarthritis grade 0/1	97/3
Congenital hip dislocation	6
Age, years	29.9 (9.2)
BMI, kg/m ²	23.2 (3.0)
Duration of pain, years	4.9 (5.6)
NRS pain lying, 0–10	3.1 (2.4)
NRS pain sitting, 0–10	3.8 (2.7)
CE angle preoperatively, degrees	17.4 (4.7)
AI angle preoperatively, degrees	13.8 (4.9)
HAGOS pain, 0–100	50.3 (18.0)
HAGOS symptoms, 0–100	49.2 (17.4)
HAGOS ADL, 0–100	55.5 (22.4)
HAGOS sport/recreation, 0–100	39.3 (20.7)
HAGOS participation, 0–100	23.0 (24.7)
HAGOS quality of life, 0–100	29.4 (14.3)
Hip flexion, Nm/kg	1.2 (0.5)
Hip abduction, Nm/kg	1.2 (0.4)
Hip adduction, Nm/kg	1.1 (0.4)
Hip extension, Nm/kg	1.8 (0.7)

Baseline characteristics are presented as mean (SD) values and as numbers. BMI, body mass index; CE, center-edge; AI, Tönnis' acetabular index; HAGOS, Copenhagen hip and groin outcome score; ADL, activities of daily living; NRS, Numeric Rating Scale.

measurements (0.72–0.92) and the standard error of measurement ranged between 9.45% and 14.44%.

The prevalence of muscle-tendon-related pain according to specific entities was: iliopsoas-related pain 56% (CI 46; 66), abductor-related pain 42% (CI 32; 52), adductorrelated pain 14% (CI 8; 22), Hamstring-related pain 6% (CI 2; 13) and rectus abdominis-related pain 4% (CI 1; 10). Twenty-six percent of the patients reported no muscle-related pain, as defined by non-existence of pain in any of the predefined clinical entities, and the maximum number of pain-full clinical entities in individual patients was four. The distribution of muscle-tendon-related pain in clinical entities was as follows: pain in one entity (38%), pain in two entities (27%), pain in three entities (6%) and pain in four entities (3%).

Both the crude and adjusted linear regression proved an inverse linear association between muscle-tendon-related pain and the self-reported HAGOS score (Table III). Besides the adjusted association between muscle-tendon related pain and hip extension an inverse linear association between muscle-tendon-related pain and isometric hip muscle strength was found in both crude and adjusted analyses (Table IV).

DISCUSSION

Patients with symptomatic hip dysplasia are characterized by a high prevalence of muscle-tendon-related pain assessed with the clinical entity approach, and muscle-tendon-related pain evidently affects patients' self-reported hip disability and muscle strength. Moreover, the findings suggest that muscle strength and hip disability may potentially be improved through exercise therapy focusing on reducing muscle-tendon-related lower extremity pain.

To our knowledge, no previous studies have systematically assessed presence of muscle-tendon-related pain in a large cohort of hip dysplasia patients scheduled for PAO. One cross-sectional study on 16 patients with symptomatic hip dysplasia documented pathology of the psoas tendon in three hips [12], and another cross-sectional study on hip dysplasia patients treated with PAO 24 months earlier reported non-specific soft-tissue injury in 17% [6]. In a sample of sports-active persons with long-standing groin pain muscle-tendon-related pain in clinical entities was systematically assessed [15], and adductor- and iliopsoasrelated pain were reported as the most prevalent entities (58% and 36%, respectively). The higher prevalence of adductor-related pain in that study probably reflects that the population is dominated by males and soccer players opposed to our female and non-specific sports-active study population [15, 20, 25]. What was notable in our cohort was the large proportion of patients (42%) with abductor-related pain. This fits well with the results of a previous study reporting increased hip abduction and external rotation torques in patients with hip dysplasia [7]. Possibly, the higher torques reported among patients with hip dysplasia exist due to the shallow acetabulum and reduced weightbearing of the hip, where the muscles acting close to the hip may present with overuse-related pain in order to maintain a levelled pelvis during ambulation.

Abductor- and iliopsoas-related pain may potentially be improved by introducing heavy slow strength training using the side-lying hip abduction exercise and the standing hip flexion exercise [26, 27], both performed in full active range of motion [26, 27]. The heavy slow strength training including an eccentric emphasis could be an effective way of reducing muscle-tendon-related pain and improve hip disability as has been shown in patients with achilles and patellar tendinopathy [28–30]. In a randomized trial, improvement in adductor-related pain was documented in sports-active persons with longstanding groin pain [31], and in a cohort study, reduction of pain and successful return to sport were reported in runners with iliotibial band syndrome [32]. Similar exercise approaches seem feasible in patients with symptomatic hip dysplasia.

Our results showed significant associations between muscle-tendon-related pain and all six subscales of HAGOS, and the associations proved a linear relationship between the number of clinical entities with muscle-tendon-related pain and the reported HAGOS scores. This

Table III. Associations between muscle-tendon-related pain and self-reported disability (n = 100)

	Crude	Crude		Adjusted	
HAGOS points (0-100)	β Coefficient (95% CI)	P value	β Coefficient (95% CI)	P value	
HAGOS Pain	-6.79 (-10.12; -3.46)	< 0.001	-6.90 (-10.18; -3.61)	< 0.001	
HAGOS Symptoms	-6.26 (-9.52; -3.01)	< 0.001	-6.34 (-9.61; -3.07)	< 0.001	
HAGOS ADL	-7.17 (-11.41; -2.93)	0.001	-7.51 (-11.53; -3.49)	< 0.001	
HAGOS Sport/rec	-7.12 (-11.01; -3.23)	< 0.001	-7.39 (-11.22; -3.56)	< 0.001	
HAGOS Participation	-5.73 (-10.55; -0.92)	0.020	-6.08 (-10.89; -1.27)	0.014	
HAGOS Quality of life	-3.19 (-5.98; -0.41)	0.025	-3.35 (-6.12; -0.58)	0.018	

Linear regression of muscle-tendon-related pain on the self-reported HAGOS score reported as crude and adjusted β coefficients (95% confidence interval). Adjustments were made for age and gender.

ADL, activities of daily living; sport/rec, sport/recreation.

	Crude		Adjusted		
Hip muscle strength (Nm/kg)	β Coefficient (95% CI)	P value	β Coefficient (95% CI)	P value	
Flexion	-0.12(-0.23; -0.02)	0.021	-0.11 (-0.21; -0.01)	0.038	
Abduction	-0.10 (-0.19; -0.01)	0.023	-0.11 (-0.19; -0.03)	0.011	
Adduction	-0.12 (-0.21; -0.03)	0.009	-0.12 (-0.20; -0.03)	0.010	
Extension	-0.14 (-0.28; -0.01)	0.037	-0.12(-0.25; 0.01)	0.077	

Table IV. Associations between muscle-tendon-related pain and muscle strength (n = 100)

Linear regression of muscle-tendon-related pain on the muscle strength values reported as crude and adjusted β coefficients (95% confidence interval). Adjustments were made for age and gender.

means that per added painful entity a patient experiences, the lower that patient will score in HAGOS. Patients with muscle-tendon-related pain in more than one entity is normally presented in our cohort (represent 36%). The HAGOS ADL score among these patients is minimum 15 points lower than in patients with no pain [i.e. a patient with pain in one entity reports a 7.5 points lower score than a patients with no pain, and a patient with pain in two entities reports a 15 points (2×7.5) lower score than a patient with no pain, Table III (adjusted analysis)]. A HAGOS ADL score of 15 points is higher than the Minimal Important Change of 11.8 points [19]. This means, that the impact of muscle-tendon-related pain on hip disability is of clinical relevance among patients with muscle-tendon-related pain, presenting with more than one entity. Based on this, the clinical entity approach may be used as a fast and in-expensive screening approach to select hip dysplasia patients with substantial disability in activities of daily living that is associated with the presence of muscle-tendon-related pain.

The isometric muscle strength tests likewise showed a linear and significant association between the number of clinical entities with muscle-tendon-related pain and muscle strength. This means that per added clinical entity with muscle-tendon-related pain the lower strength will that patient have. The relative lower strength values in a patient with muscle-tendon related pain in one clinical entity is approximately 10% and in two clinical entities is approximately 20%. The latter is the same as the recommended meaningful difference of 20% reported by the Cochrane Musculoskeletal Group [33] and higher than the SEM% values reported in this study, and the lower strength values indicate the relevance of muscle strength training.

Our study has a number of limitations. The analysis of inter-rater reliability showed slight to moderate agreement of the clinical entity approach. Compared with the

reported inter-rater values of a previous study on sportsactive people with long-standing groin pain our values are systematically lower [14]. This discrepancy may exist because the second test was performed 3 days after the first test and not on the same day, and because the kappa coefficient depends on the prevalence [34]. The prevalence of pain is low in the iliopsoas palpation lower abdomen (LA) test, the hamstrings palpation test and the hamstrings against resistance test, and the k values of these three tests should be interpreted with caution. The assessment of isometric hip muscle strength are also exposed to measurement error because of the assessor-dependent approach. Our values of the SEM% are similar but higher than the results reported in a previous study on inter-tester reliability of isometric hip muscle strength test using belt fixation [35]. However, the SEM% is lower than the 20% border reported by the Cochrane Musculoskeletal Group [33], and we included a large cohort where the measurement error has lesser impact. Based on the latter two arguments, we find the variability of our muscle strength tests acceptable. Another limitation is that we did not include a control group, and therefore we have no knowledge of the presence of muscle-tendon-related pain in healthy subjects. Presence of muscle-tendon-related pain in our study was however based on provocation of earlier experienced pain, which are probably unusual in subjects categorizing themselves as healthy. A third limitation is, that we included patients with both uni- and bilateral symptoms, which is similar to previous studies in this area [6, 36-38]. It cannot be ruled out that presence of hip dysplasia in one side of the body could have had influence on muscle-tendonrelated pain of the other side.

The results of this study provide evidence that there is a high prevalence of muscle-tendon-related pain in patients with symptomatic hip dysplasia. Previously, labral tears and acetabular cartilage lesions have been described as the primary cause of pain at the groin and/or lateral to the hip [5, 6]. In the present study, we also found, a high prevalence of muscle-tendon-related pain in clinical entities dominated by a high prevalence of iliopsoas- and abductorrelated pain. The implications of our results are that clinicians and scientists have to re-evaluate the cause of pain from hip dysplasia as solely being derived from the hip joint, and consider the impact of muscle-tendon-related pain on hip disability and muscle strength when assessing and planning conservative or surgical treatment in patients with hip dysplasia.

SUPPLEMENTARY DATA

Supplementary data are available at *Journal of Hip Preservation Surgery* online.

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CONFLICT OF INTEREST STATEMENT None declared.

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Paper 2

Muscle-tendon-related abnormalities detected by ultrasonography are common in symptomatic hip dysplasia

ORTHOPAEDIC SURGERY



Muscle-tendon-related abnormalities detected by ultrasonography are common in symptomatic hip dysplasia

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Abstract

Introduction Hip dysplasia is characterized by reduced acetabular coverage of the femoral head leading to an increased mechanical load on the hip joint and the acting hip muscles. Potentially, the muscles and tendons functioning close to the hip joint may present with overuse-related ultrasonography findings. The primary aim was to report the prevalence of muscle–tendon-related abnormalities detected by ultrasonography in 100 patients with symptomatic hip dysplasia. The secondary aim was to investigate correlations between muscle–tendon-related abnormalities detected by ultrasonography and clinically identified pain related to muscles and tendons.

Materials and methods One hundred patients (17 men) with a mean age of 29 ± 9 years were included. Muscle-tendon-related abnormalities were detected with a standardized ultrasound examination. Correlations between muscle-tendon-related abnormalities detected by ultrasonography and clinically identified pain related to muscles and tendons were tested with Spearman's rank correlation coefficient.

Results The most prevalent ultrasonography findings were identified in the iliopsoas tendon [50% (95% CI 40; 60)], the adductor longus tendon [31% (95% 22; 40)] and the gluteus medius/minimus tendons [27% (18; 36)]. Significant correlations between ultrasonography findings and pain related to muscles and tendons were only found for the iliopsoas tendon ($\rho = 0.24$ and p = 0.02) and the gluteus medius/minimus tendons ($\rho = 0.35$ and p < 0.001).

Conclusions Muscle–tendon-related abnormalities detected by ultrasonography in the hip and groin region are common in patients with symptomatic hip dysplasia, and the ultrasonography findings of the iliopsoas and gluteus medius/minimus tendons are weakly to moderately correlated to pain related to muscles and tendons in these structures. Both the iliopsoas and the gluteus medius/minimus have a pronounced stabilizing role in the dysplastic hip joint, and the common muscle–tendon-related abnormalities in these patients may be caused by injuries related to excessive use or degenerative changes in the muscle–tendon tissue.

Keywords Hip dysplasia · Hip dislocation, congenital · Ultrasound · Ultrasonography · Muscle · Tendon

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Introduction

Hip dysplasia is characterized by reduced acetabular coverage of the femoral head [1-4] leading to an increased mechanical load on the hip joint and the acting hip muscles [3, 5-8]. The acetabular labrum plays a major role in load transfer and joint stability of the hip [4, 7]. Excessive stress on the labrum in the dysplastic hip joint results in labral injuries in 49–83% of dysplastic hips [9, 10]. However, the muscles acting close to the hip joint also play a vital role in load transfer and in maintaining the femoral head in place of the acetabular socket [3, 5-8].

The iliopsoas tendon and the anterior hip capsule are anatomically closely related [11]. The iliopsoas muscle has an anterior stabilizing role to the hip joint due to the location of the iliopsoas close to the capsulo-labral complex [12]. The gluteus medius and minimus muscles act as important lateral stabilizers to the hip joint maintaining a leveled pelvis during single limb support [13]. The function of the iliopsoas and the gluteus medius and minimus muscles may be even more essential in the dysplastic hip joint, due to the steep and shallow acetabular roof. Potentially, the muscles acting close to the hip joint may present with pain related to the muscles or tendons.

Pain related to muscles and tendons has been registered by clinical tests in 74% of patients with symptomatic hip dysplasia [14], and in 17% by patient-reported questionnaires [15]. Moreover, muscle-tendon-related abnormalities have been verified in the iliopsoas tendon in 18% of patients with symptomatic hip dysplasia undergoing hip arthroscopy [16]. Muscle-tendon-related abnormalities have also been detected by magnetic resonance imaging (MRI) [17] and musculoskeletal ultrasonography in sports-active subjects with long-standing groin pain [18]. Musculoskeletal ultrasonography is gaining acceptance as a diagnostic tool in hip pathology [19-21], and standardized protocols for hip evaluation have been published [19, 22-24]. Of note, a MRI study has previously demonstrated that some muscle-tendon-related abnormalities in the hip were not uncommon in asymptomatic controls [17], underscoring the need to correlate imaging findings to clinical symptoms of pain. To our knowledge, no prior studies have examined muscle-tendon-related abnormalities with musculoskeletal ultrasonography in patients with symptomatic hip dysplasia.

The primary aim of this study was to report the prevalence of muscle-tendon-related abnormalities detected by ultrasonography in 100 patients with symptomatic hip dysplasia. The secondary aim was to investigate correlations between muscle-tendon-related abnormalities detected by ultrasonography and clinically identified pain related to muscles and tendons.

Materials and methods

Ethical approval was obtained from the Danish Committee on Biomedical and Research Ethics in January 14, 2014 (5/2014). The Danish Data Protection Agency gave permission to the handling of personal data (1-16-02-47-14), and the study was registered at ClinicalTrials.gov (20140401PAO). This study is one out of two parallel studies on the same subjects designed simultaneously with individual outcome measures and aims. The other study identified pain related to muscles and tendons using clinical tests [14]; in the current study, muscle–tendon-related abnormalities were examined with ultrasonography.

Subjects

One hundred patients with bilateral or unilateral hip dysplasia were recruited consecutively between May 2014 and August 2015 from the Division of Hip Surgery at Aarhus University Hospital in Denmark [14]. Inclusion criteria were Wiberg's center-edge angle $< 25^{\circ}$ [25], groin pain in the last 3 months and scheduled periacetabular osteotomy [14, 26]. Patients were excluded if they had co-morbidities and a history of surgical interventions affecting the function of their hip [14].

Outcome measures

All outcomes measures were collected at a clinical examination prior to surgery. The clinical examination was completed by two experienced physical therapists (CMS and JSJ). They had 5 and 7 years of experience of assessing patients with hip dysplasia. The clinical examination included examination for muscle–tendon-related abnormalities using musculoskeletal ultrasonography, examination of pain related to muscles and tendons and registration of baseline characteristics.

Baseline characteristics

Baseline characteristics were registered using a standardized protocol [14]. The center-edge angle [25], Tönnis' acetabular index angle [27], and Tönnis' osteoarthritis grade [27] were measured by a single rater (SSJ) using anteroposterior radiographs, while hospital charts provided data on unilateral or bilateral hip involvement and other pathologies. Hip disability was recorded with The Copenhagen Hip and Groin Outcome Score (HAGOS) [28]. HAGOS has been shown to be a valid, reliable and responsive measure of hip disability and associated problems in young- to middle-aged physically active patients with long-standing hip and/or groin pain [28]. HAGOS consists of six separate subscales rating hip disability from 0 to 100 points [28]. Hip-related groin pain was assessed and recorded as number of positive tests using the FABER (Flexion/Abduction/External Rotation) test and the FADIR (Flexion/Adduction/Internal Rotation) test [20, 29]. Furthermore, occurrence of internal snapping hip was recorded using a standardized clinical test [30].

Ultrasonography findings

The ultrasound examination was carried out by two experienced physical therapists in accordance with a standardized protocol (Online Resource 1) based on the study by Nestorova et al. [23]. The ultrasound examination included an examination of the iliopsoas tendon, the gluteus medius/ minimus tendons, the adductor longus tendon, the hamstrings tendons, the pubic symphysis and the acetabular labrum.

A Noblus, Hitachi-Aloka Medical (Zug, Switzerland) ultrasound system and a multi-frequency linear transducer (5–18 MHz) (EUP-L64, Zug, Switzerland) were used for all examinations. Ultrasonography findings were defined as heterogeneous echogenicity with loss of normal fibrillar pattern, abnormal fluid intra- and/or extra-substantial, irregular bone configuration, enthesophytes, and/or calcifications [23]. The ultrasonography findings were registered as normal or abnormal during the examination by the two physical therapists (CMS or JSJ) (for example, Figs. 1, 2), and muscle–tendon-related abnormalities were assessed in the index limb. During the examination, we recorded images and movie sequences of the anatomical structures in all 100

Fig. 1 Transverse ultrasound image of a normal and homogeneous iliopsoas tendon with normal fibrillar pattern (**a**). Transverse ultrasound image of a thickened heterogeneous iliopsoas tendon with loss of normal fibrillar pattern and diffuse margin appearance (**b**). Iliopsoas tendon (1), iliopsoas muscle (2), and acetabular rim (3) patients (Online Resource 1), and the images and movie sequences were stored on an external disc.

To ensure valid image reading, we included a two-phase procedure. In the first phase, the two physical therapists pilot tested the ultrasound protocol by capturing and registering normal and abnormal finding in ten subjects (patients with symptomatic hip dysplasia and healthy subjects), and a radiologist specialized in musculoskeletal ultrasonography (LB) supervised the training in five subjects. In the second phase, data collection was initiated. We used the approach by Branci et al. [17], who based image findings on consensus. The radiologist specialized in musculoskeletal ultrasonography (LB) evaluated images and movie sequences of the initial 50 patients together with CMS and JSJ. Eighteen percent of the initial ultrasound registrations caused discussion between raters, and final consensus between all three raters was obtained. The two physical therapists (CMS or JSJ) performed the rating of the last 50 patients and had the possibility to contact the specialist in case of any doubts. In this second phase, the specialist was contacted in five cases, and he approved the ultrasound registrations in all five cases.

Pain related to muscles and tendons

Pain related to muscles and tendons was assessed in clinical entities using a standardized clinical entity approach originally proposed by Hölmich et al. [31, 32] and modified by the Doha consensus statement [33]. The standardized clinical entity approach is based on a number of pain provocation tests including anatomical palpation, resistance testing and passive muscle strength. Since the standardized clinical



Fig. 2 Longitudinal ultrasound image of normal and homogeneous gluteus medius and minimus tendons with normal fibrillar pattern and bone configuration (**a**). Longitudinal ultrasound image of thickened hypoechoic gluteus medius and minimus tendons with loss of normal fibrillar pattern and irregular bone configuration (**b**). Greater trochanter (1), gluteus medius and minimus tendons (2), and greater trochanteric bursitis (3)



entity approach does not include identification of pain in the hamstrings and abductors, we included these two entities in our study. Identification of pain related to muscles and tendons in the hamstrings and abductors followed the same principle as the other clinical entities. Furthermore, rectus abdominis-related pain [31, 32] was the focus in this study instead of the inguinal-related pain defined in the Doha consensus [33]. Inguinal-related pain is less relevant in the female-dominated study population, because the anatomy of the inguinal canal is different in women compared to men [14]. Muscle-tendon-related pain was assessed in the index limb.

Intra- and inter-rater reliability

Two raters assessed pain related to muscles and tendons and the inter-rater reliability of these measures was reported in Jacobsen et al. [14]. Similarly, two raters carried out the ultrasound examination, and the intra- and inter-rater reliability of this examination was investigated. Saved images and movie sequences of 50 patients were evaluated twice by the same rater (JSJ), with a period of median 10 (7–13) days between each evaluation. Furthermore, the radiologist specialized in musculoskeletal ultrasonography (LB) later evaluated the saved images and movie sequences of the same 50 patients, and the inter-rater reliability was investigated.

Statistics

Normal distribution was checked with histograms and probability plots, and data were presented as mean \pm one standard deviation if data were normally distributed. The categorical variables were presented as prevalence with 95% confidence intervals. Correlations between muscle-tendon-related abnormalities detected by ultrasonography and pain related to muscles and tendons identified clinically within each entity were tested with Spearman's rank correlation coefficient on the 100 dysplasia patients. The reliability of the ultrasound examination was reported as percentage of agreement and with Cohen's κ -coefficient. Furthermore, the interpreted agreement of Cohen's κ -coefficient was reported according to Landis [34]. The significance level was 0.05 and the STATA 14 (StataCorp, College Station, TX) software package was used for data analysis.

Results

A consecutive sample of 135 patients was assessed for eligibility; of those, 100 patients were included in the study [14]. Baseline characteristics of the included patients are reported in Table 1.

The intra-rater reliability of the ultrasound examination ranged from 76 to 92% with κ -coefficients ranging from 0.51 to 0.70 (Table 1, Online Resource 2). The inter-rater reliability of the ultrasound examination ranged from 64 to 84% with κ -coefficients ranging from 0.19 to 0.46 (Table 2, Online Resource 2).

The prevalence of labral- and muscle-tendon-related abnormalities detected by ultrasonography ranged from 9 to 55% (Table 2). The three most prevalent muscle-tendon-related abnormalities were related to iliopsoas, adductor longus and gluteus medius/minimus. In 19% of the patients, no muscle-tendon-related abnormalities were detected by ultrasonography. Furthermore, 43% had muscle-tendon-related abnormalities in one entity, 26% in two entities, 11% of patients had muscle-tendon-related abnormalities in three entities and 1% of patients in four

 Table 1 Baseline characteristics in 100 consecutive patients with hip dysplasia

Outcomes	Patients (SD)
Men	17
Bilateral hip dysplasia	89
Tönnis osteoarthritis grade 0 [27]	97
Age	29.9 (9.2)
BMI	23.2 (3.0)
Duration of pain, years	4.9 (5.6)
CE angle preoperatively	17.4 (4.7)
AI angle preoperatively	13.8 (4.9)
Clinical sign of labral pathology (positive FADIR test)	83
Clinical sign of labral pathology (positive FABER test)	74
Clinical sign of internal snapping hip (positive pain- provocation test [30])	30
HAGOS pain	50.3 (18.0)
HAGOS symptoms	49.2 (17.4)
HAGOS ADL	55.5 (22.4)
HAGOS sport/recreation	39.3 (20.7)
HAGOS participation	23.0 (24.7)
HAGOS quality of life	29.4 (14.3)

Baseline characteristics are presented as mean (SD) values and as percentage (%)

BMI body mass index, *CE* center-edge, *AI* Tönnis' acetabular index, *FADIR* flexion/adduction/internal rotation, *FABER* flexion/abduction/ external rotation, *HAGOS* Copenhagen hip and groin outcome score, *ADL* activities of daily living

entities. We tested correlations between muscle-tendonrelated abnormalities detected by ultrasonography and pain related to muscles and tendons identified clinically and found significant correlations between ultrasonography findings and pain related to the iliopsoas tendon and the gluteus medius/minimus tendons (Table 3).

Discussion

Eighty-one percent of patients with symptomatic hip dysplasia presented with muscle-tendon-related abnormalities and most prevalent were muscle-tendon-related abnormalities of the iliopsoas, adductor longus and gluteus medius/minimus. Furthermore, ultrasonography findings of the iliopsoas and gluteus medius/minimus tendons were correlated with pain identified with the clinical entity approach, whereas ultrasonography findings related to the adductor longus tendon, the hamstrings tendons and the pubic symphysis were not correlated to pain related to muscles and tendons in these structures.

Clinical implication

In our previous study on patients with hip dysplasia [14], we identified pain related to muscles and tendons with clinical tests and found a high prevalence of pain in the iliopsoas and hip abductors. However, pain in the hip adductors, the hamstrings and pain related to the pubic symphysis was low. In this study, the prevalence of adductor longus-related abnormalities was high, but the ultrasonography findings in the adductor longus tendon did not correlate with pain. Furthermore, the prevalence of ultrasonography abnormalities in the hamstrings and pubic symphysis was low and in line with the findings of our previous study [14].

Muscle-tendon-related abnormalities detected by MRI have previously been reported among asymptomatic controls and asymptomatic soccer players [17]. Moreover, a cohort study on 34 male athletes failed to show ultrasonography-detected differences between athletes with and without history of previous injury [35]. This suggests that chronic structural changes probably exist as a consequence of previous injuries and/or microtears unrelated to current symptoms [17]. Hence, we believe that the structural changes in the adductor longus tendon, the hamstring tendons and the pubic

Table 2 Labral- and muscle-tendon-related abnormalities detected by ultrasonography in 100 patients with hip dysplasia

Tissue	Transducer placement	Abnormali- ties (95%
		CI)
Iliopsoas tendon	Transverse scan with the femoral artery as medial landmark	50 (40; 60)
Glut. med./min. tendons	Longitudinal and transverse scan with the greater trochanter as landmark	27 (18; 36)
Adductor longus tendon	Longitudinal scan with the inferior ramus of the pubis as proximal landmark	31 (22; 40)
Hamstring tendons	Longitudinal and transverse scan with the ischial tuberosity as landmark	15 (8; 22)
Pubic symphysis	Transverse scan at the symphyseal cleft	9 (3; 15)
Acetabular labrum	Longitudinal scan parallel to the long axis of the femoral neck	55 (45; 65)

Abnormalities are reported as prevalence (%). The sum of abnormalities in the individual patients is above 100% because a patient can have abnormalities in more than anatomical structure

glut. med./min. gluteus medius/minimus

				· ·
Clinical entities	lliopsoas tendon US	Clinical entities	Glut. med./min. tendons US	
	<i>p p</i> value		φ	<i>p</i> value
Iliopsoas-related pain	0.24 0.02	Abductor-related pain	0.35	<0.001
Clinical entities	Adductor longus tendon US	Clinical entities	Hamstring tendons US	
	<i>p p</i> value		σ	<i>p</i> value
Adductor-related pain	0.04 0.68	Hamstring-related pain	0.04	0.69
Clinical entities	Pubic symphysis US			
	p value			
Rectus abdominis-related p	iin 0.11 0.26			
Correlations between muscl man's ρ)	e-tendon-related abnormalities detected by	ultrasonography (US) and the correspond	ling clinical entities reported as Spear	rman's rank correlation coefficient (Spear-

symphysis detected by ultrasonography are less clinically relevant and probably exist because of injuries, microtears and/or overuse earlier in life.

The high prevalence of iliopsoas- and gluteus medius/ minimus-related abnormalities correlated with pain in the same anatomical structures, which was supported by the findings of our previous study [14], where we found a high prevalence of pain in the iliopsoas and in the hip abductors. Abnormality of the iliopsoas tendon probably manifests as a consequence of the shallow and oblique acetabulum causing reduced weight bearing in the dysplastic joint [1-4] and increased load on the anterior capsulo-labral complex [4] and possible also the iliopsoas [12]. Furthermore, patients with hip dysplasia also present with increased femoral anteversion [36, 37] causing further load on the anterior capsulolabral complex [4] and the iliopsoas [12]. An increased load may also explain the high prevalence of internal snapping hip identified in our study (30%), which was also reported among patients with increased femoral anteversion undergoing hip arthroscopy [12]. Abnormalities related to gluteus medius/minimus possibly also manifest as a consequence of the reduced weight bearing in the dysplastic joint [1-4]. where the hip abductors have to generate higher forces to maintain a leveled pelvis during ambulation as previously documented [38].

Previous ultrasound studies

glut. med./min. gluteus medius/minimus

This study is the first to detect muscle-tendon-related abnormalities with ultrasonography in a consecutively included cohort of patients with symptomatic hip dysplasia. Four previous studies have reported muscle-tendon-related abnormalities detected by ultrasonography in patients with hip and/or groin pain [18, 35, 39, 40]. Using a standardized protocol, Kälebo et al. [18] detected muscle-tendon-related abnormalities in 36 patients with groin pain (not patients with hip dysplasia). In 28 of the 36 patients, ultrasonography detected abnormalities in the region of the painful areas [18]. Abnormalities of the hamstrings and adductor tendons were most prevalent [18]. Abnormalities of the rectus femoris, gluteal and rectus abdominis tendons were less common; abnormality of the iliopsoas tendon was not assessed [18]. The higher prevalence of abnormalities of the hamstring tendons compared to our results may be explained by the study being conducted 25 years ago and since the ultrasound technology has developed significantly. In a retrospective study by Bass et al. [39], ultrasonography findings were detected in the origin of the tensor fascia lata muscle in 12 symptomatic athletes with anterior groin pain. The symptomatic athletes presented with enlarged tendons, hypoechoic areas at the iliac crest and point tenderness at the iliac crest. These findings were compared to asymptomatic controls, and no ultrasonography findings were detected in the asymptomatic

controls. In another study by Long et al. [40], 877 patients with so-called greater trochanteric pain syndrome underwent ultrasound examination. Among these patients, 50% had gluteal tendinitis, 20% had trochanteric bursitis, 29% had a thickened iliotibial band and 2% had gluteal tendon tears. Despite our cohort being much younger than the patients in the study by Long et al. [40] with a mean age of 54 years, we also identified a high prevalence of abnormalities related to gluteus medius/minimus. In our cohort, we believe that the gluteus medius/minimus-related abnormalities were linked to the reduced lateral acetabular coverage of the femoral head, which requires the abductors to be overly active and may lead to injury or to overuse tendinopathy caused by excessive use.

Based on the previous studies [18, 35, 39, 40], ultrasound examination of the hip seems justifiable and capable of differentiating findings between symptomatic and asymptomatic structures [18, 39]. An advantage of ultrasonography compared with MRI is the possibility to assess both image and tenderness of the structure in focus by applying pressure during examination [40]. The latter is of great importance, since previous studies have reported muscle-tendon-related abnormalities in asymptomatic individuals [17, 35, 41]. Therefore, ultrasonography of the hip cannot stand alone and should be used as a supplement to clinical tests and anamnesis. Pain related to muscles and tendons should be identified by clinical tests and secondary by an ultrasound examination, which may be used to image and specify the structural changes. It is essential always to use a standardized ultrasound protocol and to be aware of the possible high prevalence of asymptomatic structural changes, which is of no clinical importance. Finally, despite the challenges of adding an ultrasound examination as an extra modality, ultrasonography might potentially help clinicians monitor tendon structure and bursitis while treating painful structures.

Limitations of our results

This study has a number of limitations. First, our evaluation of reliability indicated that the applied ultrasound examination was rater dependent. The low inter-rater reliability of our ultrasound examination is in accordance with previous studies on reliability of ultrasound [41, 42], where the findings of minor structural abnormalities have been described as particularly difficult due to inability to separate minor structural changes from ultrasound artifacts such as anisotropy. The reliability evaluation was performed after our two-phase procedure; although the two-phase procedure indicated a positive learning curve, we cannot rule out that the low inter-rater reliability may have affected our overall findings. Second, abnormality of the iliopsoas tendon was only assessed at the acetabular rim and not at the lesser trochanter because the attachment at the lesser trochanter is difficult to detect by ultrasonography [23]. Finally, using ultrasonography, only the anterior superior labrum can be visualized, and we have no knowledge of possible abnormalities in the posterior part of the labrum. However, a previous study has reported a positive predictive value of ultrasonography of 88% with MRI as the gold standard. This means that there is a high probability that an acetabular labral tear is present if detected by ultrasonography in patients with hip dysplasia [43]. Furthermore, the prevalence of labrum abnormality in this study was in line with the findings of previous studies [9, 10].

Muscle-tendon-related abnormalities in the hip and groin region are common in patients with symptomatic hip dysplasia, and the ultrasonography findings of the iliopsoas and gluteus medius/minimus tendons are weakly to moderately correlated to pain related to muscles and tendons in these structures. Both the iliopsoas and the gluteus medius/minimus have a pronounced stabilizing role in the dysplastic hip joint and the common muscle-tendon-related abnormalities in these patients may be caused by injury due to excessive use or degenerative changes in the tendon tissue.

Further studies are needed to assess if the structural changes present due to increased load on the tendons and/or due to impingement secondary to hypertrophy of the acetabular labrum. Furthermore, a positive effect on pain and structural changes of both exercise and surgical interventions should be investigated in future prospective studies.

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Compliance with ethical standards

Conflict of interest Julie Sandell Jacobsen, Lars Bolvig, Per Hölmich, Kristian Thorborg, Stig Storgaard Jakobsen, Kjeld Søballe, and Inger Mechlenburg declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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Paper 3

Patient-reported outcome and muscle-tendon pain after periacetabular osteotomy are related: 1-year follow-up in 82 patients with hip dysplasia





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Patient-reported outcome and muscle-tendon pain after periacetabular osteotomy are related: 1-year follow-up in 82 patients with hip dysplasia

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Background and purpose — Larger prospective studies investigating periacetabular osteotomy (PAO) with patientreported outcome measures developed for young patients are lacking. We investigated changes in patient-reported outcome (PRO), changes in muscle-tendon pain, and any associations between them from before to 1 year after PAO.

Patients and methods — Outcome after PAO was investigated in 82 patients. PRO was investigated with the Copenhagen Hip and Groin Outcome Score (HAGOS). Muscle– tendon pain in the hip and groin region was identified with standardized clinical tests, and any associations between them were analyzed with multivariable linear regressions.

Results — HAGOS subscales improved statistically significantly from before to 1 year after PAO with effect sizes ranging from medium to very large (0.66–1.37). Muscletendon pain in the hip and groin region showed a large decrease in prevalence from 74% (95% CI 64–83) before PAO to 35% (95% CI 25–47) 1 year after PAO. Statistically significant associations were observed between changes in HAGOS and change in the sum of muscle–tendon pain, ranging from –4.7 (95% CI –8.4 to –1.0) to –8.2 (95% CI –13 to –3.3) HAGOS points per extra painful entity across all subscales from before to 1 year after PAO.

Interpretation — Patients with hip dysplasia experience medium to very large improvements in PRO 1 year after PAO, associated with decreased muscle–tendon pain. The understanding of hip dysplasia as solely a joint disease should be reconsidered since muscle–tendon pain seems to play an important role in relation to the outcome after PAO. Traditionally, hip dysplasia is considered a joint disease with insufficient coverage of the femoral head, which is related to early painful degenerative changes (Mechlenburg 2008, Ross et al. 2011). Pain and physical function can be improved by periacetabular osteotomy (PAO) (Hartig-Andreasen et al. 2012, Lerch et al. 2017), a well-established surgical treatment of symptomatic hip dysplasia in young patients. We have previously challenged this traditional understanding as we reported a high prevalence of muscle–tendon pain in young patients with hip dysplasia, which negatively affected patient-reported outcome (PRO) (Jacobsen et al. 2018b).

PAO is commonly investigated with patient-reported outcome measures (PROMs) developed for older patients with osteoarthritis (Hartig-Andreasen et al. 2012, Clohisy et al. 2017). In young patients, however, a high score on a PROM designed for older patients does not necessarily indicate an acceptable health status, as more strenuous activities such as sports and recreational activities are not evaluated.

Only a few previous studies have investigated PRO after PAO with PROMs developed for young and physically active patients (Jacobsen et al. 2014, Khan et al. 2017). In these studies, outcomes were investigated with the Non Arthritic Hip Score (NAHS) and the Copenhagen Hip and Groin Outcome Score (HAGOS). The results of the studies showed medium to very large effect sizes. The NAHS, however, was developed for and validated in patients with hip osteoarthritis (Khan et al. 2017), while the study using HAGOS was fairly small and focused on objective gait characteristics rather than PRO (Jacobsen et al. 2014). Therefore, it is warranted to investigate the outcome of the PAO with PROMs designed for young and active patients, including the possible negative effect of muscle–tendon pain.

We investigated changes in PRO, changes in muscle–tendon pain, and any associations between them from before to 1 year after PAO.

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Patients and methods

Patients from the Department of Orthopaedics at Aarhus University Hospital in Denmark were prospectively included from May 2014 to August 2015. They were part of a study population from a previous study (Jacobsen et al. 2018b) and were included if Wiberg's centre-edge (CE) angle was $< 25^{\circ}$ (Wiberg 1939), if they had had groin pain for at least 3 months, and if they were scheduled for PAO. Furthermore, only patients < 45 years, with BMI < 30, normal range of motion (minimum 110° of hip flexion), and with Tönnis's osteoarthritis grade < 2 (Tönnis 1987) were operated on. Patients with comorbidities and previous surgical interventions affecting their hip function were excluded. Further details on study design are reported in our previous studies on the same study population, reporting prevalence of muscle–tendon pain and structural abnormalities before PAO (Jacobsen et al. 2018a, 2018b).

Before PAO, patient characteristics including age, sex, and duration of pain were recorded based on standardized questions. A single rater measured the CE angle, the Tönnis acetabular index (AI) angle (Tönnis 1987), and the Tönnis osteoarthritis grade on standing anteroposterior radiographs. Information on comorbidities and previous treatments was extracted from hospitals charts. Pain was recorded using the FABER (Flexion/Abduction/External Rotation) test and the FADDIR (Flexion/Adduction/Internal Rotation) test (Troelsen et al. 2009, Martin et al. 2010). Additionally, a standardized test was used to record occurrence of internal snapping hip (Tibor and Sekiya 2008).

Periacetabular osteotomy

The minimally invasive transsartorial approach for PAO was performed by 2 experienced orthopedic surgeons via 3 separate osteotomies (Troelsen et al. 2008). In short, an approximately 7 cm incision was made alongside the sartorius muscle beginning at the anterior superior iliac spine. The sartorius muscle was divided parallel with the direction of its fibers. The medial part of the split muscle was retracted medially together with the iliopsoas muscle, and this was followed by osteotomies. The patients were presented with a standardized post-surgery rehabilitation program on the ward, and discharged after approximately 2 days of hospitalization. Partial weight-bearing was allowed in the first 6–8 weeks. Moreover, all patients were offered an individual-based rehabilitation program of 2 weekly training sessions starting 6 weeks after PAO and lasting generally for 2–4 months.

Patient-reported outcome measure

The HAGOS was completed before and 1 year after PAO by all patients prior to assessment of muscle–tendon pain. HAGOS consists of 6 separate subscales covering pain, symptoms, physical function in daily living (ADL), physical function in sports and recreation (sports/recreation), participation restriction (PA), and quality of life (QOL) (Thorborg et al. 2011). HAGOS is tailored to reflect physically active young and middle-aged patients with long-standing hip and/or groin pain. HAGOS measures the patient's hip-related disability during the past week on a scale from 0 to 100 points, where 100 points indicates best possible outcome.

Pain at rest was measured before and 1 year after PAO on a numeric rating scale (NRS) from 0 (no pain) to 10 (unbearable pain).

Muscle-tendon pain

We assessed muscle-tendon pain before and 1 year after PAO with standardized clinical examinations originally proposed by Hölmich et al. (2004) and modified by the Doha consensus statement (Weir et al. 2015). The standardized examination covers a number of pain-provoking tests including anatomical palpation, resistance testing, and passive muscle stretch in specific anatomical regions, named clinical entities (Weir et al. 2015). In our study, we added identification of pain in the hamstrings and abductors following the same principle as the other clinical entities, since these structures were considered important in our study. Moreover, pain related to the rectus abdominis (Hölmich et al. 2004) was the focus in this study as an alternative to inguinal-related pain defined in the Doha consensus since most patients were women. Muscle-tendon pain was assessed in 5 anatomical entities: the iliopsoas, the abductors, the adductors, the hamstrings, and the rectus abdominis. Muscle-tendon pain was investigated within each entity and as the sum of positive clinical entities for each patient, ranging from 0 to 5. The outcome of each entity test was dichotomous (pain yes or no).

Sample size considerations

The aim of this study was to investigate 1-year outcome of the PAO using HAGOS. Moderate effect sizes were considered relevant, which would require a sample size of 85 patients to show an effect size of 0.5 from before to 1 year after PAO. This sample size is based on a power of 90% and a significance level of 5%.

Statistics

Parametric continuous data were reported as means with standard deviations (SD) if normally distributed, otherwise reported as medians with interquartile ranges (IQR). Histograms and probability plots were used to test for normality. Categorical data were reported as numbers of events and percentage with a 95% confidence interval (CI). Changes in each HAGOS subscale measured before and 1 year after PAO were considered important and were tested with paired t-tests. Similarly, changes in each muscle–tendon pain entity from before to 1 year after PAO were considered equally important. These were tested with the McNemar test. Effect sizes of HAGOS and muscle–tendon pain were calculated from the paired t-test as Cohen's d on the formula:

Effect size

Cohen's d

1.37

0.99

1.25

1.02

0.66

1.11

0.74

p-value

< 0.001

< 0.001

< 0.001

< 0.001

< 0.001

< 0.001

< 0.001

Difference

mean (CI)

26 (22-30)

19 (15-23)

27 (22-31)

25 (20-31)

21 (14-28)

28 (22-33)



Flowchart of the study process. 100 consecutive patients with symptomatic hip dysplasia scheduled for periacetabular osteotomy (PAO) were included from Department of

Orthopedic Surgery, Aarhus University Hospital, Denmark.

Table 2. Patient-reported outcome of PAO in 82 patients with hip dysplasia

Before PAO

mean (SD)

50 (17)

48 (17)

55 (22)

39 (21)

23 (24)

29 (14)

3 (2-5)

Outcome score

Symptoms

Sport/recreation

Quality of life

NRS Pain (IQR)

HAGOS

Pain

ADL

PA

1 year

after PAO

mean (SD)

76 (17)

67 (19)

81 (18)

64 (23)

44 (33)

57 (25)

 $0(\dot{0}-2)$

Abbreviations: HAGOS = Copenhagen Hip and Groin Outcome Score (0–100 points), ADL = physical function in daily living, PA = preferred physical activity participation, NRS = numeric rating scale, IQR = interquartile range.

Table 1. Characteristics of 82 consecutive patients with hip dysplasia

Patient characteristics	Before PAO	1 year after PAO
Age, years ^a BMI ^a Men, n Duration of pain, years ^b Bilateral hip dysplasia, n CE angle (°) ^a Al angle (°) ^a Tönnis's osteoarthritis grade 1, n Positive FADIR test, n Positive FABER test, n Positive internal snapping hip test, n	30 (9) 23 (3) 11 3 (1-6) 74 17 (5) 14 (5) 3 70 62 0 25	31 (9) 24 (3) - - 30 (5) 3 (4) 5 55 47 16

Characteristics are presented as numbers or

^a mean values (standard deviation),

^b median values (interquartile range)

Abbreviations: CE = centre-edge, AI = Tönnis's acetabular index,

FADIR = Flexion/Adduction/Internal Rotation,

FABER = Flexion/Abduction/External Rotation.

t statistic/ $\sqrt{(n)}$, and from McNemar test as Cohen's w on the formula: w statistic/ $\sqrt{(n)}$. Finally, crude and adjusted multivariable linear regression analyses were performed to assess associations between changes in HAGOS (pain, symptoms, ADL, sport/recreation, PA, and QOL) and change in the sum of muscle-tendon pain entities (i.e., the sum of positive clinical entities for each patient) from before to 1 year after PAO. Changes in each HAGOS subscale were the dependent variables, and the sum of muscle-tendon pain entities for each patient was the independent variable. Potential co-variates were identified using causal diagrams for observational research, based on knowledge from previous studies (Greenland et al. 1999). Co-variates included in the analysis were CE angles measured before and 1 year after PAO (continuous), age (continuous), and sex (dichotomous). Crude and adjusted β -coefficients were estimated and the assumptions

(independent observations, linear association, constant variance of residuals, and normal distribution of residuals) of the regression models were met. The β -coefficients refer to the slope of the regression line, indicating a decrease in changed PRO per unit increase in muscle–tendon pain. The STATA 14.0 (StataCorp, College Station, TX, USA) software package was used for data analysis, and results were considered statistically significant if p < 0.05.

Ethics, registration, funding, and potential conflicts of interest

This study was conducted and reported in accordance with the WMA declaration of Helsinki and the STROBE statement. All patients gave informed consent to participate, and ethical approval was obtained from the Central Denmark Region Committee on Biomedical Research Ethics (5/2014). The Danish Data Protection Agency (1-16-02-47-14) authorized the handling of personal data, and the protocol was registered at ClinicalTrials.gov (20140401PAO). This study was funded by the Danish Rheumatism Association, the Aase and Ejnar Danielsen Fund, and the Fund of Family Kjaersgaard, Sunds. The authors declare that they have no potential conflicts of interest.

Results

Informed consent was obtained from 100 consecutive patients before PAO. 18 patients were lost to follow-up (Figure), leaving 82 patients for this study (Table 1). We found no statistically significant differences in any of the listed patient characteristics between the 18 patients lost to follow-up and the analyzed patients (data not shown).

Patient-reported outcome

We found statistically significant increases in all HAGOS subscales from before to 1 year after PAO (Table 2). The effect

Table 3. Muscle-tendor	ı pain in 8	32 patients	with hip	dysplasia
------------------------	-------------	-------------	----------	-----------

Clinical entities Before	ore PAO 1 year aft 5 (CI) % (C	er PAO Difference CI) % points (CI	Effect size) Cohen's w	p-value
Iliopsoas-related pain54Abductor-related pain37Adductor-related pain12Hamstrings-related pain6Rectus-abdominis-related pain4Patients with minimum 1positive clinical entity74	(42-65) 22 (1) (26-48) 15 (8) (6-21) 7 (3) (2-14) 1 (0) (0-10) 0 (0) (64-83) 35 (2)	$\begin{array}{rrrr} 4-32) & -32 & (-46 & \text{to} -24) & -22 & (-36 & \text{to} -4) & -22 & (-36 & \text{to} -4) & -15) & -5 & (-16 & \text{to} & 6) & -7) & -5 & (-12 & \text{to} & 2) & -0) & -4 & (-9 & \text{to} & 2) & -0 & -4 & (-9 & \text{to} & 2) & -5 & \text{to} & 47) & -39 & (-54 & \text{to} -4) & -39 & (-54 $	$\begin{array}{rrrrr} 17) & -1.96\\ 8) & -1.12\\ 0 & -0.11\\ 0 & -0.29\\ & -0.33\\ 24) & -2.46 \end{array}$	< 0.001 0.002 0.5 0.2 0.3 < 0.001

Table 4. Associations between change in HAGOS (0–100 points) and change in muscle–tendon pain (n = 82)

HAGOS	Crude β coefficient (CI)	p-value	Adjusted ^a β coefficient (CI)	p-value
Pain	-4.7 (-8.5 to -0.9)	0.02	-4.7 (-8.4 to -1.0)	0.01
Symptoms	-4.8 (-8.6 to -1.0)	0.02	-4.7 (-8.6 to -0.9)	0.02
ADL	-6.1 (-10 to -1.9)	0.005	-6.2 (-10 to -2.1)	0.004
Sport/recreation	-5.9 (-11 to -1.0)	0.02	-6.0 (-11 to -0.9)	0.02
PA	-1.2 (-7.9 to 5.5)	0.7	-1.2 (-7.9 to 5.6)	0.7
Quality of life	-8.2 (-13 to -3.3)	0.001	-8.2 (-13 to -3.3)	0.001

 $^{\rm a}$ Adjusted for CE angles measured before and 1 year after PAO, age, and sex. Abbreviations: See Table 2

sizes ranged from 0.66 to 1.37, corresponding to medium to very large effect sizes. Moreover, 26/82 patients reported a sport/recreation score of 0–50 points 1 year after PAO, 14/82 patients reported a sport/recreation score of >50–70 points, while 42/82 patients reported a sport/recreation score >70 points 1 year after PAO. Similarly, NRS pain decreased statistically significantly, corresponding to a medium effect size of 0.74.

Muscle-tendon pain

The analysis of the individual entities showed a significant decrease in iliopsoas-related pain and abductor-related pain from before to 1 year after PAO, whereas the decrease in the other 3 entities was not statistically significant (Table 3). Moreover, the proportion of patients with minimum 1 positive muscle–tendon pain entity decreased by 39 percentage points (CI 24–54) 1 year after PAO.

Associations between changes in HAGOS and change in muscle-tendon pain

Apart from HAGOS PA, both crude and adjusted analyses showed statistically significant negative linear association between changes in HAGOS and change in the sum of muscle–tendon pain entities, ranging from -4.7 to -8.2 HAGOS points per extra painful entity across all subscales from before to 1 year after PAO (Table 4).

Discussion

We investigated changes in PRO, changes in muscle-tendon pain, and any associations between them from before to 1 year after PAO. Our patients reported clinically relevant improvements in all HAGOS subscales with effect sizes ranging from medium to very large. All improvements were higher than the minimally important change (MIC) of the HAGOS (Thomeé et al. 2014). Nevertheless, 1 year after PAO, one-third of the patients still experienced muscle-tendon pain, most commonly affecting the iliopsoas and the hip abductors. Furthermore, our regression analyses showed that

change in the sum of muscle-tendon pain was associated with changes in PRO of the PAO.

Only 2 previous studies have investigated the outcome of PAO with PROMs tailored to reflect activity levels of young and active patients. Jacobsen et al. (2014) reported PRO after PAO, applying HAGOS, and found medium to very large improvements corresponding to effect sizes from 0.78 to 1.75 in a study population of 29 patients with hip dysplasia. Similarly, a consecutive study on 168 patients with hip dysplasia reported very large patient-reported improvement corresponding to an effect size of 1.5 measured with the NAHS (Khan et al. 2017). The HAGOS subscale scores, we found, ranged from 44 to 81 points, which is in accordance with the study by Jacobsen et al. (2014), reporting scores of 50 to 90 HAGOS points 1 year after PAO in another series of patients. The association between change in HAGOS PA and change in the sum of muscle-tendon pain entities was not statistically significant. However, the lack of association between change in HAGOS PA and change in muscle-tendon pain can be explained since HAGOS PA measures patients' selfperceived ability to participate in a preferred physical activity (Thorborg et al. 2011), which is not related to specific functions and activities like the other HAGOS subscales. Therefore, it is not surprising that perceived participatory capacity is not reflected in change in muscle-tendon pain and vice versa.
We did not include a healthy control group; however, an age- and sex-matched healthy control group was included in a previous study, investigating the outcome 1 year after PAO using HAGOS (Jacobsen et al. 2014). All healthy subjects reported a PRO of 84–100 HAGOS sport/recreation points, which was different from the HAGOS sport/recreation score measured 1 year after PAO in the patients with hip dysplasia (Jacobsen et al. 2014). In this study, half of the patients reported a HAGOS score \leq 70 sport/recreation points 1 year after PAO. This indicates that patients still experience a low functional level, associated with muscle–tendon pain.

Our patients showed a clinically relevant reduction in pain related to the iliopsoas and the hip abductors. This decrease may be a result of both surgical reorientation and the intensive individual-based rehabilitation program. The effect of muscle-tendon pain on changes in HAGOS score was 5–8 HAGOS points for every change in number of painful clinical entities across all HAGOS subscales, which is in line with the MIC of HAGOS (Thomeé et al. 2014). This suggests that resolving just 1 painful clinical entity after PAO has a clinically relevant impact on the outcome 1 year after PAO.

Muscle-tendon affection in patients with hip dysplasia has only been reported in 1 previous study, which reported muscle-tendon affection among one-fifth of the patients identified by hip arthroscopy (Domb et al. 2014). However, associations between muscle-tendon affection and patient-reported outcomes were not investigated.

Methodological considerations and limitations

As reported in our previous study on the same study population, we found low inter-rater reliability of the muscle-tendon pain assessment, indicating a high random variation in our estimates (Jacobsen et al. 2018b). The potentially negative impact of this is small because we included a large study population. The associations between changes in HAGOS and change in the sum of muscle-tendon pain were mainly driven by patients who either reduced many painful entities or increased the number of painful entities 1 year after PAO. The same analysis without these patients would have resulted in smaller associations or even lack of significant associations between HAGOS and muscle-tendon pain.

Summary

Patients with hip dysplasia experience medium to very large improvements in PRO 1 year after PAO, associated with decreased muscle–tendon pain. The understanding of hip dysplasia as solely a joint disease should be reconsidered as muscle–tendon pain seems to play an important role in relation to the outcome after PAO. Future intervention studies ought to investigate the optimal treatment for patients with hip dysplasia and coexisting muscle–tendon pain. All authors were involved in the planning and writing of the manuscript. IM, KT, PH, and LB gave supervision on design and methods. KS and SSJ included and operated on all patients. JSJ examined patients, while SSJ made all radiologic evaluations. JSJ coordinated all elements, wrote the first description of the study, did all analyses, and wrote the first draft of the manuscript.

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Paper 4

Does the physical activity profile change in patients with hip dysplasia from before to 1 year after periacetabular osteotomy?



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Does the physical activity profile change in patients with hip dysplasia from before to 1 year after periacetabular osteotomy?

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Background and purpose — Knowledge of physical activity profiles among patients with hip dysplasia is lacking. We investigated whether patients with hip dysplasia change physical activity profile from before to 1 year after periace-tabular osteotomy. Furthermore, we investigated associations between change in accelerometer-based physical activity and change in self-reported participation in preferred physical activities (PA).

Patients and methods — Physical activity was objectively measured at very low to high intensity levels with accelerometer-based sensors. Subjectively, PA was recorded with Copenhagen Hip and Groin Outcome Score (HAGOS) in 77 patients. Associations between the 2 were analyzed with simple linear regression analyses.

Results — Changes in accelerometer-based physical activity ranged from -2.2 to 4.0 % points at all intensity levels from baseline to 1-year follow-up. These changes represent very small effect sizes (-0.16 to 0.14). In contrast, self-reported PA showed a statistically and clinically relevant increase of 22 (CI 14–29) HAGOS PA points 1 year post-surgery. Associations between change in accelerometer-based physical activity and change in self-reported PA were, however, not statistically significant and correspond to a percentage change in physical activity of only -0.87% to 0.65% for a change of 10 HAGOS PA points.

Interpretation — Patients with hip dysplasia do not seem to change physical activity profile 1 year post-surgery if measured with objective accelerometer-based sensors. This is interesting as self-reported PA indicates that patients' ability to participate in physical activity increases, suggesting that this increased self-reported participatory capacity is not manifested as increased objectively measured physical activity.

Hip dysplasia is a pathological development of the hip joint, presenting in early adulthood. The clinical presentation of symptomatic hip dysplasia is pain caused by intra-articular injury (Nunley et al. 2011) and coexisting muscle–tendon pain (Jacobsen et al. 2018b). The pain prevents patients from participating in their preferred physical activities (Jacobsen et al. 2013), including higher intensity activities such as running (Novais et al. 2013).

Periacetabular osteotomy (PAO) is the preferred joint-preserving treatment for patients with symptomatic hip dysplasia (Troelsen et al. 2008). PAO has been shown to result in pain relief, restoration of function, and high hip survival rates (Lerch et al. 2017). Furthermore, previous studies on selfreported physical activity have shown that patients increase their ability to participate in their preferred physical activities 1 year after PAO (Jacobsen et al. 2014, Klit et al. 2014, Khan et al. 2017) and spend more time on physical activities at higher intensities (Novais et al. 2013). Discrepancies between selfreported physical activity and objectively measured physical activity have been reported (Sallis and Saelens 2000, Harding et al. 2014). However, it is important to recognize that selfreported physical activity captures the capability to complete a given task, while the ability to measure the actual performance is limited (Smuck et al. 2017). Accelerometer-based measures of physical activity allow us to evaluate if patients with hip dysplasia change objectively measured physical activity profile, alongside with subjective measured levels of improved pain, physical function, and quality of life after PAO.

We investigated whether patients with hip dysplasia change physical activity profile from before to 1 year after periacetabular osteotomy, measured by accelerometer-based sensors and self-reported physical activity. Furthermore, we investigated associations between change in accelerometer-based physical activity and change in self-reported participation in preferred physical activities (PA).

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Patients and methods

Patients

100 consecutive patients with unilateral and bilateral symptomatic hip dysplasia were included in this study from May 2014 to August 2015 at the Department of Orthopedics, Aarhus University Hospital, Denmark. Inclusion criteria to participate in this study was Wiberg's center-edge (CE) angle < 25 degrees (Wiberg 1939), groin pain for at least 3 months, and scheduled PAO. Patients with known co-morbidities and a history of previous surgical interventions affecting the hip function were excluded. Further details on study design was reported in our previous studies on the same study population, reporting ultrasonography-detected abnormalities and prevalence of muscle–tendon pain prior to PAO (Jacobsen et al. 2018a, b).

Baseline characteristics

Baseline characteristics were recorded at baseline by standardized questions. Pain at rest was measured on a numeric rating scale (NRS), and radiographic acetabular angles and Tönnis's osteoarthritis grade were measured by a single rater using standing anteroposterior radiographs. Hospital charts were used to retrieve data on previous surgeries and co-morbidities.

Periacetabular osteotomy

2 experienced orthopedic surgeons used the minimally invasive approach for PAO. The surgical procedure involves reorientation of the acetabulum through 3 separate osteotomies and correction of the insufficient coverage of the femoral head. Compared with other PAO procedures, the minimally invasive approach involves minor incision of the soft tissue and enables early mobilization (Troelsen et al. 2008). Post-surgery, all patients underwent an in-hospital standardized rehabilitation program, and only partial weight bearing with a maximum load of 30 kg was allowed in the first 6–8 weeks. Patients were discharged after approximately 2 days.

Accelerometer-based physical activity

The patients' habitual physical activity profile was objectively measured with a commercial tri-axial accelerometer-based sensor (Gulf Coast Data Concepts, Waveland, MS, USA) during 7 consecutive days (working and leisure days) at baseline and 1 year after PAO. The sensor was taped to the lateral non-affected upper leg of patients using hypo-allergenic double-sided tape (3M, Maplewood, MN, USA). The position of the sensor was at the mid-thigh between the trochanter and lateral condyle, with the y-axis of the sensor along the axis of the femur (van Laarhoven et al. 2016). The sensor was worn during waking hours for a minimum of 8 hours per day. It was removed for the night and during both showering and swimming activities. Data from –6g to 6g were sampled at 50 Hz.

The raw activity data were transferred to a computer and processed using a validated algorithm (Lipperts et al. 2017). Data were visually divided into separate days using a MatLab (https://www.mathworks.com/products/matlab.html) script designed for the purpose, and non-worn days were excluded. All data were calibrated manually by selecting a period of level walking in the dataset of each day to adapt variations in height, morphology, sensor placement, walking style, and speed (Lipperts et al. 2017). After calibration, the data were run through an algorithm based on a decision tree, and divided into resting, standing, cycling, level walking, walking on stairs (upstairs and downstairs), and running. Further details are described by Lipperts et al. (2017). In addition, the algorithm constructed an intensity variable on the distribution of the average signal intensity in 10-second intervals grouped into 4 intensity levels. The intensity levels were: (i) Very low intensity such as sitting and standing (0–0.05g), (ii) Low intensity such as standing and shuffling (0.05-0.1g), (iii) Moderate intensity such as slow and normal walking (0.1-0.2g), (iv) High intensity such as brisk walking, running, and jumping (> 0.2g).

Self-reported physical activity

Self-reported physical activity was subjectively measured as preferred physical activity participation (PA) using the Copenhagen Hip and Groin Outcome Score (HAGOS) (Thorborg et al. 2011), and completed by the patients at baseline and 1 year after PAO. Besides participation in physical activities, the HAGOS outcome score captures pain, symptoms, physical function in daily living (ADL), physical function in sports and recreation, and quality of life on a scale from 0 to 100 points, where 100 points indicate the highest outcome. HAGOS is a valid, reliable, and responsive outcome measure developed for young patients with longstanding hip and groin pain (Thorborg et al. 2011). Additionally, time spent on preferred PA per week was recorded at baseline and 1 year after PAO.

Sample size consideration

The purpose of this study was to investigate whether patients change physical activity profile from before to 1 year after surgery. We considered moderate effect sizes to be of importance, which required 85 patients for detecting an effect size of 0.5 from before to 1 year after surgery. This calculation was based on a power of 90% and a significance level of 5%.

Statistics

Parametric continuous outcome measures were reported as means (SD) if normally distributed; otherwise reported as medians with either interquartile ranges (IQR) or 95% confidence intervals (CI). Normality was assessed with histograms and probability plots. Categorical data were reported as number of events and percentage with CI. Time spent on physical activities was normalized to total accelerometer-based wear time before surgery and 1 year after surgery. Number



Figure 1. Flowchart of the study process among 100 consecutive patients with symptomatic hip dysplasia scheduled for periacetabular osteotomy (PAO).

of events at baseline were normalized to average daily accelerometer-based wear time at baseline, and the number of events at 1-year follow-up were normalized to average daily accelerometer-based wear time at 1-year follow-up. Differences between baseline and 1-year follow-up were tested with a paired t-test if assumptions were met and otherwise tested with the non-parametric Wilcoxon signed-rank test. Effect sizes were calculated from the paired t-test as Cohen's d on the formula: t statistic/ $\sqrt{(n)}$ for parametric data and otherwise from the non-parametric Wilcoxon signed-rank test on the formula: z statistic/ $\sqrt{(n)}$. Furthermore, simple linear regression analyses were performed assessing associations between change in objectively measured physical activity at 4 intensity levels (very low, low, moderate, and high intensity) and change in subjectively measured HAGOS PA from baseline to 1 year post-surgery. Crude ß-coefficients were estimated, and the assumptions (independent observations, linear association, constant variance of residuals, and normal distribution of residuals) for the linear regression analyses were met. The crude ß-coefficients refer to the slope of the regression line (the increase in objectively measured physical activity for every unit increase in subjectively measured HAGOS PA). STATA 14.0 (StataCorp, College Station, TX, USA) software package was used for data analysis and significant results were presented if p < 0.05.

Table 1. Baseline characteristics of 97 consecutive patients with hip dysplasia

Outcomes	Baseline
Men	15
Age, years (SD)	30 (9)
BMI, kg/m ² (SD)	23 (3)
CE angle, degrees (SD)	17 (4.7)
Al angle, degrees (SD)	14 (4.8)
Tönnis osteoarthritis grade 1	3
Bilateral hip dysplasia	86
Hours spent on self-reported preferred	
physical activities/week, n	
<2.5	13
2.5 to <5	18
5 to <10	40
≥10	26
Self-reported preferred physical activities, n	
Fitness	27
Running	19
Team sports	13
Gymnastics	6
Horseback riding	6
Bicycling	5
Dancing	3
Other	16
No one	2

Abbreviations: SD (standard deviation); BMI (body mass index), CE (center-edge), AI (Tönnis' acetabular index).

Ethics, registration, funding, and potential conflict of interests

This study was done in accordance with the STROBE statement and in compliance with the Helsinki Declaration. The study was notified to the Central Denmark Region Committee on Biomedical Research Ethics on January 14, 2014 (5/2014). The Danish Data Protection Agency gave permission for the handling of personal data (1-16-02-47-14), and the protocol was registered at ClinicalTrials.gov (20140401PAO). All patients gave informed written consent. This study was funded by the Danish Rheumatism Association [grant number: A3280], the Aase and Ejnar Danielsen Fund [grant number: 10-000761/LPJ], and the Fund of Family Kjaersgaard, Sunds [date: 01-05-2018]. The authors have no competing interests.

Results

100 consecutively enrolled patients gave informed consent and were included in this study. Data on objective accelerometer-based physical activity were lost on 3 patients at baseline. At 1-year follow-up 17 patients were lost to follow-up and objective accelerometer-based physical activity data were lost on further 3 patients (Figure 1).

Baseline characteristics of the included patient are reported in Table 1. Pain at rest measured on an NRS was 3.0 (1.5-4.0) Table 2. Accelerometer-based physical activity and self-reported physical activity in hip dysplasia (n = 77)

Outcomes	Baseline mean (SD)	1-year follow-up mean (SD)	Difference mean % points (CI)	Effect size	p-value
Percent of time measured by	acceleromete	er-based sensors			
Very low intensity	74 (9.1)	76 (8.9)	1.6 (-0.89 to 4.0)	0.14	0.2
Low intensity	14 (5.1)	14 (5.3)	-0.66 (-2.2 to 0.89)	-0.096	0.4
Moderate intensity	6.8 (2.9)	6.4 (2.6)	-0.40 (-1.1 to 0.31)	-0.13	0.3
High intensity	4.6 (2.0)	4.3 (2.0)	-0.32 (-0.77 to 0.13)	-0.16	0.2
Self-reported physical activity	/	, , , , , , , , , , , , , , , , , , ,	· · · · · · · · · · · · · · · · · · ·		
HAGOS PA a	23 (24)	45 (33)	22 (14 to 29)	0.67	< 0.001
Hours in PA/week ^{b,c}	0.0 (0.0–2.3	3) 1.0 (0.0–3.0)	_`_`	0.18	0.1

^a HAGOS (Copenhagen Hip and Groin Outcome Score, 0-100 points),

^b PA (preferred physical activity participation)

^c Non-parametric data presented as median (interquartile range).

Table 3. General physical activity profile based on objective data on patients with hip dysplasia

Outcomes	Baseline (n = 97) median (CI)	1-year follow-up (n = 78) median (CI)
Cadence as steps/min Events/day, n	n 99 (98–100)	100 (98–102)
Total steps	7,404 (6,645-8,418)	7,925 (6,637-8,612)
Steps (level)	6,923 (6,192–7,709)	7,322 (6,081-8,217)
Steps (up)	266 (194–403)	235 (171–313)
Steps (down)	155 (134–183)	146 (123–169)
Total wear time, h/day	/ 14 (14–15)	15 (14–15)
Time as percentage		
Resting	64 (61–68)	63 (59–66)
Standing	23 (22–27)	26 (23–27)
Walking	11 (9.9–13)	11 (9.3–13)
Cycling	0.15 (0.063-0.33)	0.084 (0.046-0.18)
Running	0.011 (0.0042-0.020)	0.0078 (0.0040-0.025)

at baseline, and at 1-year follow-up it was 0.0 (0.0-1.3). A sensitivity analysis of the 17 patients lost to follow-up revealed no differences in age, sex, pain, and radiological angles compared with the analyzed patients.

Accelerometer-based physical activity

The accelerometer-based sensor was worn for a median of 7 days (3–8) at both baseline and 1-year follow-up; only 6 patients had worn the sensor for less than 5 days. Changes in objectively measured physical activity ranging from -2.2 to 4.0 % points, across all intensity levels (covering very low, low, moderate, and high intensity) from baseline to 1-year follow-up (Table 2). This was, however, not statistically significant, and represents very small effect sizes ranging from -0.16 to 0.14. A general physical activity profile of the patients is reported in Table 3.

Self-reported physical activity

Subjectively measured HAGOS PA increased statistically sig-

Change in accelerometer-based PA

Figure 2. Scatter plot of the prediction of change in accelerometerbased physical activity (PA) at high intensity as a linear function of change in self-reported preferred physical activity participation (PA) measured by the Copenhagen Hip and Groin Outcome Score (HAGOS) from baseline to 1 year post-surgery.

nificantly from baseline to 1-year follow-up with a moderate effect size. Similarly, a statistically non-significant change in hours spent on preferred physical activities at 1-year follow-up was present, represented by a very small effect size (Table 2).

Associations between accelerometer-based physical activity and self-reported physical activity

Associations between change in accelerometer-based physical activity and change in HAGOS PA ranged from -0.00087 to 0.00065, covering very low, low, moderate, and high intensity from baseline to 1-year follow-up. These were, however, not statistically significant and correspond to a percentage change in physical activity of only -0.87% to 0.65% for a change of 10 HAGOS PA points. The individual associations were as follows: Very low intensity: $\beta = -0.00011$ (CI -0.00087 to 0.00065), p = 0.8. Low intensity: $\beta = -0.00012$ (CI -0.00050 to 0.00046), p = 0.9. Moderate intensity: $\beta = 0.000044$ (CI -0.00018 to 0.00027), p = 0.7. High intensity: $\beta = 0.000072$ (CI -0.000066 to 0.00021), p = 0.3 (Figure 2).

Discussion

Using accelerometer-based sensors, we found that the objectively measured physical activity profile was the same before and 1 year after PAO at all the measured physical activity intensity levels, indicated by very low effect sizes. In contrast, subjectively measured physical activity showed a moderate increase, and this was higher than the minimal important change (MIC) of HAGOS PA (Thomeé et al. 2014). Our linear regression analyses showed absence of any statistically significant and clinically relevant associations between objectively and subjectively measured physical activity as a change of 10 HAGOS PA points would maximally result in a change of physical activity of 1%.

In a systematic review, Tudor-Locke et al. (2011) reported minimum international recommendations for physical activity in healthy populations. The minimum number of steps for adults was 7-8,000 steps per day with an average cadence of 100 steps per minute indicating moderate intensity walking (Tudor-Locke et al. 2011). The general physical profile (Table 3) of our patients shows that their overall level of physical activity was at level with reference values for both steps and cadence at baseline and at the 1-year follow-up, indicating that the patients followed current public health guidelines. Similarly, an American study reported daily strides by a step watch in adults with hip dysplasia and in healthy adults. No differences were seen between the 2 groups (Harris-Hayes et al. 2012). The average number of strides per day was 4,627 (i.e., 9,254 steps) among the adults with hip dysplasia, similar to the average number of steps reported among our patients. Additionally, physical activity was grouped into 4 different intensity levels based on strides per minute. No differences between the groups were found, and the effect sizes were very low (Harris-Hayes et al. 2012). Overall, these 4 intensity levels were comparable to the 4 intensity levels for physical activity in our study, and the results were similar to our results. This suggests that the physical activity profile among Danish patients with hip dysplasia is comparable to that of healthy American adults both before and 1 year after PAO, when measured objectively with accelerometer-based sensors.

This finding is in line with observations among patients undergoing total hip arthroplasty. A previous study measured physical activity with objective accelerometer-based sensors in 19 patients (mean age 69 years) with hip osteoarthritis before and 6 months after total hip arthroplasty (Harding et al. 2014). Similar to our findings, no significant increase in objectively measured physical activity was found after surgery. Self-reported physical activity after surgery has been reported in 6 previous studies of patients with hip dysplasia (Novais et al. 2013, Jacobsen et al. 2014, Beaulé et al. 2015, Clohisy et al. 2017, Hara et al. 2017, Khan et al. 2017). In 1 prospective, multicenter study, the physical activity level was measured subjectively with the University of California, Los Angeles (UCLA) activity scale in 371 patients (mean age 25 years) with hip dysplasia (Clohisy et al. 2017). The patients' physical activity level had increased statistically significantly 2 years post-surgery, alongside with improvement in self-reported pain, physical function, and quality of life. These results are in line with the results of 4 other previous studies in patients with hip dysplasia reporting statistically significantly and clinically relevant increases in self-reported physical activity levels after surgery (Novais et al. 2013, Beaulé et al. 2015, Hara et al. 2017, Khan et al. 2017). In a 6th study, a statistically significantly and clinically relevant increase in HAGOS PA was reported among 32 patients (mean age 34 years) with hip dysplasia 1 year after PAO compared with baseline (Jacobsen et al. 2014). Overall, the results of the 6 previous studies showed statistically significantly and clinically relevant increases in subjectively measured physical activity levels after surgery (Novais et al. 2013, Jacobsen et al. 2014, Beaulé et al. 2015, Clohisy et al. 2017, Hara et al. 2017, Khan et al. 2017); this corroborates our findings.

Difficulties in participating in preferred physical activities are reported as important components of disability among patients with hip pain (Novais et al. 2013). We observed increased HAGOS PA and unchanged objectively measured physical activity 1 year post-surgery. The discrepancy probably exists because HAGOS PA and accelerometer-based methods measure different aspects of physical activity. Accelerometer-based methods provide an objective measure of physical activity, while HAGOS PA measures the patients' self-perceived ability to participate in preferred physical activity. Moreover, age, employment status, culture, and geography have been shown to be associated with activity level (Hirata et al. 2006, Sechriest II et al. 2007, Althoff et al. 2017). Changing one's physical activity profile is complex (Harding et al. 2014), because it is under the influence of one's lifestyle and thus both patients and health professionals need to be aware that PAO alone is unlikely to change the physical activity profile from before to 1 year after PAO.

Limitations

We included no healthy controls and estimates of both accelerometer-based physical activity and self-reported physical activity could therefore not be compared with estimates in healthy controls. The negative impact of this is presumably small since it was possible to compare our findings with the findings of a previous study that included a control group (Jacobsen et al. 2014). Processing of the accelerometer-based physical activity data does involve some measure of subjectivity as the researcher has to calibrate the algorithm manually (Lipperts et al. 2017). To reduce potentially systematic effects, we processed all data in pairs, and in this way processing of baseline data was followed by processing of 1-year follow-up data in each patient. Still, we cannot rule out that the subjective element may increase the overall variability. The intensity variable shows the percentage of time at 4 different intensity levels, and other thresholds may have given other results. However, a previous study on young and middle-aged adults with hip disorders found similar results, even though their intensity levels were based on strides per minute (Harris-Hayes et al. 2012). This similarity suggests that our findings are valid.

Summary

Patients with hip dysplasia do not seem to change physical activity profile 1 year post-surgery if measured with objective accelerometer-based sensors. This is interesting as selfreported PA indicates that patients' ability to participate in physical activity increases, suggesting that this increased participatory capacity is not manifested as increased objectively measured physical activity. These findings are similar to another study on patients undergoing total hip arthroplasty where no increase in accelerometer-based physical activity was found after surgery.

All authors took part in planning the study and writing of the present manuscript. IM, KT, PH, and LB concentrated on the design and use of methods. JSJ tested the participants. KS and SSJ were responsible for inclusion of patients, and SSJ made the radiologic evaluations. JSJ coordinated all elements and made the first draft of the manuscript.

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13. Supplementary files

Standardised clinical examinations

Entity	Procedure	Palpation	Resistance or stretch
Iliopsoas-related pain	Palpatory pain of the muscle through the lower lateral part of the abdomen and/or just distal of the inguinal ligament and pain with passive stretching during modified Thomas' test (47,48,54).		
Abductor-related pain	Palpatory pain at the insertion point at the greater trochanter and pain with side-lying abduction against resistance		
Adductor-related pain	Palpatory pain at the muscle origin at the pubic bone and pain with adduction against resistance (47,48,54)		at the second se
Hamstring-related pain	Palpatory pain at the muscle origin at the tuber ischii and pain with extension against resistance		
Rectus-abdominis- related pain	Palpatory pain of the distal tendon and/or the insertion at the pubic bone and pain at contraction against resistance (47,54)		

Tissue	Findings	Procedure	Illustration
Iliopsoas tendon Transverse scan with the femoral artery as medial landmark	Non- homogeneous echogenicity, diffuse margin appearance, abnormal fluid intra- and/or extra-substantial (iliopsoas bursitis), calcifications, and/or hypertrophy compared with the contralateral side.	Patient assessed is in the supine position with hip and knee in neutral position. The probe is placed in a sagittal oblique plane parallel to the long axis of the femoral neck with the acetabular rim centred. The probe is then rotated until it is parallel to the inguinal ligament with the femoral artery medial to the tendon. A movie sequence was recorded in this position.	
Gluteus medius/mini mus tendons Longitudinal and transverse scan with the greater trochanter as landmark	Non- homogeneous echogenicity, abnormal fluid intra- and/or extra-substantial (trochanteric bursitis), calcifications, and/or hypertrophy compared with the contralateral side.	Patient assessed is in the side-lying position with hip and knee in neutral position. The probe is placed parallel to the femoral diaphysis. A movie sequence is recorded starting proximal to the greater trochanter and ending distal to the greater trochanter. Afterwards, the probe is rotated 90 degrees with the greater trochanter centred, and a movie sequence is recorded starting anterior to the greater trochanter and ending posterior to the greater trochanter	
Adductor longus tendon Longitudinal scan with the inferior ramus of the pubis as proximal landmark	Non- homogeneous echogenicity, abnormal fluid intra- and/or extra-substantial, calcifications, enthesophytes, and/or hypertrophy compared with the contralateral side.	Patient assessed is in the supine position with thigh abducted and externally rotated with 90 degrees knee flexion. The probe is placed parallel to the femoral diaphysis. A movie sequence is recorded starting at the myotendinous insertion and ending at the inferior ramus of the pubis.	

Standardised ultrasonographic examinations

Hamstring tendons Longitudinal and transverse scan with the ischial tuberosity as landmark	Non- homogeneous echogenicity, abnormal fluid intra- and/or extra-substantial (ischiogluteal bursitis), calcifications, and/or enthesophytes.	Patient assessed is in the prone position with hip and knee in neutral position. The probe is placed perpendicular to the femoral diaphysis with the ischial tuberosity centred. A movie sequence is recorded starting proximal to the ischial tuberosity and ending distal to the ischial tuberosity. Afterwards, the probe is rotated 90 degrees and an image* is recorded with the probe parallel to the femoral diaphysis with the ischial tuberosity as the proximal landmark.	
Pubic symphysis Transverse scan at the symphyseal cleft	Irregular bone surfaces, non- homogeneous echogenicity, abnormal fluid intra- and/or extra-substantial, and/or calcifications.	The patient assessed is in the supine position with hip and knee in neutral position. The probe is placed over the symphyseal cleft perpendicular to the long axis of the body. An image* is recorded in this position.	

Acetabular	Non-	Patient assessed is in the supine	
labrum	homogeneous	position with hip and knee in	
	echogenicity,	neutral position. The probe is	
Longitudinal	labrum tear,	placed in a sagittal oblique plane	
scan parallel	abnormal fluid	parallel to the long axis of the	
to the long	intra- and/or	femoral neck. A movie sequence	
axis of the	extra-substantial,	is recorded from medial to lateral	
femoral neck	calcifications,	visualising the anterior superior	
	and/or	labrum.	
	hypertrophy		
	compared with		
	the contralateral		
	side.		

*Recording the movie sequence was time consuming. To reduce the total scan time, two entities were stored as images. Similar table published as supplementary material, Paper 2.

14. Declarations of co-authorship



Declaration of co-authorship concerning article for PhD dissertations

Full name of the PhD student: Julie Sandell Jacobsen

This declaration concerns the following article/manuscript:

Title:	Muscle-tendon-related pain in 100 patients with hip dysplasia: prevalence and associations with self-reported hip disability and muscle strength
Authors:	Julie Sandell Jacobsen, Per Hölmich, Kristian Thorborg, Lars Bolvig, Stig Storgaard Jakobsen, Kjeld Søballe, Inger Mechlenburg.

The article/manuscript is: Published \boxtimes Accepted \square Submitted \square In preparation \square

If published, state full reference: Jacobsen JS, Hölmich P, Thorborg K, Bolvig L, Jakobsen SS, Søballe K, Mechlenburg I. Muscle-tendon-related pain in 100 patients with hip dysplasia: prevalence and associations with self-reported hip disability and muscle strength. Journal of Hip Preserving Surgery 2018;5:39-46.

If accepted or submitted, state journal:

Has the article/manuscript previously been used in other PhD or doctoral dissertations?

No \boxtimes Yes \square If yes, give details:

The PhD student has contributed to the elements of this article/manuscript as follows:

- A. Has essentially done all the work
- Has done most of the work (67-90 %) B.
- Has contributed considerably (34-66 %) C.
- Has contributed (10-33%) D.
- No or little contribution E.
- F. N/A

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Element	Extent (A-F)
1. Formulation/identification of the scientific problem	В
2. Development of the method	С
3. Planning of the experiments and methodology design and development	А
4. Involvement in the experimental work/clinical studies/data	Α
collection/obtaining access to data	
5. Development of analysis plan and preparation of data for analysis	А
6. Planning and conducting the analysis of data	А
7. Interpretation of the results	В
8. Writing of the first draft of the manuscript	В
9. Finalization of the manuscript and submission	В



Signatures of first- and last author, and main supervisor

Date	Name	Signature
20.05.2019	Julie Sandell Jacobsen	Julii Sandelle Jacobson
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Signature of the PhD student



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Authors:	Julie Sandell Jacobsen, Lars Bolvig, Per Hölmich, Kristian Thorborg, Stig Storgaard Jakobsen, Kjeld Søballe, Inger Mechlenburg.

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Signature of the PhD student



Declaration of co-authorship concerning article for PhD dissertations

Full name of the PhD student: Julie Sandell Jacobsen

This declaration concerns the following article/manuscript:

Title:	Patient-reported outcome and muscle-tendon pain after periacetabular osteotomy are related: 1-year follow-up in 82 patients with hip dysplasia.
Authors:	Julie Sandell Jacobsen, Kjeld Søballe, Kristian Thorborg, Lars Bolvig, Stig Storgaard Jakobsen, Per Hölmich, Inger Mechlenburg.

The article/manuscript is: Published \boxtimes Accepted \square Submitted \square In preparation \square

If published, state full reference: Jacobsen JS, Søballe K, Thorborg K, Bolvig L, Jakobsen SS, Hölmich P, Mechlenburg I. Patient-reported outcome and muscle–tendon pain after periacetabular osteotomy are related: 1-year follow-up in 82 patients with hip dysplasia. Acta Orthopaedica 2019;90:40–5.

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2. Development of the method	C
3. Planning of the experiments and methodology design and development	Α
4. Involvement in the experimental work/clinical studies/data	Α
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Signature of the PhD student



Declaration of co-authorship concerning article for PhD dissertations

Full name of the PhD student: Julie Sandell Jacobsen

This declaration concerns the following article/manuscript:

Title:	Does the physical activity profile change in patients with hip dysplasia from before to 1 year after periacetabular osteotomy?
Authors:	Julie Sandell Jacobsen, Kristian Thorborg, Per Hölmich, Lars Bolvig, Stig Storgaard Jakobsen, Kjeld Søballe, Inger Mechlenburg.

The article/manuscript is: Published \boxtimes Accepted \square Submitted \square In preparation \square

If published, state full reference: Jacobsen JS, Thorborg K, Hölmich P, Bolvig L, Jakobsen SS, Søballe K, Mechlenburg I. Does the physical activity profile change in patients with hip dysplasia from before to 1 year after periacetabular osteotomy? Acta Orthopaedica 2018; 89(6): 622-627.

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