Evaluation of Periacetabular Osteotomy in Patients with Hip Dysplasia

An Investigation of Adverse Events, Functional Performance, Patient-Reported Outcomes, and Radiographic Measurements.

PhD thesis

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2025

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Contents

Abbreviations

ADL	Activity limitations of Daily Living
AI-angle	Acetabular Index of Tönnis
BMI	Body Mass Index
CE-angle	Centre-Edge angle of Wiberg
CINAHL	Cumulative Index to Nursing and Allied Health Literature
DNPR	Danish National Patient Registry
EMBASE	Excerpta Medica Database
FAIS	Femoral impingement syndrome
FEAR	Femoral-Epiphyseal Acetabular Roof
GEE	Generalized estimating equations
GRADE	Grading of Recommendations Assessment Development and Evaluation
HAGOS	the Copenhagen Hip and Groin Outcome Score
HOOS	the Hip disability and Osteoarthritis Outcome Score
ICC	Intraclass coefficient
ICD-10	Internal Classification of Diseases 10th revision
iHOT	the International Hip Outcome Tool
IQR	Interquartile range
MCID	Minimal clinically important difference
MEDLINE	Medical Literature Analysis and Retrieval System Online
NAHS	the Non-Arthritic Hip Score
NCSP	NOMESCO Classification of Surgical Procedures
OHS	the Oxford Hip Score
OR	Odds ratios
PAO	Periacetabular osteotomy
PPV	Positive predictive value
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
REDCap	Research Electronic Data Capture
ROBINS-I	Cochrane Risk of Bias In Non-Randomized Studies – of Interventions
SHAK	Sygehus-afdelingsklassifikation (hospital department classification)
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
THA	Total hip arthroplasty
VAS	Visual Analogue Scale
QoL	Hip-related quality of life
WOMAC	the Western Ontario and McMaster Universities Arthritis Index
95% CI	95% confidence interval

1. English summary

This PhD thesis evaluates periacetabular osteotomy (PAO) for treating hip dysplasia, encompassing a systematic review, a cross-sectional study, and three cohort analyses. Together, these five papers address functional performance and muscle strength before PAO as well as adverse events, patient-reported outcomes, and radiological findings after the surgery.

The first study (Paper I) is a systematic review with meta-analysis investigating the harms and benefits of PAO through a systematic literature search. The paper included studies reporting both adverse events and patient-reported outcomes. Twenty-nine cohort studies were included, estimating a 4.3% (95% confidence interval (95% CI): 3.7;4.9) risk of a major adverse event and a 14.0% (95% CI: 13.0;15.1) risk of a minor adverse event. The benefits of PAO were clinically relevant improvements in patient-reported hip pain and function that persisted for at least 5 years after the surgery.

The second study (Paper II) is a cross-sectional study investigating functional performance and muscle strength deficits in patients with hip dysplasia scheduled for PAO compared to healthy subjects. Compared to healthy subjects, patients with hip dysplasia had significantly worse functional performance and a significant deficit in isometric hip flexion strength. For patients with hip dysplasia, better isometric muscle strength was associated with better functional performance.

The third study (Paper III) is a cohort study investigating the assumed association between the radiographic measurement of the femoral-epiphyseal acetabular roof (FEAR) index and patient-reported outcomes. Patients were divided into two groups defined by their preoperative FEAR index: (1) patients with an unstable hip, defined by a FEAR index >2° and (2) patients with a stable hip, defined by a FEAR index ≤2°. Both groups had clinically relevant improvements in patient-reported hip pain,

function and quality of life from preoperative to 6 months after PAO. No differences were found in the improvements between the two groups, and the FEAR index was thus not able to predict patient-reported outcomes after PAO.

The fourth study (Paper IV) is a cohort study investigating sports participation before and after PAO, measured preoperative and 6 months, 2, 5, 10, 15, and 20 years after the surgery. It demonstrated that the number of patients participating in sports increased from 45% (95% CI: 43;48) before PAO to 56% (95% CI: 53;59) 6 months after PAO and 60% (95% CI: 57;63) 2 years after PAO. The number of sports participants remained higher than before the surgery throughout the follow-up period. Being sports-active, having a higher education, and having a better pain score before PAO increased the odds of participating in sports after PAO.

The fifth study (Paper V) is also a cohort study, investigating the registration completeness of the Aarhus PAO-database, which served as the basis for the two above-mentioned cohort studies. The registration completeness between the Aarhus PAO-database and the Danish National Patient Registry was 94.7% (95% CI: 93.3;95.9), confirming its validity as a resource for investigating the effect of PAO.

The findings of this PhD thesis demonstrate that patients with hip dysplasia experience reduced hip function and that their hip function is associated with their hip muscle strength. The research has identified the risks and benefits associated with the PAO procedure, as well as the preoperative factors that affect sports participation after surgery. Additionally, it has been uncovered that the FEAR index does not affect patient-reported outcomes following PAO. These findings highlight the complex effects of PAO on patients with hip dysplasia, providing valuable insights for clinical practice and future research.

2. Dansk resumé (Danish summary)

Denne ph.d.-afhandling evaluerer periacetabulær osteotomi (PAO) som behandling af hoftedysplasi og omfatter et systematisk review, et tværsnitsstudie og tre kohortestudier. Sammen behandler disse fem artikler fysisk funktion og muskelstyrke før PAO, samt bivirkninger, patientrapporterede udfald og radiologiske fund efter operationen.

Det første studie (artikel I) er et systematisk review med meta-analyse, der undersøgte ulemper og fordele ved PAO gennem en systematisk litteratursøgning. Artiklen inkluderede studier, der rapporterede både bivirkninger og patientrapporterede udfald. På baggrund af de 29 inkluderede kohortestudier blev risikoen for en væsentlig bivirkning estimeret til 4,3% (95% konfidensinterval (95% CI): 3,7;4,9), mens risikoen for en mindre bivirkning blev estimeret til 14,0% (95% CI: 13,0;15,1). Studiet fandt desuden at fordelene ved PAO var klinisk relevante forbedringer i de patientrapporterede udfald, hoftesmerter og hoftefunktion, disse forbedringer vedblev i mindst 5 år efter operationen.

Det andet studie (artikel II) er et tværsnitsstudie, der undersøgte fysisk funktion og muskelstyrke problematikker hos patienter med hoftedysplasi, der var opskrevet til PAO, sammenlignet med raske personer. Sammenlignet med raske personer havde patienter med hoftedysplasi signifikant dårligere fysisk funktion og en betydelig nedsat isometrisk hoftefleksionsstyrke. For patienter med hoftedysplasi var bedre isometrisk muskelstyrke forbundet med bedre fysisk funktion.

Det tredje studie (artikel III) er et kohortestudie, der undersøgte den formodede sammenhæng mellem det radiologiske indeks FEAR (femoral-epiphyseal acetabular roof) og patientrapporterede udfald. Patienterne blev opdelt i to grupper baseret på deres præoperative FEAR-indeks: (1) patienter med en ustabil hofte, defineret ved et

FEAR-indeks >2° og (2) patienter med en stabil hofte, defineret med et FEAR-indeks ≤2°. begge grupper havde klinisk relevante forbedringer i patientrapporterede hoftesmerter, funktion og livskvalitet fra præoperativ til 6 måneder efter PAO. Der blev dog ikke fundet forskelle i forbedringerne mellem de to grupper og FEAR-indekset synes derfor ikke at være i stand til at forudsige patientrapporterede udfald efter PAO.

Det fjerde studie (artikel IV) er et kohortestudie, der undersøgte sportsdeltagelse før og efter PAO, målt præoperativt samt 6 måneder, 2, 5, 10, 15 og 20 år efter operationen. Studiet viste, at antallet af patienter, der deltog i sport, steg fra 45% (95% CI: 43;48) før PAO til 56% (95% CI: 53;59) 6 måneder efter PAO og 60% (95% CI: 57;63) 2 år efter PAO. Antallet af sportsdeltagere forblev højere end før operation i hele opfølgningsperioden. At være sportsaktiv, højere uddannelse og have en bedre smertescore før PAO øgede alle sandsynligheden for at deltage i sport efter PAO.

Det femte studie (artikel V) er også et kohortestudie, hvor kompletheden af registreringerne i den aarhusianske PAO-database, som har dannet grundlag for de to ovennævnte kohortestudier (artikel III og IV), blev undersøgt. Kompletheden af registreringerne mellem den aarhusianske PAO-database og Landspatientregisteret var 94,7% (95% CI: 93,3;95,9), hvilket bekræfter databasens validitet som en værdifuld ressource til at undersøge effekten af PAO.

Resultaterne af denne ph.d.-afhandling viser, at patienter med hoftedysplasi har nedsat hoftefunktion og at deres hoftefunktion er forbundet med hoftens muskelstyrke. Forskningen har identificeret risici og fordele ved PAO-proceduren samt de præoperative faktorer der påvirker sportsdeltagelse efter operationen. Derudover er det blevet afdækket at FEAR-indekset ikke har betydning for, hvordan det går patienterne efter operationen. Disse resultater understreger den komplekse indvirkning af PAO på patienter med hoftedysplasi og giver værdifuld indsigt for klinisk praksis og fremtidig forskning.

3. Introduction

The anatomy of the hip joint

The hip joint, articulation coxae, is a triaxial ball-and-socket joint formed between the caput of the femoris and the acetabulum of the pelvis. The acetabulum is a hemispherical socket and covers 50% of the caput femoris [(1)]. The caput femoris and part of the acetabulum are covered with articular cartilage to reduce the load on the joint surfaces. The femoral head is held in the acetabulum by the joint capsule, the surrounding muscles, the articular cartilage and the ligaments. The four ligaments are: (1) Ligamentum teres, (2) Iliofemoral ligament, (3) Ischiofemoral ligament and (4) Pubofemorale ligament. Together, they stabilise the joint during movement by limiting the range of movements. The muscles surrounding the hip can be categorised into; (1) The lumbar muscles, (2) The gluteal muscles and (3) The lateral rotator group (Figure 1). The lumbar muscles primarily consist of the muscle iliopsoas, which consists of the muscles psoas major and iliacus, and their function is to create hip flexion. The gluteal muscles consist of the gluteus maximus, medius and minimus, and the tensor fasciae latae. The lateral rotator group consist of the muscles piriformis, gemellus superior and inferior, quadratus femoris, obturatorius internus and externus. The movements of the hip are performed by the hip and thigh muscles. The range of motion of the hip movements is flexion 0° to 120°, extension 0° to 30°, abduction 0° to 45°, adduction 0° to 30°, external rotation 0° to 60° and internal rotation 0° to 40°.

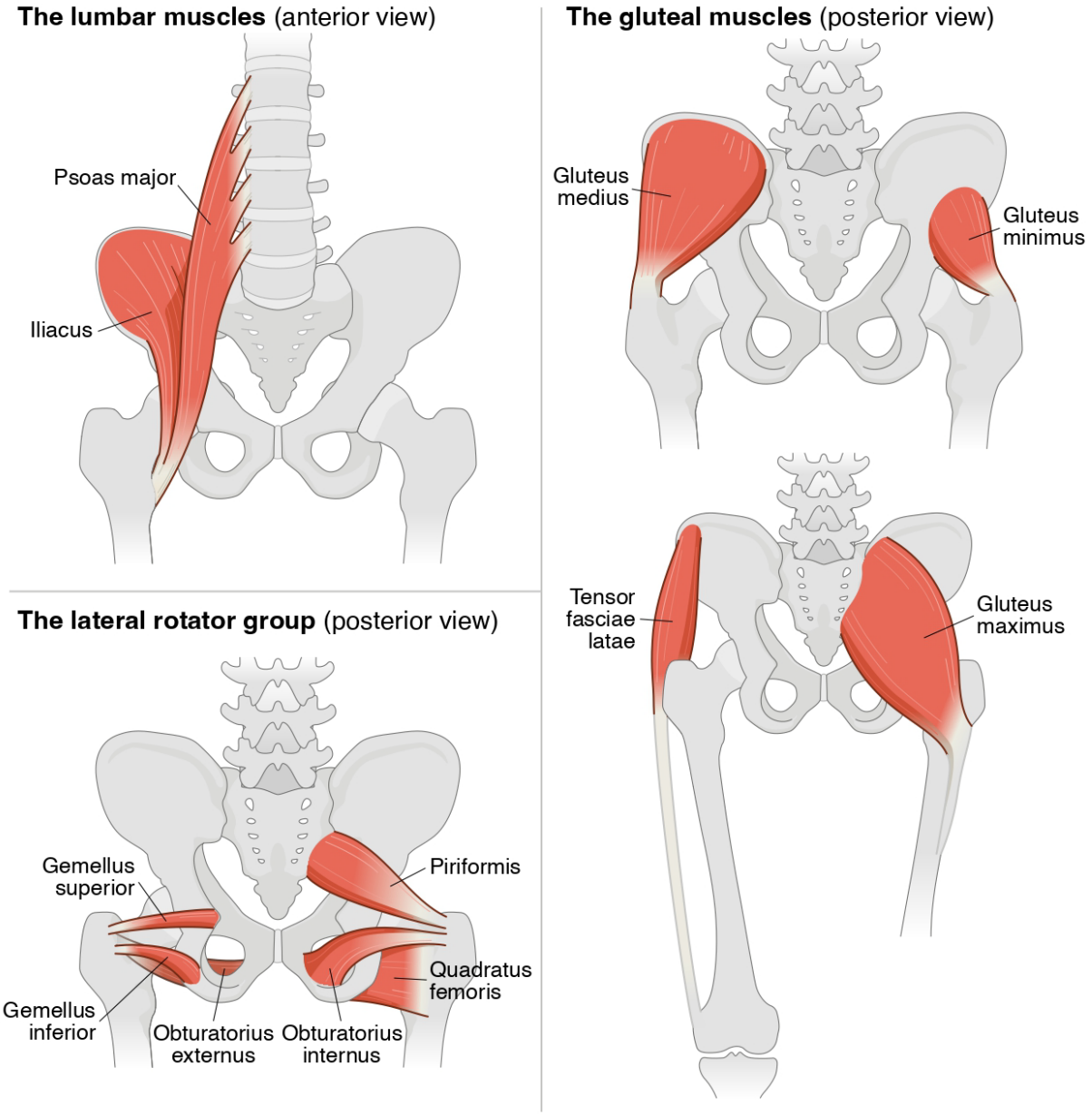

Figure 1. *Illustration of the three muscle groups surrounding the hip. The lumbar muscles (anterior view) consist of the psoas major and iliacus muscles. The lateral rotator group (posterior view) consist of the piriformis, gemellus superior, gemellus inferior, quadratus femoris, obturatorius internus and obturatorius externus muscles. The gluteal muscles (posterior view) consist of the gluteus maximus, gluteus medius, gluteus minimus, and tensor fasciae latae muscles.*

Hip dysplasia

Inadequate coverage of the femoral head by the acetabulum is called developmental dysplasia of the hip, while excessive coverage is called femoral impingement syndrome (FAIS). Hip dysplasia ranges from hip dislocation at birth to asymptomatic acetabular dysplasia in adolescents [2]. This thesis will focus on *painful acetabular dysplasia* in adolescents, which is referred to as *hip dysplasia* in the present thesis. Hip

dysplasia is a developmental joint disease characterised by a shallow and oblique acetabulum, laxity of ligamentous structures and abnormalities to the proximal part of the femur, which leads to an insufficient coverage of the femoral head [2-5]. Moreover, hip dysplasia means that the hip socket does not cover the femoral head sufficiently. Insufficient coverage is characterised by deficient lateral acetabulum coverage, sometimes accompanied by anterior or posterior deficiency [6]. Three patterns of undercoverage have been observed in dysplastic hips: (1) Anterosuperior deficiency (anterior and lateral undercoverage), (2) Global deficiency (lateral undercoverage with variable degrees of anterior and posterior undercoverage) and (3) Posterosuperior deficiency (lateral and posterior undercoverage) [6]. Nepple et al. found that the three patterns were almost equally distributed in their cohort of 50 patients with hip dysplasia [6]. The insufficient acetabulum coverage of the femoral head can result in a smaller load-bearing surface between the bones, which could increase the contact pressure on the cartilage and lead to hip instability and damage to the soft tissue structures surrounding the joint [7]. Mechlenburg et al. investigated the projected load-bearing surface of the femoral head and found that the average area was 7.4 cm^2 among patients with hip dysplasia, which was significantly smaller than observed in healthy subjects (11.8 cm^2) [5]. The abnormalities of the proximal part of the femur include an elliptic head, decreased epiphyseal height, decreased epiphyseal extension towards the femur neck, a valgus neck (coxa valga) and reduced femoral head-neck offset posteroinferiorly [8, 9].

Epidemiology

Jacobsen et al. investigated the prevalence of hip dysplasia in adults among 3,564 Danish citizens and found that the prevalence ranged from 5.4 to 12.6%, depending on the radiographic index applied [10]. In addition, Engesæter et al. found that the prevalence of hip dysplasia ranged from 1.7 to 20.0% among late teenage Norwegians, depending on the radiographic index applied [11]. Engesæter et al. further observed that

the prevalence of hip dysplasia rose from 3.3% to 20.0% when the cut-off value on the Centre-Edge angle of Wiberg (CE-angle) was changed from <20° to <25° [11].

In the Nordic countries, 2% of all primary hip replacements are registered as a result of hip dysplasia [11]. Hip dysplasia is associated with several risk factors, of which biological sex is the most reported, and evidenced by hip dysplasia occurring four times more often among females than males [11-14]. Genetics as familial predisposition has been demonstrated to be a predisposing factor for developing hip dysplasia with a combined relative risk at 1.39 (95% confidence interval (95% CI): 1.23;1.57) [15]. Breech presentation is also a well-established risk factor, leaving persons with a 3.75 higher risk for developing hip dysplasia when born in a breech position compared to non-breech births [15]. Ethnicity and cultural differences have also been found to be risk factors since the incidence of hip dysplasia varies substantially between different ethnicities [12]. In addition, being the firstborn has a combined relative risk of 1.44 (95% CI: 1.12;1.86) [15].

Damage to soft tissue

As described above, hip dysplasia is a bone-related hip diagnosis, however, the soft tissues around the femoroacetabular joint are also important due to their stabilising role [16]. Jacobsen et al. found that 56% of 100 patients with hip dysplasia had iliopsoas-related pain, and 42% had abductor-related pain [17]. Furthermore, 14% had adductor-related pain, 6% had hamstrings-related pain, and 4% had rectus abdominis-related pain [17]. This could be due to the reduced weight-bearing area, which is associated with an increased load on the muscle structures [18, 19]. Labrum degeneration or injury is also highly prevalent in people with hip dysplasia, ranging from 49-83% [20, 21].

Microinstability

In recent years, hip dysplasia, among other hip problems such as connective tissue disorders, microtrauma, etc., has been suggested to cause hip microinstability, leading to hip pain and disability [16, 22, 23]. The theory is that hip dysplasia causes microinstability by persistent excessive hip motion due to the reduced acetabular coverage [22, 24]. A recent Delphi study from 2021 collected opinions on diagnostic criteria for hip microinstability from 27 experts (24 orthopaedic surgeons and three physiotherapists from around the world) to make a consensus and develop a diagnostic tool on how to diagnose hip microinstability [22]. The diagnostic tool involved 34 criteria based on the patient's history, a clinical examination and radiographic findings. To be diagnosed with hip microinstability, the patient must fulfil at least all 14 major factors, including hip pain, radiographic signs of hip dysplasia and a Femoral-Epiphyseal Acetabular Roof (FEAR) index >5° [22], which is described in detail in the "Outcome measurements" section under "Radiographic measurement of hip instability". However, the clinical relevance of hip microinstability still remains to be investigated.

Development of osteoarthritis

The smaller load-bearing area seen among people with developmental dysplasia of the hip is believed to result in higher contact pressure on the cartilage, causing degenerative changes and potential osteoarthritis of the hip joint [5, 7, 25]. Jacobsen et al. found that hip dysplasia was associated with high odds of hip osteoarthritis in 2232 Danish women and 1336 Danish men [10]. Hip osteoarthritis is often assessed by the Tönnis grade, where the sign of hip osteoarthritis based on an anterior-posterior radiograph is classified into four categories: (0) no sign of osteoarthritis, (1) slight narrowing of joint space, slight lipping at joint margin and slight sclerosis of the femoral head or acetabulum, (2) small cysts in the femoral head or acetabulum, increasing narrowing of joint space and moderate loss of sphericity of the femoral

head, (3) large cysts, severe narrowing or obliteration of joint space, severe deformity of the femoral head and avascular necrosis [26, 27].

Wyles et al. studied the natural history of hip dysplasia over time, using the Tönnis grade classification system and found that patients with hip dysplasia had a statistically significantly higher risk of progression from a Tönnis grade of 0 to a Tönnis grade of 3 or receiving a total hip arthroplasty (THA), with a hazard ratio of 5.0 (95% CI 1.1;22.1, p =0.036), compared to patients with a normal hip morphology [28]. Further, Wyles et al. found that over 10 years, the probability of no transition from a Tönnis grade 0 at 10 years was 9% lower for a dysplastic hip compared to hips with a normal hip morphology. Additionally, the probability of transitioning to a Tönnis grade 1 or 2 was 3% higher, and the probability of transitioning to a Tönnis grade 3 or a THA was 2% higher for dysplastic hips than hips with a normal hip morphology [28]. Therefore, according to Wyles et al., early joint preservation intervention in patients with hip dysplasia seems to be beneficial [29]. However, the study has an important limitation, as all the recruited patients could be considered a selected subgroup of patients as they had all undergone THA in the contralateral hip, possibly implying a higher risk of developing osteoarthritis than patients who had not undergone THA [28]. Moreover, an earlier THA could result in a modified physical activity behaviour, again affecting the risk of developing osteoarthritis in the opposite hip. A study on the natural history of the hip in patients with hip dysplasia who have not undergone THA in the contralateral hip would address this knowledge gap.

Consistent with the findings by Wyles et al., Mechlenburg et al. found that the projected load-bearing area was increased to the level of hips with a normal morphology after undergoing periacetabular osteotomy (PAO) [5]. This indicates that surgery could prevent or decrease the degeneration of the joint, however, irreparable damage to the cartilage could already have occurred, which means that the former dysplastic hips could still degenerate despite undergoing PAO [5]. In addition, Jacobsen et al. found no significant difference in the reduction of joint space width between

people with hip dysplasia and controls without hip dysplasia, followed for 10 years [30]. In addition, Thomas et al. also found that radiographic findings of hip dysplasia and FAIS were associated with hip osteoarthritis among 670 hips from women aged 44-67 years [31]. On the contrary, Anderson et al. found that radiographic findings of dysplasia and FAIS were not associated with hip osteoarthritis among 1001 hips from senior athletes [32].

Diagnostics

To assess if a patient is suffering from hip dysplasia, a clinical evaluation and anteroposterior radiographs of the pelvis must be obtained [33]. The radiographic measures used to diagnose hip dysplasia are the CE-angle and the Acetabular Index of Tönnis (AI-angle) (Figure 2).

Radiographic measurements

In 1939, the CE-angle was introduced as a measure of the development of acetabulum and displacement of the femoral head [34]. As shown in Figure 2, The CE-angle is obtained by finding the centre of both femoral heads and drawing a horizontal line between the two centres. A vertical line through the femoral head and perpendicular to the horizontal line is then drawn, as well as a line from the lateral edge of the acetabular roof and through the centre of the femoral head. The CE-angle is then calculated by calculating the angle between the last two lines [35]. Wiberg stated that a normal hip has a CE-angle a more than 25°, while a dysplastic hip has a CE-angle at less than 20° [34]. A hip with a CE-angle between 20° and 25° is considered borderline dysplastic (19). A CE-angle less than 25° is considered dysplastic at Aarhus University Hospital.

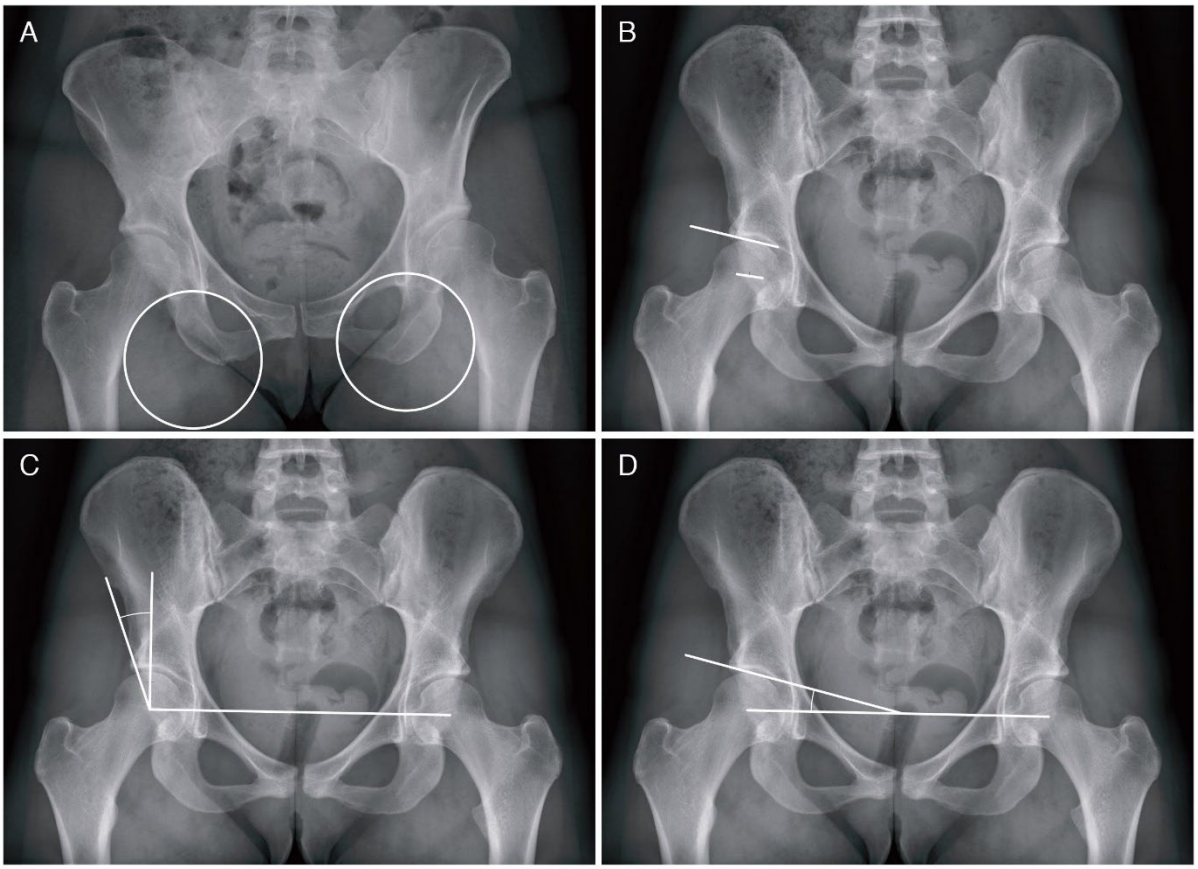

Figure 2. *Radiographic presentation of the following four radiographic measurements measured in patients with hip dysplasia before undergoing periacetabular osteotomy: (A) broken Shenton's line (on the left hip), (B) femoral-epiphyseal acetabular roof index, (C) centre-edge angle of Wiberg and (D) acetabular index of Tönnis. The figure is the same as Figure 1 in Paper III (appendix 3).*

Besides the CE-angle, the AI-angle is also a part of the radiographic diagnosis of hip dysplasia. The AI-angle is defined as the angle formed between the horizontal inter-teardrop line and a line extending from the lateral to the medial point of the weight-bearing region of the acetabulum [(35)], (Figure 2). The AI-angle can be classified into three groups, a normal hip range (ranging from 0-10°), a decreased acetabular inclination (AI-angle <0°) and an increased acetabular inclination (AI-angle >10°) [(36)]. An increased inclination is considered a sign of hip dysplasia and structural instability [(36)].

Clinical presentations

Clinical presentations of hip dysplasia are hip pain located to the groin area and deep interior pain, often shown by the C-sign, where the patient forms a C sign with their hand and places it around the trochanter major. The pain can be sharp, sudden and

sometimes radiate towards the knee [37]. A changed gait pattern, such as the Trendelenburg gait pattern, could be a sign of hip dysplasia. As described by Gala et al., range of motion (ROM) is mostly not affected, however, in some patients, the hip adductor and flexor muscles could be tight, leading to some stiffness when performing hip abduction and extension [33]. Two recent systematic reviews and meta-analyses (in which I serve as co-author) based on 62 and 24 studies, respectively, found that patients with hip dysplasia had worse pain levels, hip function and quality of life than healthy subjects [38, 39]. In addition, O'Brien et al. found that most patients with hip dysplasia had hip impingement, reduced hip muscle strength in abduction and flexion and reduced physical performance compared to healthy subjects [39]. Patients with hip dysplasia also had an affected walking pattern, as they had a lower peak hip extension angle and a lower peak hip extension and flexion moment during walking, compared to healthy subjects [39].

Conservative treatment

When searching the literature, surgical treatment seems like the only possible treatment for symptomatic hip dysplasia. However, many studies have investigated the effect of conservative treatment in patients with hip dysplasia. Since the goal of the surgery is not only to relieve pain but also to prevent the development of osteoarthritis, it would seem unethical to offer patients with hip dysplasia conservative treatment. However, the number of patients who postpone their surgery indicates that patients could benefit from conservative treatment [3]. In addition, Kapron et al. did not find a difference in radiographic measurements between a painful and a non-painful hip [40]. This indicates that factors other than the bony hip morphology might influence whether a patient experiences pain or not from a dysplastic hip. Further, one of the proposed treatments for hip microinstability is strengthening the hip muscles, as well as the muscles around the abdomen and lower back, and activity changes [22, 24].

Only a few studies have investigated the effects of exercise treatment on patients with hip dysplasia. In 2018, Mortensen et al. published a feasibility study where 17 patients with hip dysplasia scheduled for PAO had received 8 weeks of progressive resistance training in exercise machines [41]. The supervised resistance training was found feasible and resulted in improved pain levels, patient-reported outcomes and improved hip flexion muscle strength [41]. Based on this, a randomised controlled trial investigating if PAO followed by progressive resistance training is more efficient than exercise alone was initiated, the PreserveHip trial, however, as the trial is still ongoing, we do not have results yet [42]. In addition, Jacobsen et al. investigated the feasibility and acceptability of a 6-month exercise and patient education intervention in patients with hip dysplasia who were not eligible for PAO [43]. As the intervention was found feasible and acceptable with improvements in pain levels, muscle strength and hip function, a randomised controlled trial was initiated (the MovetheHip trial) [44]. As for the PreserveHip trial, MovetheHip is also ongoing, and data collection has not been finished yet. The lack of information on rehabilitation after PAO, as well as conservative treatment, is problematic when attempting to organise and offer the best treatment to hip dysplasia patients. In addition, Sucato et al. clarified the importance of focusing on rehabilitation as well as the worth of investigating the effect of preoperative resistance training among these patients [45].

A recent Delphi study with a panel of 15 physiotherapists and the purpose of presenting rehabilitation guidelines for patients with hip dysplasia resulted in a consensus guideline regarding conservative treatment for patients with hip dysplasia [46]. The guideline consists of 16 principles involving evaluation, activity modifications, exercise progression, activity/sports return and indications for referral to a physician. The guideline is meant to help reduce practice variation as well as identify patients that would benefit from conservative treatment [46].

Periacetabular Osteotomy

There are several surgical interventions for patients with hip dysplasia [47, 48], but for this thesis, the focus is on the Bernese periacetabular osteotomy (PAO), which was developed by Reinhold Ganz in 1988 to change the hip morphology and thus prevent or postpone the development of hip osteoarthritis [25]. The osteotomy allows for the acetabulum to be reoriented in three dimensions and thus increases the coverage of the femoral head (Figure 3). Over the years, multiple variances of the original surgical procedure have been developed, and at Aarhus University Hospital, the minimally invasive transartorial approach is used [49]. Indications for PAO differ between countries and hospitals [50]. The indications mainly used are radiographically verified hip dysplasia, persistent hip pain, reduced function and skeletal maturity [29, 51, 52]. There is also no consensus regarding contraindications. However, signs of osteoarthritis, lack of hip congruence, a high Body Mass Index (BMI) and older age have been found to influence the results of the surgery negatively [52-54]. The goal of the PAO is to reduce pain, improve hip function and prevent degeneration of the hip joint. The radiographic goal is to achieve a CE-angle between 30°-40° and an AI-angle between 0°-10° [49].

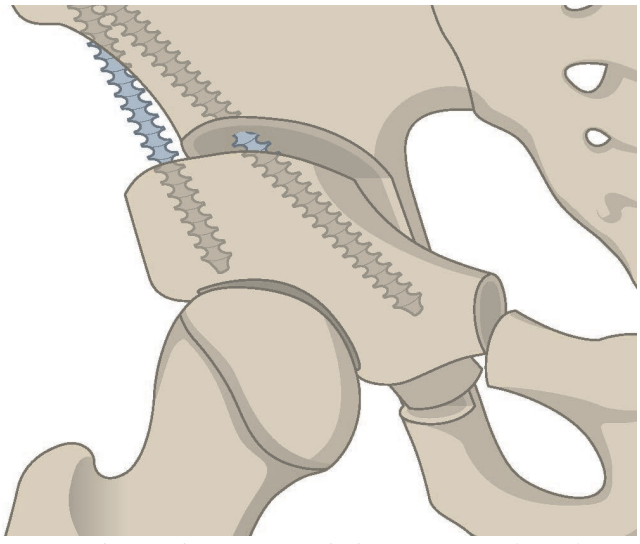

Figure 3. *Illustration of the surgical procedure periacetabular osteotomy (PAO) using the minimally invasive approach in a hip with hip dysplasia.*

Post-surgical rehabilitation

After surgery, patients at Aarhus University Hospital are instructed in mobilisation and are allowed to partially weight bear, with a maximum of 30 kg, within the first 6-8 weeks [3]. After hospital discharge, the patients receive 4 months of rehabilitation to gain basic hip function. The content of the rehabilitation program depends on the patient's needs and their local rehabilitation unit. The content can thus include home-based training, group-based training, and individual sessions, depending on the local conditions [55].

Harms related to periacetabular osteotomy

Complications and adverse events followed by PAO can be divided into major and minor complications/adverse events [56]. A systematic review from 2009 found that major complications were present in 6-37% of the hips, followed by PAO [50]. The most common major complication found in the literature was symptomatic heterotopic ossification, wound hematomas, nerve palsies, intraarticular osteotomies, loss of fixation and malreductions [50]. The surgical learning curve could affect the complication rate since PAO is a complex surgical technique [50]. Larsen et al. found that 1.1% of the included hips where PAO was performed after the surgical learning curve had a serious complication (non-union, superficial wound infection and revision) [29].

Outcomes of periacetabular osteotomy

Patient-reported outcome measures are widely used to assess hip-related pain, hip function and quality of life after PAO. Based on 62 studies on patients with hip dysplasia, O'Brien et al. concluded that hip-related pain, daily activities and hip-related quality of life (QoL) improved after PAO, and the improvements appeared to last for at least 7 years [38]. Despite the improvements, patients did not reach the same level as healthy subjects. Meta-analysis on three studies revealed that the standardised paired difference for pain scores was 1.35 (95% CI: 1.02;1.67) from before to 1 year after PAO, and meta-analysis on four studies revealed that the standardised paired

difference was 1.35 (95% CI: 1.16;1.54) from before to 2 years after PAO. For the activities of daily living scores, the standardised paired difference was 1.22 (95% CI: 1.09;1.35) from before to 1 year after PAO and 1.06 (0.9;1.22) from before to 2 years after PAO. The standardised paired difference for QoL scores also improved at 1 year after PAO (1.36, 95% CI: 1.22;1.5) and 2 years after PAO (1.3, 95% CI: 1.1;1.5) [38]. The most frequently used patient-reported outcome measure was the Western Ontario and McMaster Universities Osteoarthritis index (WOMAC) (33 studies), followed by the Hip disability and Osteoarthritis Outcome Score (HOOS) (17 studies).

O'Brien et al. also investigated physical impairments in 24 studies on patients with hip dysplasia and found that patients with hip dysplasia had a reduced walking function compared to healthy subjects (reduced hip extension angle and peak hip extension moment and flexion moment) before PAO [57]. After PAO, the walking function improved to the level of the healthy subjects. In addition, walking velocity and stride length also improved 18 months after PAO, while muscle strength in hip abduction and flexion did not change, nor did walking cadence [57]. In addition, Jacobsen et al. found that their cohort of patients who had undergone PAO due to hip dysplasia did not change their objectively measured daily physical activity level in regards to walking, standing, number of steps, cadence and intensity [58].

Conversion to total hip arthroplasty

Patients with severe hip osteoarthritis can be treated with a THA, and conversion to THA has thus often been used to investigate the survivorship of PAO [29]. In a retrospective study by Lerch et al., 56% of the included hips were converted into THA within 30 years after PAO [59]. The high rate of conversions to THA within this study could be due to the indication for PAO during the study period. Hip dysplasia was the only surgical indication in the study, and 57% of the included hips had a Tönnis score higher than 0° [59]. In addition, more than 70% of the included hips were still painful and/or had developed osteoarthritis within the 30-year follow-up period. Larsen et al. found that the survival rate was 80% (95% CI: 68;88) at 14 years follow-up, meaning

that 1 out of 5 hips who had undergone PAO at Aarhus University Hospital was converted to THA within 14 years [29]. This was supported by Kristiansen et al., who found that the survival rate was 82% (95% CI: 77;85) at 15 years of follow-up among patients undergoing PAO at another Danish hospital (Odense University Hospital) [60]. Contrary to the study by Lerch et al., Larsen et al. and Kristiansen et al. excluded patients with hip osteoarthritis and patients with a BMI higher than 30 kg/m^2. Larsen et al. further only included hips where surgery was performed after the surgical learning curve.

4. Aims and hypotheses

The overall aim of the thesis was to investigate functional performance, muscle strength, adverse events, patient-reported outcomes, and radiological findings in patients with hip dysplasia undergoing PAO before and after PAO. This was done through a systematic review and meta-analysis, a cross-sectional study, two cohort studies, and a validation study.

Individual aims and hypotheses

Paper I – The systematic review

The aim of the systematic review was to investigate the benefits and harms of PAO in patients with hip dysplasia through the literature by including randomised controlled trials and observational studies (cohort studies and case-series) that reported both benefits and harms in patients with hip dysplasia undergoing PAO [47]. The hypothesis was that patients with hip dysplasia undergoing PAO would increase their scores on the different patient-reported outcome measures and that the risk of adverse events would be similar to the results that Clohisy et al. found when they performed a systematic review in 2009 on adverse events after PAO [50].

Paper II – The cross-sectional study

The aim of the cross-sectional study was to compare functional performance and isometric maximum voluntary contraction (MVC) during hip flexion, extension and abduction between patients with hip dysplasia scheduled for PAO and a group of healthy subjects. In addition, the secondary aim was to investigate associations between hip muscle strength and hip functional performance. The hypotheses were that patients with hip dysplasia would have lower functional performance and muscle

strength than healthy subjects without hip problems and that muscle strength would be associated with functional performance.

Paper III – The FEAR index study

The aim of the radiographic study was to investigate if the FEAR index was associated with the patient-reported outcome measure HOOS in patients with hip dysplasia undergoing PAO. The secondary aim was to examine the inter-rater reliability of the FEAR index alongside other radiographic measurements used to assess hip microinstability. The hypotheses were that patients with hip microinstability, defined as a FEAR index >2° before PAO, would have a worse HOOS score than patients without hip microinstability, defined as a FEAR index ≤2°. In addition, we believed that both groups would improve on HOOS from before to 6 months after PAO but that the improvement would be higher for patients with hip microinstability [61]. We believed that the inter-rater reliability of the FEAR index would be moderate (defined as an intraclass-coefficient between 0.50 and 0.75) due to the two assessors' lack of experience with the new index and their different medical fields.

Paper IV – The sports participation study

The aim of the sports participation study was to determine the proportion of patients with hip dysplasia that 1) participated in sports, 2) performed their preferred sports, and 3) reported improvements in sports performance after PAO. The secondary aim was to investigate whether specific preoperative patient characteristics (age, sex, education, BMI, CE-angle, AI-angle, pain, and quality of life) could predict the three sports-related outcomes after PAO. The hypothesis for the primary aim was not specified, as this was a descriptive aim. However, we expected that the number of patients participating in sports and performing preferred sports would increase after PAO and that the number of patients who reported an improvement in sports function would be high. The hypotheses for the secondary aim were that young age, male sex,

high educational level, low BMI, high CE-angle, low AI-angle, less pain, and high quality of life before surgery would be associated with better odds of 1) participating in sports, 2) the ability to perform preferred sports and 3) improvements in sports following PAO.

Paper V – The validation study

The validation study had three aims. The first aim of the study was to investigate the registration completeness in the Aarhus PAO-database compared to the Danish National Patient Registry (DNPR). The second aim was to examine the positive predictive value (PPV) of the diagnosis and surgical procedure from a random sample of 160 patients from the Aarhus PAO-database and 160 patients from DNPR, compared to their electronic medical records. The third aim was to investigate the PPV of the diagnosis and surgical procedure for patients with discrepancies between the two registries using electronic medical records. There were no specific hypotheses, however, we expected that the registration completeness and PPV would be high and expected that the DNPR would be more accurate than the PAO-database.

5. Materials and methods

Ethical approval

Paper I

The systematic review (Paper I) was registered on the Prospero site for systematic reviews (registration number: CRD42021253438) prior to the selection of studies, and the Paper was written in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) checklist for reporting harms in systematic reviews [62].

Paper II

The cross-sectional study (Paper II) was approved by the Central Denmark Region Committee on Biomedical Research Ethics as part of the ongoing randomised controlled trial, the PreserveHip trial (journal number 1-10-72-234-18) and registered at the Region of Central Denmark's internal list of research projects (journal number 1-16-02-120-19). Before enrolment, all patients and healthy subjects were given written and oral information, and the participants gave written consent to participate in accordance with the Declaration of Helsinki II [63].

Paper III

The FEAR index study (Paper III) relied on the official approval of the Aarhus PAO database from the Digitalization and IT Office, Region of Central Denmark (journal number 1-52-81-57-19 and 1-16-02-151-13), regarding data collection. The aim and methodological design of the study were further registered at the Region of Central Denmark's internal list of research projects (journal number: 713207) before the study was initiated. The manuscript followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [64].

Papers IV and V

The sports participation study (Paper IV) and the validation study (Paper V) also relied on the official approval of the Aarhus PAO database from the Digitalization and IT Office, Region of Central Denmark (journal number 1-52-81-57-19 and 1-16-02-151-13), regarding data collection. The aim and methodology of these studies were also registered at the Region of Central Denmark's internal list of research projects (journal number: 1-16-02-46-23) before the studies were initiated. In addition, these two studies were further approved by the Legal Office, Region of Central Denmark (journal number: 1-45-70-85-22). The manuscripts both followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [64].

Study design

The five papers that form the basis of this dissertation were a systematic review and meta-analysis (Paper I), a cross-sectional study (Paper II), and three cohort studies (Papers III, IV and V). The systematic review and meta-analysis were a synthesis of studies reporting patient-reported outcomes and adverse events after PAO [47]. Studies that had included a comparison group were further included in the meta-analysis on major and minor adverse events. Based on the Oxford Centre for Evidence-Based Medicine levels of evidence (OCEBM Levels of Evidence), a systematic review based on observational studies is placed on level 2a [65]. The cross-sectional study was part of an ongoing randomised controlled trial investigating the efficacy of PAO followed by usual care and resistance training to non-surgical treatment defined as progressive resistance training [42]. According to the OCEBM Levels of Evidence, a cross-sectional study is placed on level 3b [65]. The three cohort studies were all retrospective cohort studies with prospectively collected data, as the aims of the studies were defined after data was collected. Two of the cohort studies, Paper III [61] and Paper V also included radiological findings and information from the patient electronic journals, data collected retrospectively. According to the OCEBM Levels of Evidence, a retrospective cohort study is placed on level 2b [65].

The systematic review

Design and eligibility criteria

The systematic literature search was based on a previous literature search that the PhD candidate was involved in, focusing on patient-reported outcomes and physical impairments in patients with hip dysplasia undergoing PAO [38, 57]. The original literature search was performed in five literature databases in January 2021 and involved all observational study designs (Table 1). Studies on PAO in patients with hip dysplasia aged 15 or older at surgery, with one of the predefined hip-specific patient-reported outcome measures, were included (Table 1). In addition, studies had to have a comparator group or more than one measurement time. Studies only applying the Hip Outcome Score, the modified Harris Hip Score or patient-reported outcome measures that were not hip-specific were not included due to validity and responsiveness issues [38]. There were three independent reviewers, 2nd author (MO), 3rd author (CS) and the PhD candidate, who performed the title/abstract screening as well as the full-text reading in Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia) and a senior researcher, the 5th author (JK), resolved all disagreements. Michael O'Brien and I did the data extraction and quality evaluation using a modified version of the Downs and Black checklist. One of the items in the modified Downs and Black checklist addresses adverse events and is defined as any mention of adverse events, complications, harms, or related concerns. All studies not defined as having a high risk of bias in this item were included in the systematic review on harms and benefits, as these were the studies that had either included adverse events or had stated something about adverse events (e.g. no adverse events were found). The systematic review on benefits and harms was registered on the Prospero registration site (registration number: CRD42021253438).

Table 1. The inclusion and exclusion criteria for the systematic review (Paper I).

	Inclusion criteria	Exclusion criteria
Databases	CINAHL EMBASE MEDLINE PsychNFO Sports Discuss	
Population	Hip dysplasia as primary diagnosis Age >15 years	Down syndrome Cerebral palsy Charcot-Marie-tooth disease
Intervention	Periacetabular osteotomy Bernese osteotomy Ganz osteotomy	Rotational acetabular osteotomy Curved periacetabular osteotomy
Comparator	Sham treatment Other treatments No treatment Second-time point	Only 1 time point and no comparison group
Outcome	Patient-reported outcome measures: *HAGOS* *HOOS* *iHOT* *NAHS* *OHS* *WOMAC* Any mention of harms, adverse events or complications	Patient-reported outcome measures: *Modified Harris Hip Score* *Hip Outcome Score* *Merle d'Aubigne Score* *University of California Los Angeles activity score* *Visual Analogue Scale* No information or statement on harms, adverse events or complications
Types of studies	Randomised controlled trials Non-randomised controlled trials Prospective cohort studies Retrospective cohort studies Case series	Case-studies Animal studies

CINAHL: Cumulative Index to Nursing and Allied Health Literature. EMBASE: Excerpta Medica Database. HAGOS: Copenhagen Hip and Groin Outcome Score. HOOS: Hip disability and Osteoarthritis Outcome Score. iHOT: International Hip Outcome Tool 12 and 13. MEDLINE: Medical Literature Analysis and Retrieval System Online. NAHS: Non-Arthritic Hip Score. OHS: Oxford Hip Score. WOMAC: Western Ontario and McMaster Universities Arthritis Index.

Quality and certainty assessment

The methodological quality of the included studies was individually assessed by two reviewers (Michael O'Brien and I) using the Cochrane Risk of Bias In Non-Randomized Studies – of Interventions (ROBINS-I) [66]. Disagreements were consulted with a third reviewer, the last author (IM), and resolved. The ROBINS-I assesses the risk of bias in studies evaluating the effect of an intervention that is not randomised controlled trials, thus observational studies as cohort studies and case-control studies

where the study population has not been randomised to either the intervention or to a comparison group, but are allocated during the course of usual treatment decisions [66]. A randomised controlled trial on the effect of PAO has not yet been performed, so the ROBINS-I assessment tool was considered relevant for this systematic review. The ROBINS-I assesses the risk of bias in the following domains: (i) bias due to confounding, (ii) bias in the selection of participants into the study, (iii) bias in classification of interventions, (iv) bias due to deviations from intended interventions, (v) bias due to missing data, (vi) bias in measurement of outcomes and (vii) bias in selection of the reported result. The risk of bias for every domain is scored as either low, moderate, serious, critical or no information, and the study is given an overall score based on the worst score received in one of the seven domains [66]. Before the assessment, the following independent confounding variables were predefined: (1) Multiple surgeons, (2) Multiple previous surgeries and (3) Multiple surgical centres. Co-interventions such as concomitant procedures were a priori defined as a moderate risk of bias due to deviations from intended interventions. Missing data were a priori defined as a major risk of bias if ≥20% of data were missing and moderate if 10-19% of data were missing. If the primary aim was not specified, this was a priori defined as a major risk of bias in the selection of the reported results.

The certainty of evidence for the meta-analysis was rated using the Grading of Recommendations Assessment Development and Evaluation (GRADE), where five domains are assessed: risk of bias, inconsistency, indirect evidence, inaccuracy and publication bias [67]. The overall quality was rated very low, low, moderate or high [67]. All observational studies are, by default, defined as low-quality evidence, and the five domains can be used to downgrade the study further. In addition, a study with a large effect, a dose-response relationship or a plausible confounding factor that influenced the results would upgrade the study. Limitations were defined as the risk of bias score using the ROBINS-I, and inconsistency was assessed as the degree of heterogeneity. Heterogeneity was interpreted as not important if <25%, moderate if 25-75% and considerable if >75% [68].

Data extraction

Data extraction was done by the same two reviewers who assessed the quality of the studies, and disagreements were also resolved by including a third reviewer (IM). For each study, information on eligibility criteria, PAO procedure, patient groups and patient characteristics were extracted. If patients had undergone PAO surgery more than once, data were only extracted for the first surgery. Patient-reported outcomes were a priori defined as the six above-mentioned hip-specific patient-reported outcome measures. Adverse events were predefined as all the 26 complications described by Biedermann et al. in their paper on complications and patient satisfaction after PAO [56]. Biedermann et al.'s categorisation of complications as either major or minor was also followed. Patient-reported outcomes and adverse events were extracted for all possible time points, and the authors were contacted and asked to provide missing data if the data was inadequate.

Data sources in Papers II-V

The Aarhus PAO-database

The Aarhus PAO-database is a disease registry created in 2010 to systematically collect information on the effects of PAO at Aarhus University Hospital and Mølholm Private Hospital. Aarhus University Hospital was the first hospital in Denmark to introduce PAO surgery by orthopaedic surgeon Professor Kjeld Søballe in 1998. Later, professor Søballe started working at Mølholm Private Hospital and trained other surgeons in the procedure. PAO is thus performed in four hospitals in Denmark today (Aarhus University Hospital, Copenhagen University Hospital, Mølholm Private Hospital and Odense University Hospital), and the Aarhus PAO-database collects data from two of these. Since 2010, patients at the two hospitals have been asked to participate by answering questionnaires sent by email before surgery (preoperatively) and 6 months, 2, 5, 10, 15 and 20 years after the PAO procedure. In addition, orthopaedic surgeons report radiological findings and surgery-related information to the database. In 2014, a secretary at the Department of Orthopedic Surgery at Aarhus University Hospital

entered all data collected from 1998-2010 and stored it in paper format [29, 61, 69]. In addition, the PhD candidate entered all data collected as part of research projects from 2010-2022 after realising that some of the patients recruited in the PreserveHip trial were not found in the database. All data has thus been collected prospectively, but for patients who had undergone PAO before 2010 and some patients who had participated in a research project, data has been typed in retrospectively. The registry thus contains information on patient demographics and patient-reported outcomes collected from the patients and radiological findings and surgery-related information collected by the surgeons, and all data is stored online using the software Procordo v. 3.0 (Procordo Aps, København, Denmark).

The Danish National Patient Registry

The Danish National Patient Registry (DNPR) is a Danish national registry collecting information on every hospital contact a patient has had with a Danish public or private hospital, including surgical procedures and diagnosis [70]. Since 1978, every hospital in Denmark has been required to submit standardised data, such as the Internal Classification of Diseases 10th revision (ICD-10) codes for diagnosis and the NOMESCO Classification of Surgical Procedures (NCSP) for surgeries. DNPR collects data using the electronic medical records for each hospital, which are linked with information on date, time, and department. Even though the DNPR is based on electronic medical records, these records include much more information alongside notes and comments from healthcare professionals. Thus, medical records are considered the golden standard for healthcare information [71]. Working with data from DNPR requires that results can only be presented if they exceed the number four to minimise the risk that a person can be identified, and results with less than five entries must thus be blurred.

Patients who had undergone PAO at either Aarhus University Hospital or Mølholm Private Hospital between 2014-2021 were identified in the DNPR by using the SHAK

codes (Danish for "hospital department classification") "6620" and "6010", Aarhus University Hospital and Mølholm Private Hospital respectively. Further, only patients with the ICD-10 codes "Q658" (congenital malformation of the hips) combined with the NCSP codes "NEK59" or "NET49" (pelvic osteotomy and correction of pelvis deformity) were included. Patients younger than 15 years at the time of surgery were excluded (Table 3).

Patients

The patients included in the cross-sectional study (Paper II) were all candidates for a PAO at either Aarhus University Hospital or Odense University Hospital, while the patients included in the PAO-database and DNPR had all undergone PAO at either Aarhus University Hospital or Mølholm Private Hospital. The indications and contraindications for PAO were the same for all four observational studies and are presented in Table 2. Further, these indications and contraindications were followed by the surgeons at Aarhus University Hospital and Mølholm Private Hospital since 1998 when the PAO was introduced in Denmark, except for the following three contraindications that were added in 2016: (1) Age >45 years, (2) Body mass index (BMI) >25, and (3) Hip osteoarthritis defined as a Tönnis grade >0 or a joint space width <3 mm. The eligibility criteria for the four cohort studies were similar, however, different periods and differences in exclusion criteria were used due to the different aims of the studies. The eligibility criteria are presented in Table 3.

Table 2. Indications and contraindications for periacetabular osteotomy at Aarhus University Hospital and Mølholm Private Hospital.

Indications	Contraindications
Hip congruence. Pelvic bone maturity. Persistent hip pain. Radiographically verified hip dysplasia, defined as a CE-angle <25° and an AI-angle >10°. Reduced hip function.	Age >45 years. BMI >25. Hip osteoarthritis (defined as a Tönnis grade >0 or a joint space width <3 mm. [26, 27]). Hip subluxation. Reduced range of motion indicating lack of hip congruence, defined as internal rotation ≤15° and hip flexion ≤110°.

AI-angle: acetabular index of Tönnis [35]. BMI: body mass index. CE-angle: centre-edge angle defined by Wiberg et. [34].

Healthy subjects

The healthy subjects for Paper II were recruited through advertisements at the public hospital, the university and colleges in the city of Aarhus, social media, and the included patients' network. The healthy subjects were eligible for participation if they were >17 years old and had not experienced any hip-related pain or problems in the last 12 months (Table 3). In addition, they could not participate in the study if they had undergone any major hip, knee, ankle or back surgery or were diagnosed with any neurological or rheumatoid disease affecting their hip. The patients' index leg was defined as the hip scheduled for PAO, while the right leg was defined as the index leg for healthy subjects. For both groups, the opposite leg was defined as the contralateral leg, regardless of bilateral hip dysplasia for the patients.

Table 3. Eligibility criteria used in the four observational periacetabular osteotomy (PAO) papers.

	Paper II	Paper III	Paper IV	Paper V
Inclusion criteria	**Patients:** Age ≥18 years. AI-angle >10°. CE-angle <25°. Patients eligible for PAO between 1st of July 2019 and 1st of March 2023. Persistent hip pain. Range of motion of more than 110° hip flexion and 15° internal- and external hip rotation. **Healthy subjects:** Age ≥18 years.	All patients registered in the PAO-database from 1st of January 2018 to 31st of December 2020.	All patients registered in the PAO-database from 1st of January 1998 to 31st of December 2023.	All PAO procedures registered in the PAO-database or in DNPR between 2014-2021.
Exclusion criteria	CE-angle <10°. Diagnosis of Calvé-Legg-Perthes or epiphysiolysis. Diagnosed with a neurological or rheumatoid disease affecting the hip. Osteoarthritis >0, defined by the Tönnis classification [26, 27]. Unable to read written Danish. **Healthy subjects:** Experienced hip-related pain or problems within the past year. History of major surgery in the hip, knee, ankle or back. Diagnosed with a neurological or rheumatoid disease affecting the hip. Unable to read written Danish.	The second procedure was excluded if the patient had undergone PAO twice during the period. The second surgery was excluded for double entries, defined as two identical entries. Missing or incomplete preoperative radiographs.	Age <15 years at surgery. Calvé-Legg-Perthes reported as the primary diagnosis. Femoral osteotomy reported as the surgical procedure. No Danish civil registration number. Other primary diagnosis than hip dysplasia reported. Reported that they had not undergone surgery at any of the time points. Subluxation reported as primary diagnosis. Sports participation was not answered at any time point. The second or more procedures were excluded if the patient had undergone PAO more than once during the period.	Age <15 years at surgery. Calvé-Legg-Perthes reported as the primary diagnosis. Double entry, defined as the second PAO performed on the same hip. Femoral osteotomy reported as the surgical procedure. Missing information on date of surgery. No Danish civil registration number.

Outcome measures

The five studies in this thesis had different primary and secondary outcomes, but many of the other outcomes collected for each paper were the same or similar.

Participant characteristics

Different participant characteristics were collected for the four observational studies. Age and sex were obtained from the civil registration number for all participants. Weight and height were self-reported in the Aarhus PAO-database (Paper IV) and measured by a physiotherapist or an exercise physiologist using a Tanita weight (SC-330MA, Tanita Corporation of America, Illinois, USA) and a telescopic height measuring device from ADE (MZ10023, DES Germany Gmbh, Hamburg, Germany) in the cross-sectional study (Paper II). BMI was calculated by dividing the participant's weight in kg by the square of their height in meters. Employment status, alcohol consumption, smoking status and educational level were assessed by asking the participants. Participants in the cross-sectional study (Paper II) were also asked about their current employment status. Here, they had the following options: 1) During education, 2) In work, 3) In activation/on sick leave/available/etc., 4) Outside the labour market and 5) Other. In addition, they were asked how much alcohol they usually drink in a week, using the following options: 1) <2 drinks, 2) 2-7 drinks, 3) 8-14 drinks, 4) 15-21 drinks, 5) 22-30 drinks and 6) >30 drinks. They were also asked about their smoking status and had the following options: 1) Never, 2) Former, 3) Occasionally and 4) Daily. Educational levels were assessed differently in Papers II, III and IV, as presented in Table 4.

Table 4. Educational level as presented in Papers II, III and IV.

Paper II[a]	Paper III[b]	Paper IV[c]
Primary school	General certificate of secondary education	Primary education
High school or similar	Upper secondary school leaving	Secondary education
Vocational education	Vocational upper secondary education	
Short higher education	Short-cycle higher education	
Medium higher education	Medium-cycle higher education	
	Bachelor education	Higher education
Long higher education	Long-cycle higher education	
	PhD education	
Other education		

[a]Questions defined in the PreserveHip trial [42]. [b]Questions defined when the Aarhus PAO-database was initiated. [c]Grouping of the questions from the Aarhus PAO-database to strengthen the categories.

Adverse events

Complications and adverse events followed by PAO have already been described in the introduction, but in short, they ranged from removal of screws to non-union (healing failure) [56]. In the systematic review (Paper I), all complications and adverse events from the included studies were collected in accordance with the adverse events reported by Biedermann et al. and further divided into major and minor complications/adverse events based on the definition by Biedermann et al. [56]. The number of adverse events alongside the number of procedures (patients or hips) where the adverse event had occurred was extracted, and the proportion of the adverse event was calculated.

Radiographic measurements of hip instability

Diagnosis of hip dysplasia involves radiographic measurement of the CE- and AI-angle as described in the introduction, whereas hip osteoarthritis is assessed by the Tönnis grade and hip instability is radiographically assessed using the FEAR index. In Papers II, III and IV, the CE-angle, AI-angle and Tönnis grade were assessed as described in the introduction. In Paper III, hip instability was assessed radiographically by applying the FEAR index, Shenton's line and the femoral neck-shaft angle. Further, the extrusion index, as well as the posterior wall sign, the cross-

over sign and the cliff sign, were assessed. All radiographic measurements for Paper III were performed by an orthopaedic surgeon, the 3rd author (JB) or a radiologist, the 2nd author (MS), whereas the radiographic measurements for Paper II were done by different orthopaedic surgeons at Aarhus University Hospital and Odense University Hospital using the digital measurement tool IMPAX client 6.5 (AGFA HealthCare, Mortsel, Belgium).

The Femoral-Epiphyseal Acetabular Roof index

The FEAR index is a rather new index, developed by Wyatt et al. in 2017 to assess if a hip joint is unstable among patients with borderline hip dysplasia as a way to better classify the underlying problem as either hip dysplasia or FAIS [72]. The FEAR index is determined by the angle formed between the acetabular roof and the central third of the femoral growth plate. The angle is calculated by drawing a line that connects the most medial and lateral points of the acetabular sourcil and another line connecting the medial and lateral points of the centre of the femoral head's physeal scar (Figure 2). The angle is positive when the vertex is medial and negative when the vertex is lateral [72]. The FEAR index has shown excellent inter- and intra-rater when first published [72] and was further evaluated using magnetic resonance imaging in 2019 [73]. Batailler et al. also found excellent intra-rater reliability, but the FEAR index was more reliable on radiographs than on magnetic resonance imaging [73]. Wyatt et al. found that a cutoff of 5° was the best to distinguish between instability and FAIS in patients with symptomatic borderline hip dysplasia. A FEAR index <5° was thus considered indicative of instability, with a probability of 79% [72]. Batailler et al. found that a cutoff value of 2° was more accurate in distinguishing between a stable and unstable hip, with a 90% probability [73]. In 2023, a systematic review with the purpose of investigating the utility of the FEAR index found 11 studies that used the FEAR index, of which five studies used the FEAR index to differentiate between patients with a stable and an unstable hip among patients with hip dysplasia, defined as a CE-angle <25° [74]. Cohen et al. found that the FEAR index had a high agreement and is a useful

diagnostic tool in hip preservation surgery [74]. The index was assessed by orthopaedic surgeons, orthopaedic fellows, medical students, research assistants and radiologists.

Other radiographic measurements

Shenton's line is an imaginary arch extending from the inferior border of the femoral neck to the superior border of the obturator foramen [75]. The line should be constant, and if not, it is defined as "broken" (Figure 2). The Shenton's line has been found to be reliable and accurate with an excellent intra- and inter-observer agreement, as well as excellent specificity and good sensitivity, among patients with hip dysplasia [75]. The femoral neck-shaft angle is the angle between the femoral shaft axis and the femoral head neck axis [76] (Figure 4). Normal values for the femoral neck-shaft angle have previously been defined as an average of 135° [77], however recently a range between 120°-140° have been suggested with angles >140° considered a sign of coxa valga and an angles <120° considered a sign of coxa vara [76].

The extrusion index quantifies the bony coverage of the acetabulum by calculating the proportion of the femoral head that is uncovered by the acetabulum when a horizontal line is drawn parallel to the inter-teardrop line (Figure 4). A normal extrusion index is less than 25% [78]. The posterior wall sign is positive when the centre of the femoral head is lateral to the posterior acetabular wall [78]. In a normal hip, the centre of the femoral head is medial to the posterior wall of the acetabulum. The crossover sign is evaluated by assessing if the line of the anterior aspect of the rim crosses the line of the posterior aspect of the rim before reaching the lateral edge of the sourcil or not (Figure 4). If the crossover and posterior wall sign are both positive, the acetabulum is defined as retroverted [36, 78]. The cliff sign is a relatively new radiographic measure in patients with hip microinstability (Figure 4). The cliff sign is assessed by drawing a perfect circle around the femoral head and then assessing if the lateral femoral head fills the circle or not. If a steep drop-off from the circle in the lateral femoral head is seen, it is defined as a positive cliff sign [16].

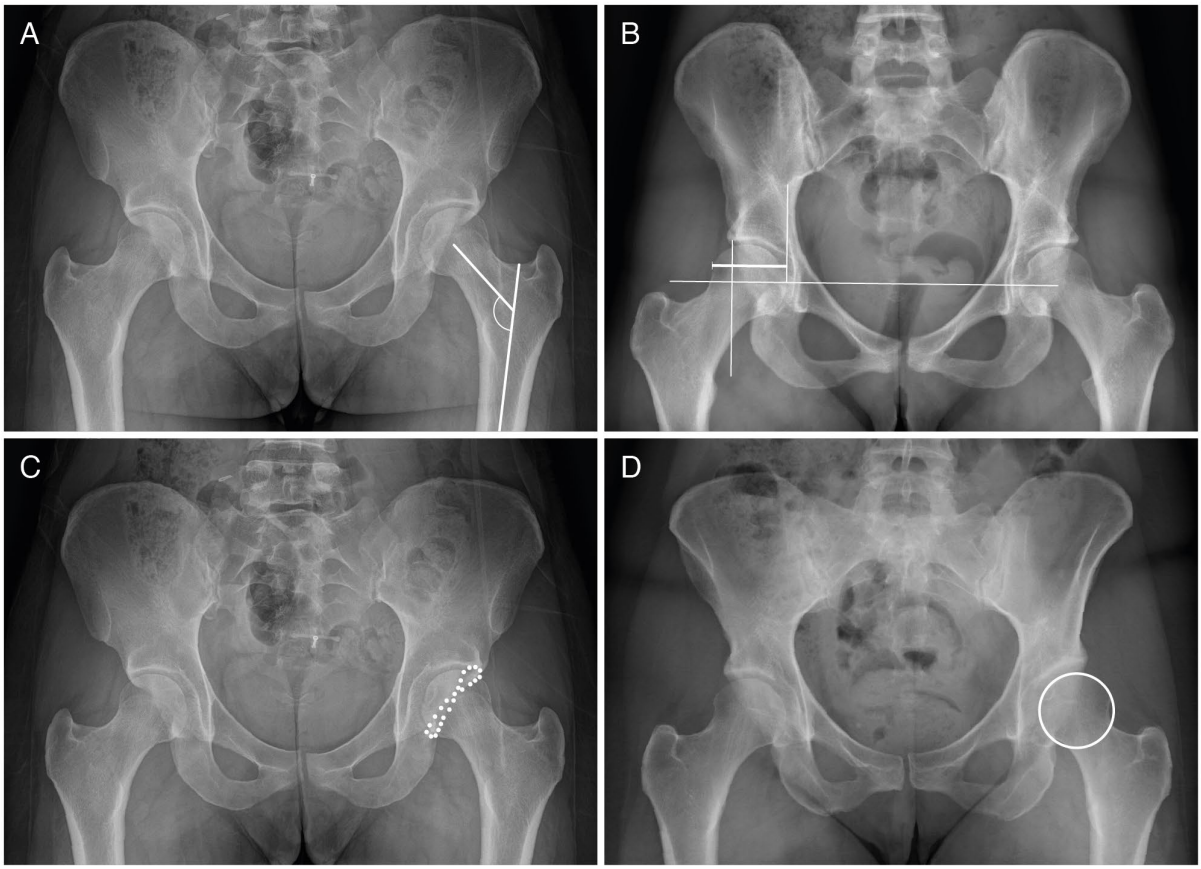

Figure 4. *Radiographic presentation of the following four radiographic measurements: (A) Femoral neck-shaft angle, (B) Extrusion index, (C) Cross-over sign, and (D) Cliff sign.*

Patient-reported outcomes

Patient-reported outcomes are useful to evaluate outcomes related to pain, activities and QoL as they focus on the patient perspective and have thus been suggested as the golden standard when assessing musculoskeletal conditions and evaluating surgeries [79, 80]. Surgical treatments used to be evaluated using outcomes where the clinician, often the surgeon, rated the result of the surgery, which was likely biased [81, 82]. In the systematic review (Paper I), six specific hip-related patient-reported outcome measures were used to assess the benefits of PAO: (1) the Copenhagen Hip and Groin Outcome Score (HAGOS), (2) HOOS, (3) the International Hip Outcome Tool (iHOT), (4) the Non-Arthitis Hip Score (NAHS), (5) the Oxford Hip Score (OHS), and (6) WOMAC. The six patient-reported outcome measures were all transformed into a score ranging from 0-100, where 0 is the worst possible outcome, and 100 is the best possible outcome. In the cross-sectional study (Paper II), the following two patient-

reported outcome measures were used: (1) The Forgotten Joint Score and (2) The Visual Analogue Scale (VAS).

The Hip disability and Osteoarthritis Outcome Score

The HOOS questionnaire was published in 2003 [83], and the translated Danish 2.0 version of the HOOS questionnaire was developed in 2008 [84]. HOOS is a patient-reported outcome measure with five subscales: pain, symptoms, activity limitations of daily living (ADL), activity limitations in sport and recreation and hip-related QoL. The symptom subscale consists of five items, the pain subscale of 10 items, the ADL subscale includes 17 items, and the sport and QoL subscale consists of four items [83]. Each item has five possible categories and is scored on a Likert Scale ranging from 0-4 points and then converted to a score between 0-100, where 0 indicates severe problems, and 100 indicates no problems [83]. The subscales have been demonstrated to have adequate internal consistency and external validity among patients with hip dysplasia undergoing PAO, and compared to the WOMAC and modified Harris hip score, HOOS has been found to be the most appropriate patient-reported outcome measure in this patient group [85]. In addition, HOOS is sensitive to measure changes over time in patients with FAIS undergoing hip arthroscopy [79] and is a valid and responsive patient-reported outcome measure among patients undergoing THA [83]. Wasko et al. estimated the minimal clinically important difference (MCID) to be 10.2 for the symptom subscale, 10.3 points for the pain subscale, 10.8 for the ADL subscale, 12.6 for the sport subscale and 11.2 for the QoL subscale among 294 patients with hip dysplasia that underwent PAO [85]. In addition, Clohisy et al. estimated the MCID to be 9 for the symptom and pain subscale, 6 for the ADL subscale, 10 for the sport subscale and 11 for the QoL subscale among 303-320 patients with hip dysplasia that underwent PAO [14].

Since the database was created, HOOS has been used to collect prospective data on physical function, pain levels and QoL among patients with hip dysplasia in the Aarhus PAO-database. The procedure for handling missing data, defined by the

authors of the HOOS, was followed. The procedure states that in cases where 1 or 2 items are missing on a HOOS subscale, the values must be substituted with the average value for the subscale [84].

The Copenhagen Hip and Groin Outcome Score

HAGOS is a modification of HOOS and the Hip Outcome Score published in 2011, as an assessment tool for young to middle-aged physically active patients with hip and/or groin pain [80]. The questionnaire consists of 6 subscales, with a total of 37 items: pain (10 items), symptoms (7 items), ADL (5 items), sport (8 items), physical activity (2 items) and QoL (5 items). Each item has five possible categories and is scored on a Likert Scale ranging from 0-4 points and then converted to a score between 0-100, where 100 indicates no problems. HAGOS is a valid, reliable and responsive patient-reported outcome measure among young patients with hip-related problems [80]. The MCID has been found to be 9.5 for the symptom subscale, 9.7 points for the pain subscale, 11.0 for the ADL subscale, 13.01 for the sport subscale, 16.9 for the physical activity subscale and 12.7 for the QoL subscale, among 502 patients with FAIS 4 months after hip arthroscopy [86].

The International Hip Outcome Tool

The iHOT-33 was also developed for younger active patients with hip-related problems and first published in 2012 [87]. The first version included 33 questions related to symptoms, physical function and QoL, but a short and timesaving version was also developed, including 12 questions (iHOT-12) [88]. Both the long and short versions result in a score between 0 and 100, ranging from severe to no problems, and both versions have been found to have excellent validity and reliability in the assessment of young patients with hip-related problems [87, 88]. The MCID has been estimated to be 6.0 among 27 young patients with hip problems who underwent hip arthroscopy [87].

The Non-Arthritic Hip Score

As for HAGOS and iHOT, the NAHS was also developed for young patients with hip-related problems in 2003 [89]. It consists of 20 items, all multiple-choice questions scored from 0 (extreme pain) to 4 (no pain) and forms a combined score ranging from 0-100 (worst to best) by multiplying the summed scores by 1.25. NAHS has demonstrated satisfactory reliability and fair validity [90]. The MCID for NAHS has been estimated to be 7.5 among 29 athletes who underwent both PAO and hip arthroscopy [91].

The Oxford Hip Score

Another hip-specific patient-reported outcome measure is the OHS, developed in 1996, which consists of 12 items, where each item is scored from 0-4 and then transformed into a total score ranging from 0-48, where 48 indicates the best possible result. The score can be further transformed into a score ranging from 0-100 (worst to best possible outcome). The OHS has been found to be reliable, valid and sensitive to changes in patients undergoing THA [92]. The MCID for OHS has been estimated to be 10.6 among 82,415 patients who received a THA [93].

The Western Ontario and McMaster Universities Arthritis Index

WOMAC was developed in 1989 to measure symptoms relevant to patients with hip or knee osteoarthritis [94]. WOMAC consist of three subscales, pain, stiffness and function, with a maximum score of 20, 8 and 68, respectively. The score can be linearly transformed into a 0-100 score, and as for the other patient-reported outcome measures, the better the score, the better the outcome. Despite being developed for older patients with hip or knee osteoarthritis, the WOMAC score has demonstrated adequate responsiveness to changes over time among patients with hip dysplasia undergoing PAO [95]. The HOOS questionnaire contains all the questions from WOMAC in the same form, meaning that a WOMAC score can be calculated from a HOOS questionnaire [83]. The MCID has been found to be 10.8 for the pain and function subscales and 12.9 for the stiffness subscale among 294 patients with hip dysplasia who underwent PAO [96].

The Forgotten Joint Score

Behrend et al. introduced the Forgotten Joint Score in 2012, a patient-reported outcome measure for patients who had undergone THA or total knee replacement, to distinguish between patients with good and excellent outcomes [97]. According to Behrend et al., the ultimate objective of a treatment is for the patient to achieve a state where they can "forget" the presence of their joint [97]. The Forgotten Joint score consists of 12 questions, and every question is scored by one of five possible responses ranging from never (1) to mostly (5). The final score is linearly transformed and reversed into a score from 0-100, where 100 indicates the best possible outcome. The Danish version of the Forgotten Joint Score was used in Paper II, which has been found to have high reliability and responsiveness and no floor or ceiling effect among patients undergoing arthroscopy due to FAIS [98]. Despite being developed for patients undergoing joint replacement, the principle of measuring whether a patient forgets their joint seems relevant regardless of the treatment.

The Visual Analogue Scale

Participants in the cross-sectional study (Paper II) rated their pain level at rest and during physical activity over the past 4 weeks on a 100-mm Visual Analogue Scale (VAS) [99]. The 100-mm VAS has been used since 1921 and ranges from no pain on the left side (0 mm.) to the worst possible pain on the right side (100 mm.). Previously, VAS was assessed in paper format, but multiple digital versions of the VAS have been developed. In study II, the participants used the Research Electronic Data Capture (REDCap) version of VAS, and most participants filled out the VAS score on a laptop, while some used their mobile phones. Delgado et al. compared a traditional paper version to a mobile phone version and a laptop version of VAS [100]. They found statistically significantly higher scores on the mobile phone version compared to the traditional paper version (1.93 mm.), but the difference was not clinically relevant (defined as ≥14 mm.) [100]. In addition, the laptop version of VAS was not significantly different from the paper version (0.03 mm.) [100].

Sports participation

The orthopaedic surgeon who created the Aarhus PAO-database defined the questions regarding sports in 2010. The first sports-related question was, *"Are you participating in sports?"* the patients could either reply yes or no. If the patients replied yes, they were further asked four sports-related questions. If the patients replied no, they were asked if a hip problem was the reason for not participating in sports (Table 5).

Table 5. Sports-related questions as defined in the Aarhus PAO-database, translated from Danish.

		Further sports question	Answer choices
Are you participating in sports?	**Yes**	What type of sports are you participating in?[a]	Athletics, Badminton, Cycling, Dancing, Fitness, Golf, Gymnastics, Handball, Horseback riding, Martial arts, Other, Running, Sailing, Soccer, Swimming, Walking, Tennis
		At what level do you participate in sports?	Recreational, Elite
		Are you able to participate in the sports you prefer with your present hip function?	Yes, No
		Has PAO improved your sports performance?[b]	Yes, No
	No	Are your lack of sports participation due to a hip problem?	Yes, No

[a]Multiple answers allowed. [b]This question was applied after PAO. PAO: periacetabular osteotomy.

The question regarding the type of sports was categorised into three categories following the definition by Leopold et al. [101]: (1) High-Impact Sports (athletics, badminton, dancing, gymnastics, handball, martial arts, running, soccer and tennis), (2) Low-Impact Sports (cycling, fitness, golf, horseback riding, sailing, swimming and walking), and (3) Others (all type of sports not specified above).

Physical function

The cross-sectional study (Paper II) involved two physical function tests, the single-leg hop for distance test [102, 103] and the Y Balance Test [104, 105], both requiring strength, flexibility, neuromuscular control, stability, and balance.

The single-leg hop test

The single-leg hop test was conducted with the participants barefoot, and their arms were held behind their backs during the test (Figure 5). Testing began with the right leg, followed by the left leg. Participants stood with their toe behind a marked starting line and hopped as far as possible on one leg, ensuring balance was maintained for 2 seconds after landing [103]. The distance from the starting line to the heel was measured. Each participant completed two familiarisation trials, followed by three maximal effort trials. Additional trials were performed if the third trial exceeded the second by more than 10 cm, continuing until the increase was less than 10 cm [103]. Only the longest hop distance was recorded, and the distance was further normalised to the participant's height by dividing the longest hop distance by the participant's height [102]. Kemp et al. investigated the reliability of the single-leg hop test and stated that a difference >14% could be considered greater than 0 [106], and a difference ≥15% on the single-leg hop test was therefore considered clinically relevant in the cross-sectional study (Paper II).

A: starting position for the single-leg hop test B: end position for the single-leg hop test

Figure 5. *Starting position (A) and ending position (B) for the single-leg hop test, as performed in Paper II. The figure is a part of Figure 1 in Paper II.*

The Y Balance Test

After the single-leg hop test, participants performed the Y Balance Test using the Y Balance Test Kit™ (Perform Better, West Warwick, Rhode Island). Prior to the assessment, the participants' limb length was measured using the Y Balance Test procedure, where the assessor measures the distance between the anterior superior iliac spine to the distal edge of the medial malleolus while the participant lies supine on an examiner table [104]. The assessor demonstrated the test before participants performed six familiarisation trials on each leg for each test direction. The participants were tested barefoot, stood with their toes behind the line on the platform, and pushed the moveable indicator as far as possible with the other foot while maintaining a single-leg stance (Figure 6) [105]. A trial was successful if the foot returned to the platform without losing balance. Trials were repeated if the participant lost balance, lifted the heel, lost contact with the distance indicator, or used it for support. Participants performed three trials in the anterior, posteromedial, and posterolateral directions, starting with the right leg. The longest reach distance in each direction was recorded and summed to form a composite reach distance normalised to limb length [105].

A: anterior direction B: posteromedial direction C: posterolateral direction

Figure 6. *End position for the Y Balance Test in (A) anterior direction, (B) posteromedial direction and (C) posterolateral direction, as performed in Paper II. The figure is a part of Figure 1 in Paper II.*

Jacobsen et al. defined a difference or change of >15% as clinically relevant among patients with hip dysplasia [43], based on results by Linek et al., who estimated the minimal detectable change of the normalised reach distances to be 8.54% for the anterior direction, 13.5% for the posterolateral direction and 13.7% for the posteromedial direction among 38 athletes with a mean age of 15.6 years (range 14-17) [107]. In addition, Foldager et al. estimated the minimal detectable change of the normalised reach distances to be 11% for the anterior direction, 7% for the posterolateral direction 6% for the posteromedial direction and 5% for the composite score among 51 healthy subjects with a mean age of 28 years (SD 7.2) [108]. In the cross-sectional study (Paper II), a difference >15% on the Y Balance Test was defined as clinically relevant as per Jacobsen et al. [43]. The intra- and interrater reliability for the Y Balance Test has been found to be excellent [104, 108].

Muscle strength

The cross-sectional study (Paper II) also involved assessment of isometric maximum voluntary contraction (MVC) in hip abduction, flexion and extension. Isometric muscle strength was assessed using an isokinetic muscle dynamometer (Humac Norm, CSMi, Stoughton, MA, USA), as motor-driven dynamometry is the gold standard for assessing muscle strength [109]. The procedure for hip abduction followed the test procedure described by Meyer et al. [109], while the hip flexion and extension procedure followed the procedure described by Kierkegaard et al. [110]. The assessment procedure started with a 10-minute warm-up on an ergometer bicycle, followed by the isometric hip abduction test for the right leg, followed by the left leg, then hip flexion and hip extension for the right leg and finally, hip flexion and extension for the left leg.

Jacobsen et al. defined a difference or change of >15% as clinically relevant among patients with hip dysplasia [43], based on results by Krantz et al., who estimated the minimal detectable change of the isometric muscle strength in an isokinetic muscle

dynamometer to be 12.5% for hip flexion and 30.5% for hip extension [111] and Thorborg et al., who estimated the minimal detectable change of isometric hip muscle strength using a handheld dynamometer to be >10% for all hip muscles [112]. In the cross-sectional study (Paper II), a difference >15% was defined as clinically relevant as per Jacobsen et al. [43].

Hip abduction

The participants were placed in a side-lying position for the hip abduction assessment, with the test leg placed on top of the non-tested leg (Figure 7). The rotation axis of the dynamometer arm was aligned with the proximal edge of the greater trochanter, and the length of the dynamometer arm was adjusted so the edge of the dynamometer pad was aligned with the superior border of the patella at full knee extension. The non-tested hip was kept in a 45° hip flexion, and bands were attached around the leg and waist to minimise rotation of the torso. The isometric hip abduction test was performed at 10° of hip abduction, and two familiarisation trials were performed, followed by three MVC trials. After each trial, a rest period of 30 seconds was applied. The trial was excluded if the participant rotated the leg while performing the test.

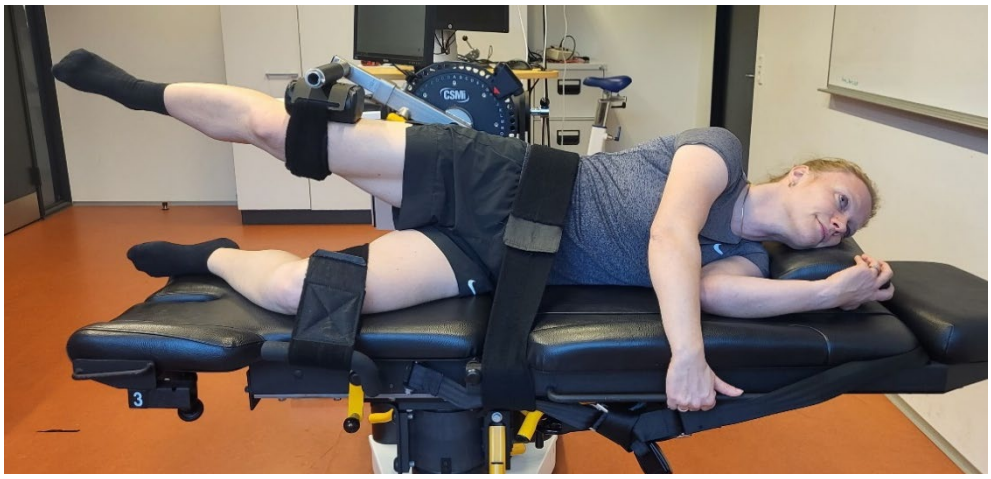

Figure 7. *Assessment of isometric hip abduction muscle strength using the isokinetic muscle dynamometer, as performed in Paper II. The figure is a part of Figure 1 in Paper II.*

The standardised verbal instructions were:

"We need to find out how strong you are in your hip muscles. To measure this, you must push as hard as possible against the dynamometer arm. At each direction, you will get two test trials where you must push with approximately 50% of what you can. After this, the test will start. You will get three attempts, and between each attempt, there is a 30-second rest period. When you push, do not kick the dynamometer arm and make sure not to pull your leg down before you push. You must push as hard and fast as possible against the dynamometer arm when I say go. Make sure not to pull your leg down before you push. Are you ready? All right, 3-2-1-go, push, push, push, push - stop".

Hip flexion and extension

The participants were placed in a supine position on the dynamometer chair with the backrest inclined 15° to reduce the lumbar curve and increase comfort (Figure 7). The rotation axis of the dynamometer arm was aligned with the proximal edge of the greater trochanter, and the dynamometer arm was placed approximately 5 cm proximal to the lateral femoral epicondyle of the tested leg. The participants were instructed to cross their arms over their chest and keep the non-tested leg flexed with the foot placed on the chair. The tested leg was barefoot to reduce weight, while the non-tested leg was wearing a shoe to keep the foot from sliding on the chair. A band was placed around the participant's hip, and the isometric hip flexion and extension test was performed at a further 45° hip flexion (Figure 8). As for hip abduction, two familiarisation trials were performed, followed by three MVC trials and a rest period of 30 seconds between each trial. The standardised verbal instructions were almost the same for the three directions, however for hip extension, the participant was asked to make sure they did not raise their leg before pulling.

Figure 8. *Assessment of isometric hip flexion and extension muscle strength using the isokinetic muscle dynamometer, as performed in Paper II. The figure is a part of Figure 1 in Paper II.*

Statistics

All handling of data was done using Microsoft Excel version 2412 (Microsoft Corporation, Redmond, WA, USA), Stata version 16.0-18.0 (StataCorp LLC, College Station, TX, USA) and the secure and web-based software platform REDCap hosted at Aarhus University [113, 114]. All statistical analysis was done using Stata version 16.0-18.0, and all graphical illustrations were done using Stata version 16.0-18.0 and GraphPad Prism version 10 (GraphPad Software, Boston, MA, USA). In all five studies, continuous data was assessed for normality and presented as mean with standard deviation (SD) or mean with 95% CI if data followed a normal distribution and as medians with interquartile range (IQR) (25^{th} and 75^{th} percentiles) if skewed (not normally distributed). Categorical data was presented as numbers with proportion in percentage. The different statistical analyses are presented in the following sections. For most of the analyses, an estimate with a p-value <0.05 was considered statistically significant except for the prediction analysis in Paper IV, where the p-value was Bonferroni corrected, meaning that the usual p-value cutoff at 0.05 was divided with the number of variables to counteract for the problem regarding multiple comparisons [115].

The systematic review and meta-analysis

Harms were extracted as the number and proportion of events with 95% CI. Meta-analysis was performed for studies with a comparator group using risk ratios, and a random-effect model was used due to differences in outcome measurements as well as PAO procedures, expected to result in considerable heterogeneity [47]. The heterogeneity of the meta-analysis results was predefined as substantial if I^2 were >50%. The I^2 statistic is the most commonly used measurement of heterogeneity, offering an estimate of the variability proportion caused by differences between the studies in a meta-analysis [116]. For the six patient-reported outcome measures, means and standard deviations were considered most relevant. Therefore, mean scores were approximated from the median scores, and standard deviations were approximated from the range scores if mean and standard deviations were unavailable. In addition, the change scores were used to calculate the preoperative or postoperative score if one was missing. The preoperative standard deviation was further used as the standard deviation for the postoperative score if this was missing [38]. The extracted data from the six patient-reported outcome measures were normalised to a scale ranging from 0-100 (worst possible outcome to best possible outcome), and weighted mean scores, with the number of patients as the weighted component, were calculated for each patient-reported outcome measure at all reported time points [47].

Subgroups

Different subgroups were analysed or presented in the different papers. In Paper III, patients were divided into patients with hip instability if their FEAR index was >2° before PAO and patients without hip instability if their FEAR index was ≤2°. In Paper IV, patients were divided into responders (defined as patients who had answered the question about sports participation) and non-responders (defined as patients who had not answered the question about sports participation but had reached the given time point) for each time point. In addition, patients who reported that they were sports-active before PAO were defined as (self-)categorised athletes and further divided into

elite- or recreational-level athletes, depending on their answer to the question about sports level.

Statistical tests

All comparisons between two groups or 2-time points were made using the chi-square test for proportions and the Student's *t*-test or regression analysis for continuous variables, while the generalised estimating equations (GEE) model was used for binary outcomes with multiple time points.

The Chi-square

The Chi-square test is used to assess whether the proportion of patients who possess specific characteristics (i.e. being a woman) is the same in two groups by testing the discrepancy between the observed frequencies and the expected frequencies if the proportion between the groups were equal [117]. The Chi-square test requires that data are categorical and that each patient only occurs once.

The Student's t-test

The Student's *t*-test is a statistical method for testing the null hypothesis, which is that there is no difference between two groups or time points (114). The Student's t-test requires that data are continuous and follow a normal distribution. Normality was assessed by QQ-plots and histograms.

Regression analysis

In Paper II, simple and multiple linear regression analyses were used to investigate the association between muscle strength and functional performance. The linear regression analysis is a statistical method to investigate the relationship between two continuous variables (an independent and a dependent variable) [117]. If there is a linear relationship between the two variables, a change in the dependent variable will be caused by a change in the independent variable. The assumptions for the linear

regression analysis are: (1) A linear relationship between the independent and dependent variable, which was assessed by plotting the two variables against each other, (2) The residuals (the difference between the observed and estimated value) follows a normal distribution, which was assessed using histograms and QQ-plots and (3) The residuals have the same variance for all the fitted variables, which was assessed by plotting the residuals against the fitted values [117]. In addition, (4) The observations must be independent, and (5) The independent variable must be measured without error. The regression coefficients describing the difference in the dependent variable expected with a 1-unit difference were presented with 95% CI for both analyses. The multiple linear regression analysis was adjusted for age, sex, height and weight, and the adjusted coefficient of determination (R^2) was reported as a measure of model fit, sometimes called the goodness of fit, as it represents the percentage of the variation in the dependent variable that the relationship with the independent variables can explain [117].

Generalised estimating equations

GEE modelling [118] is a marginal model for longitudinal data with multiple time points that take into account that the outcomes over time from the same participant tend to be correlated [119]. GEE analyses do not acquire that data is normally distributed, data can be binary and the model includes all available data [117]. GEE was used to assess if patient characteristics before PAO (age, sex, education, BMI, CE-angle, AI-angle, pain and QoL) could predict sports participation, ability to perform preferred sport and improvements in sports performance after PAO. The patient characteristics were thus the independent variables, whereas the sports outcomes were the dependent variables. The results of the GEE analysis were presented as odds ratios (OR) with 95% CI for each independent variable, as well as a combined model where the different variables adjusted for each other. Age, BMI, CE-angle, AI-angle, HOOS pain and HOOS QoL were included continuously, while sex (man or woman) and education level (primary, secondary or higher) were included categorically. The dependent variables were all dichotomous (yes or no). Complete-case analysis was used for this analysis.

Reliability

The intraclass coefficient (ICC) and Cohen's Kappa statistics were applied to assess the inter-rater reliability of the radiographic measurements indicative of hip instability (Paper III). The inter-rater reliability is the variation between two or more raters [117], in Paper III, the orthopaedic surgeon and the radiologist. The ICC is a statistical method to assess the agreement between raters when the outcome is continuous by calculating the proportion of variance between the raters out of the total variance [117]. The ICC was interpreted using the categorisation set by Koo and Li, who categorised the ICC scores in the following way: poor reliability: <0.50, moderate reliability: 0.50-0.75, good reliability: 0.75-0.90 and excellent reliability: >0.90 [120].

Cohen's Kappa coefficient is a statistical method to assess the agreement between two raters when the outcome is categorical by measuring the frequencies of which the raters agree and the expected frequencies if the outcome was measured at random and thereby includes the possibility of an agreement occurring by chance [117]. The Cohen's Kappa coefficient was interpreted using the categorisation set by Landis and Koch, who categorised the coefficients in the following way: poor agreement: <0.00, slight agreement: 0.00-0.20, fair agreement: 0.21-0.40, moderate agreement: 0.41-0.60, substantial agreement: 0.61-0.80 and perfect agreement: >0.80 [121].

Validation

Registration completeness

Registration completeness between the Aarhus PAO-database and DNPR in Paper V was defined as the percentage of patients registered in both registries and calculated by dividing the number of hips that had undergone PAO due to hip dysplasia and were registered in both registries by the number of hips registered in only one of the registries. Completeness was presented with 95% CI for the entire period and each year separately (2014-2021). A sensitivity analysis was performed, adding the date of PAO to the analysis by defining a more than 1-day difference as a discrepancy.

Positive predictive value

To further investigate discrepancies, a computer-generated random selection of 20 entries (hips) from both the Aarhus PAO-database and DNPR for each year (2014-2021) was validated by confirming the information in the two registries by the patient's electronic medical journals. The positive predictive value (PPV) is the proportion of patients with a positive result, meaning the proportion of patients that have the given disease [117], in this case, the proportion of patients that had actually undergone PAO due to hip dysplasia. PPV was therefore calculated as the proportion of confirmed diagnoses and procedures in the two registries by electronic medical records. PPV was also calculated for confirmed diagnoses and procedures among patients that only occurred in either the Aarhus PAO-database or DNPR.

6. Results

Overall patient characteristics

The characteristics of patients with hip dysplasia from all five studies have been presented in Table 6. Despite the big differences in number of patients with hip dysplasia in the five cohorts, comparable characteristics were found. The proportion of women in the five cohorts ranged from 80%-89%, and the patients' age ranged from 27-30 years. The patients in Paper II (patients included in the ongoing PreserveHip trial) were a bit younger than patients with hip dysplasia in general. BMI ranged from 23-24 kg/m^2, with the self-reported BMI in the PAO-database being slightly lower than the BMI measured by an assessor in Paper II and the BMI found in the literature in Paper I.

Table 6. Participant characteristics (number of patients, women, age at the time of surgery and body measurements) in each of the five papers.

	Paper I PAO patients across studies[a]	**Paper II** Hip dysplasia patients	**Paper III** Total cohort	**Paper IV** Total cohort[b]	**Paper V** Patients included in both registries
Patients	3484	59	122	1891	967
Women	2787 (80%)	51 (86%)	198 (89%)	1588 (84%)	1010 (86%)
Age	29 (.)	27 (5.6)	28 (9.4)	30 (10.1)	29 (9.6)
Weight	.	70.6 (11.0)	.	66.8 (10.7)	.
Height	.	1.71 (0.1)	.	1.71 (7.9)	.
BMI	24 (.)	24.2 (3.1)	.	22.8 (2.9)	.

[a]Data was combined across studies. [b]Body measurement was self-reported in the Aarhus PAO-database. Age at surgery is presented in years, weight in kg., height in meters and BMI in kg/m^2. Categorical values are presented as numbers with percentages, while continuous data are presented as means with standard deviations. .: no information available. (.): inconsistency in reporting variations, with some studies not reporting variations at all.

Paper I – The systematic review

The original systematic review on patient-reported outcomes by O'Brien et al. consisted of 62 studies [38]. For the systematic review and meta-analysis on benefits and harms, 33 studies were excluded due to not reporting or mentioning harms (n=28 studies), not reporting any of the harms defined by Biedermann et al. [56] (n=3 studies) and only reported outcomes before PAO (n=2 studies). Twentynine studies with the prespecified information on both harms and benefits were thus included. Figure 1 in Paper I (appendix 1) shows the flow chart of the study selection. The studies were overall comparable, however, the type of PAO the patients underwent varied, and nine different methods were found. The number of included patients and hips varied greatly ranging from 16-112 patients and 16-1385 hips. In addition, 12 studies used a different classification system than the one by Biedermann et al.: 10 studies used a modified Clavien-Dindo score [14, 122-130], one study classified the patients' WOMAC scores into poor, good and very good [131], and one study used five classifications based on treatment and morbidity [132]. Table 1 in Paper I (appendix Paper I) summarises the 29 included studies, including patient characteristics and the type of PAO.

Quality assessment

The methodological quality assessment was done using ROBINS-I and revealed that 24 studies had an overall serious risk of bias, two had a moderate risk of bias, and three had a low risk of bias. Lack of blinding when measuring the primary outcome was the most frequent reason for bias, often due to using a patient-reported outcome as the primary outcome, where the assessor is the patient themselves and thus not blinded. Selection of reported results, defined as multiple comparisons or no primary outcome specified, was the second most frequent risk of bias. In addition, five studies had a serious risk of bias due to missing data from more than 19% of their included patients. The quality assessment is presented in Figure 2 in Paper I (appendix 1). Despite the risk of bias, all studies were included in the analysis to include as much data as possible.

Minor and major adverse events

From the 29 included studies, 4260 procedures were done, of which a major adverse event occurred in 182 procedures and a minor adverse event in 598. The proportion of major adverse events was thus 4.3% (95% CI: 3.7;4.9) and 14.0% (95% CI: 13.0;15.1) for a minor adverse event. The amount of specific adverse events is presented in Figure 9 and Figure 10. Of the major adverse events, ischial fracture, arterial thrombosis, resubluxation and acetabular fragment migration or displacement, were not reported in any of the included studies. The minor adverse event, avulsion of iliac crest was also not reported. The adverse events that could not be classified according to Biedermann et al. are presented in Table 3 in Paper I (appendix 1). It is worth noting that five studies reported on conversion to THA, where 115 hips out of 1870 were converted to a THA. Thus, the proportion of THA conversions was 6.1% (95% CI: 5.1;7.3).

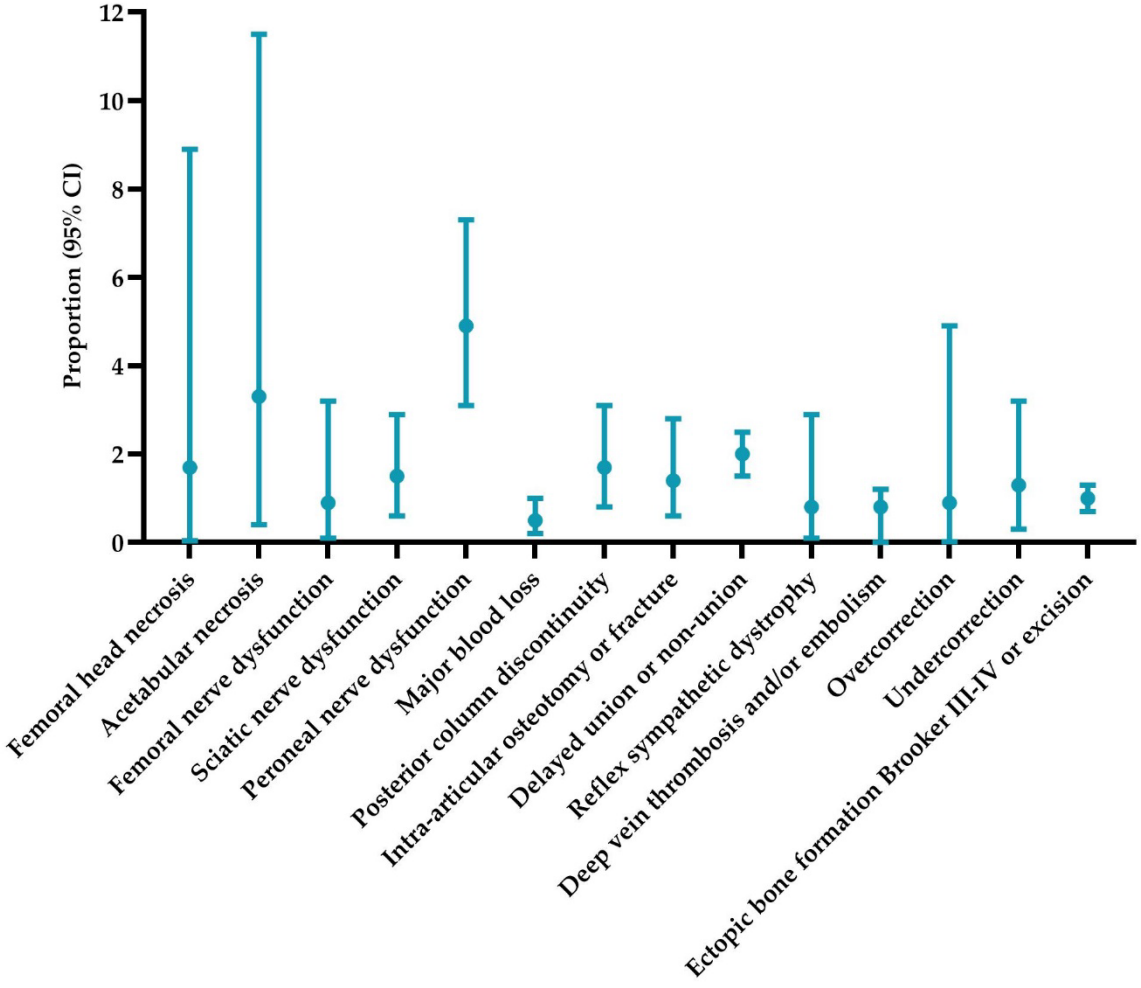

Figure 9. *Proportion of major complications following periacetabular osteotomy from the studies included in the systematic review with 95% confidence interval (95% CI). The figure presents the data in Table 2 in Paper I.*

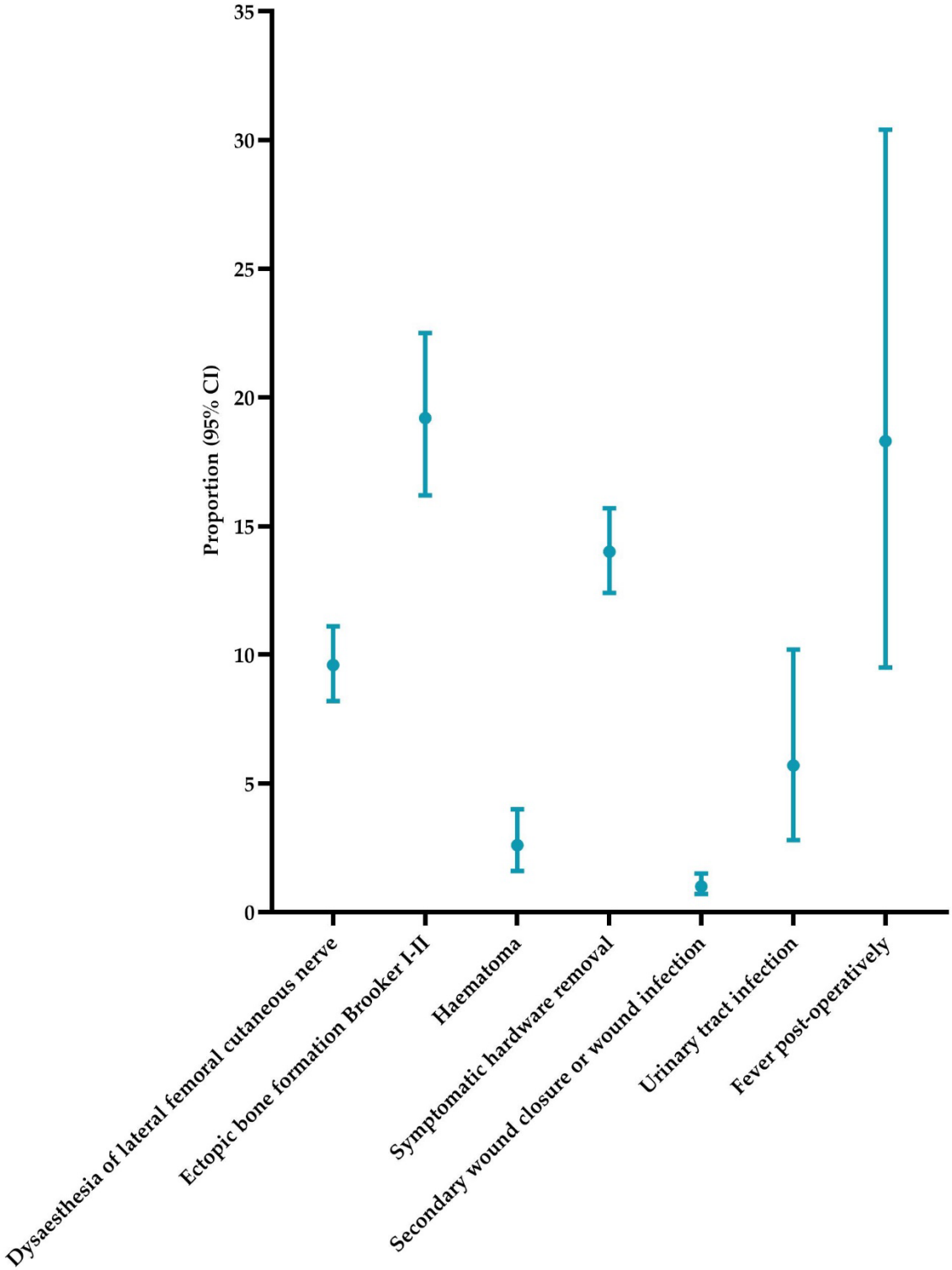

Figure 10. *Proportion of minor complications following periacetabular osteotomy from the studies included in the systematic review with 95% confidence interval (95% CI). The figure presents the data in Table 2 in Paper I.*

Meta-analysis

Six of the 29 included studies included a comparison group, making meta-analysis for these groups possible. The forest plots for the meta-analysis on major and minor adverse events are found in Figure 3 and Figure 4 in Paper I (appendix I).

PAO versus THA

Garbuz et al. [133] and Hsieh et al. [134] both included patients who had undergone PAO and patients who had undergone THA and found five major and seven minor adverse events among the group of patients that had undergone PAO, and one major and one minor adverse events among the group of patients that had undergone THA [133, 134]. The risk ratio was thus 4.30 (95% CI: 0.70;26.57) for a major and 5.70 (95% CI: 1.03;31.60) for a minor adverse event, which means that patients undergoing PAO have a 330% higher risk of a major adverse event and a 470% higher risk of a minor, compared to patients undergoing THA. The risk ratio was only statistically significant for the minor adverse event.

Severe versus mild hip dysplasia

Grammatopoulos et al. [123] and Ricciardi et al. [125] reported adverse events in patients with severe hip dysplasia and patients with mild hip dysplasia separately. Grammatopoulos et al. defined severe hip dysplasia as an AI-angle >15° and a CE-angle <15°, while Ricciardi et al. defined severe dysplasia as a CE-angle ≤17°. Mild hip dysplasia was thus defined as an AI-angle <15° and a CE-angle >15° by Grammatopoulos et al. and as a CE-angle between 18-25° by Ricciardi et al. [123, 125]. Together, they found eight major and two minor adverse events among patients with severe hip dysplasia and two major and one minor adverse event among patients with mild hip dysplasia [123, 125]. The risk ratio was thus 1.10 (95% CI: 0.23;5.25) for a major and 0.66 (95% CI: 0.09;4.99) for a minor adverse event. This means that patients with severe hip dysplasia undergoing PAO have a 10% higher risk of a major adverse event and a 44% lower risk of a minor compared to patients with mild hip dysplasia undergoing PAO. The risk ratio was not statistically significant.

PAO versus PAO with arthroscopy or arthrotomy

Ricciardi et al. [127] and Thanacharoenpanic et al. [128] both included a group of patients who had undergone PAO and patients who had undergone PAO concomitant with hip arthroscopy or arthrotomy. Together, they found four major and 14 minor adverse events among the group of patients that had undergone PAO and six major and 39 minor adverse events among the group of patients that had undergone PAO concomitant with hip arthroscopy or arthrotomy [127, 128]. The risk ratio was thus 0.71 (95% CI: 0.21;2.42) for a major and 0.53 (95% CI: 0.13;2.16) for a minor adverse event. This means that patients undergoing PAO have a 29% lower risk of a major adverse event and a 47% lower risk of a minor compared to patients undergoing PAO concomitant with hip arthroscopy or arthrotomy. The risk ratio was not statistically significant.

Certainty assessment

The GRADE assessment for the three comparison groups showed very low certainty of evidence for the six meta-analyses (Table 7). As all six studies were observational cohort studies, they started by default at low-quality evidence and were further downgraded due to a high risk of bias found in the quality assessment. Two of the meta-analyses would have been further downgraded due to heterogeneity if not already on the lowest possible level (Table 7).

Table 7. The GRADE evidence profiles of the six meta-analyses.

Outcome (number of studies/ patients)	Patients vs. controls	Quality assessment					Risk ratio (95% CI)	Overall quality
		Limitations	Inconsistency (I^2)	Indirectness	Imprecision	Publication bias		
Major complications (2/124)	PAO vs. THA	High risk of bias	0.79%[a]	No serious indirectness	Wide confidence interval	Not found	4.30 (0.70;26.57)	⊕⊖⊖⊖
Major complications (2/463)	Severe dysplasia vs. mild dysplasia	High risk of bias	0.00%	No serious indirectness	None found	Not found	1.10 (0.23;5.25)	⊕⊖⊖⊖
Major complications (2/189)	PAO vs. PAO+A	High risk of bias	0.00%	No serious indirectness	None found	Not found	0.71 (0.21;2.42)	⊕⊖⊖⊖
Minor complications (2/124)	PAO vs. THA	High risk of bias	0.00%	No serious indirectness	Wide confidence interval	Not found	5.70 (1.03;31.60)	⊕⊖⊖⊖
Minor complications (2/463)	Severe dysplasia vs. mild dysplasia	High risk of bias	0.00%	No serious indirectness	None found	Not found	0.66 (0.09;4.99)	⊕⊖⊖⊖
Minor complications (2/189)	PAO vs. PAO+A	High risk of bias	49.69%[a]	No serious indirectness	None found	Not found	0.53 (0.13;2.16)	⊕⊖⊖⊖

[a]Downgrading due to considerable (>75%) or moderate (30-75%) heterogeneity. ⊕⊖⊖⊖ = very low overall quality. CI: confidence interval. THA: total hip arthroplasty. PAO: periacetabular osteotomy. PAO+A: periacetabular osteotomy combined with hip arthroscopy or arthrotomy.

Patient-reported outcomes

Data on patient-reported outcomes was available for 26 of the included 29 studies, as two studies had only presented their patient-reported outcomes graphically, and one study had used a combined HOOS score, which deviated from the intended design of the HOOS. None of the included studies used HAGOS or OHS. All the included patient-reported outcomes showed considerable clinically relevant improvements from before PAO and up to 2 years after, as the weighted mean scores exceeded the MCID values (Table 8). The improvements were maintained for at least 5 years after PAO for all six patient-reported outcomes and were still clinically relevant.

Table 8. The weighted mean scores for the six patient-reported outcome scores across the included studies, from before PAO (time point 0) and up to more than 10 years after. The results are extracted from Paper I, Figure 5 [47].

Years after PAO	0	<1	1 to <2	2 to <3	3 to <4	4 to <5	5 to <10	10 to ∞	MCID
iHOT	34.7	68.7	76.7	73.9	.	.	66.3	.	6
HOOS Pain	54.2	83.0	.	83.3	.	.	83.0	78.0	10.3
HOOS Function	66.5	89.0	.	90.5	.	.	91.0	84.0	10.8
NAHS	59.6	.	.	82.4	.	.	92.0	.	7.5
WOMAC Pain	59.3	.	75.3	84.5	87,4	84.3	76.8	87.0	10.8
WOMAC Function	61.1	.	76.9	85.4	85.6	73.7	73.8	.	10.8

iHOT: International Hip Outcome Tool 12 and 33. HOOS: Hip Dysfunction and Osteoarthritis Outcome Score. MCID: minimal clinically important difference. NAHS: Non-Arthritic Hip Score. PAO: periacetabular osteotomy. WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index. .: no information.

Paper II – The cross-sectional study

Baseline data on 59 Danish patients with hip dysplasia were extracted from the ongoing randomised controlled PreserveHip trial and compared with 39 healthy subjects. The patients with hip dysplasia had a mean age of 27.5 years (SD 5.6), and 86% were women. The healthy subjects' mean age was 26.6 (SD 4.9), and 74% were women. There was a statistically significant difference in the mean BMI ($p<0.001$), where patients with hip dysplasia had a 2.0 kg/m^2 (95% CI: 0.8;3.1) higher BMI than the healthy subjects, which could indicate a healthier lifestyle among the healthy subjects (appendix Paper II). The healthy subjects had a median Forgotten Joint Score at 100 (IQR: 100;100) and a median VAS score at 0 mm. (IQR: 0;0) in rest and activity. The median Forgotten Joint Score for patients with hip dysplasia was 20.8 (IQR: 12.5;35.4), while the median VAS score in rest was 55 mm. (IQR: 30;68), and the median VAS score in activity was 65 mm. (IQR: 50;73). The pain level in both rest and activity and the awareness of the hip joint was thus statistically significantly worse for patients than healthy subjects. The participant characteristics are in Table 1 in Paper II (appendix Paper II).

Functional performance

The mean normalised single-leg hop test was 41.9 cm/m (95% CI: 37.7;46.1) for patients index leg and 44.4 (95% CI: 40.1;48.6) for their contralateral leg (Figure 11). The patients were thus able to hop 2.4 cm/m (95% CI: 0.2;4.7) longer on their contralateral leg compared to the index leg. The difference was statistically significant ($p=0.03$), however, not clinically relevant as the mean difference was 5.8%. The mean normalised single-leg hop distance was 61.2 cm/m (95% CI: 57.0;65.4) for the healthy subjects' right leg and, therefore, 19.3 cm/m (95% CI: 13.1;25.4) longer than the hop distance for the patients' index leg ($p<0.001$). The mean difference was 37.4% and thus more than twice as high as the threshold for clinical relevance.

The mean normalised Y Balance Test for the patients' index legs was 62.9% (95% CI: 60.3;65.4) for the anterior reach, 104.5% (95% CI: 100.3;108.8) for the posteromedial reach, 99.9% (95% CI: 95.6;104.3) for the posterolateral reach and 89.1% (95% CI: 85.6;92.6) for the composite reach. The mean normalised Y Balance Test for the patients' contralateral leg was comparable to that of the index leg (Figure 11). The healthy subjects were 10.1% (95% CI: 6.0;14.2) better in the anterior direction compared to the patients' index leg, 18.6% (95% CI: 12.6;24.5) better in the posteromedial direction, 16.9% (95% CI: 10.8;22.9) better in the posterolateral direction and 15.2% (95% CI: 10.3;20.1) better in the composite reach score. The healthy subjects were thus statistically significantly better in all the Y Balance Test directions compared to the patients' index leg ($p<0.001$) (Figure 11). The point estimate exceeded the threshold for being clinically relevant for all directions except for the anterior direction. However, the lower limit of the 95% CI was below the thresholds for all directions.

Isometric hip muscle strength

The mean isometric hip muscle strength was 57.6 Nm (95% CI: 50.5;64.6) in hip abduction, 62.7 Nm (95% CI: 55.4;70.1) in hip flexion and 153.2 Nm (95% CI: 134.6;171.8) in hip extension for the index leg in patients with hip dysplasia (Figure 11). For the contralateral leg, the hip abduction strength was 62.3 Nm (95% CI: 56.1;68.4), the hip flexion strength was 66.3 Nm (95% CI: 59.3;73.2), and the hip extension strength was 157.9 Nm (95% CI: 141.6;174.2). Isometric hip muscle strength thus seemed to be a bit higher for the contralateral leg than the index leg, but the difference was not statistically significant nor clinically relevant. For the healthy subjects, the hip abduction strength was 67.8 Nm (95% CI: 59.0;76.6), the hip flexion strength was 77.6 Nm (95% CI: 68.4;86.8), and the hip extension strength was 169.9 Nm (95% CI: 149.2;190.7). The difference in hip abduction and extension strength between the patients' index leg and the healthy subjects was not statistically significantly different, however hip abduction was clinically relevant, as the mean percentage difference was 16.3%. The mean difference in hip flexion strength was 14.9 Nm (95%

CI: 3.9;26.4) and thus statistically significantly higher for the healthy subjects compared to the patients' index leg, and clinically relevant as the mean difference was 21.2% (appendix Paper II).

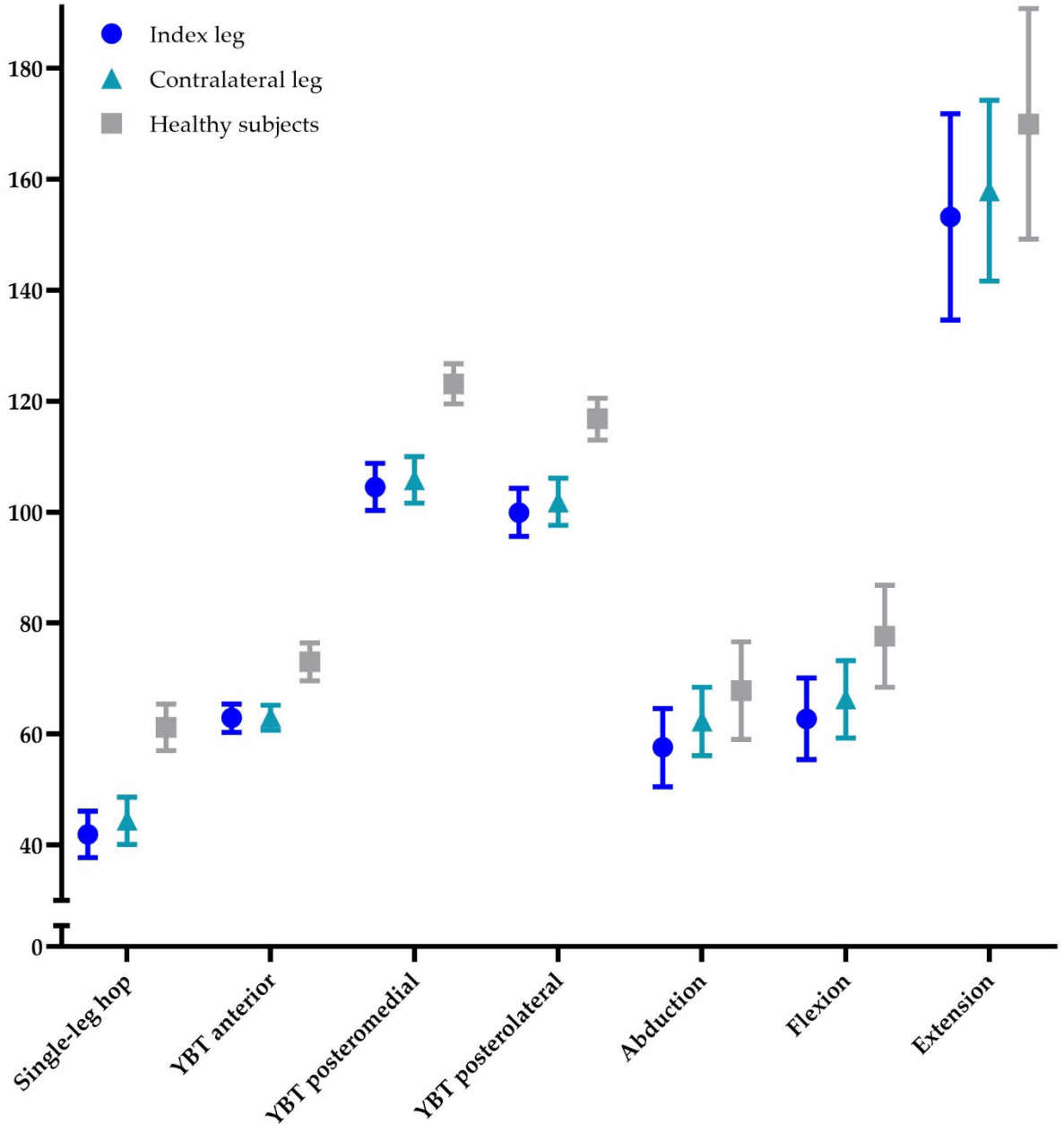

Figure 11. *Normalised single-leg hop test, normalised Y Balance test (YBT) in the anterior, posteromedial and posterolateral directions, and isometric hip abduction, flexion and extension muscle strength for patients with hip dysplasia, presented in cm/m, % and Nm with 95% confidence interval, respectively. Scores are marked with a circle for the index legs, a triangle for the contralateral legs, and a square for healthy subjects. The figure presents the data in Table 2 in Paper II.*

Associations between functional performance and isometric hip muscle strength

The single-leg hop test was statistically significantly associated with hip muscle strength in both the index and contralateral legs for patients with hip dysplasia after adjusting for age, sex, height and weight (p=0.001). The regression coefficient ranged from 0.22-0.70, meaning that the single-leg hop test is expected to increase 2.2-7.0 cm for each 10 Nm more muscle strength a patient has (Table 9). The determination coefficient ranged from 0.36-0.51, and the association model was thus able to explain 36%-51% of the variance between the single-leg hop test and the isometric muscle strength tests.

Table 9. Associations between the single-leg hop test and isometric hip muscle strength in patients with hip dysplasia. The analysis was adjusted for age, sex, height and weight. The table represents Table 3 in Paper II.

		Single-leg hop test, cm				
		Crude		Adjusted		
		β (95% CI)	P-value	β (95% CI)	R^2	P-value
Muscle strength, Nm	Index leg					
	Abduction	0.51 (0.27;0.75)	<0.001	0.47 (0.20;0.74)	0.36	0.001
	Flexion	0.46 (0.22;0.69)	<0.001	0.49 (0.21;0.76)	0.36	0.001
	Extension	0.19 (0.10;0.28)	<0.001	0.22 (0.11;0.33)	0.40	<0.001
	Contralateral leg					
	Abduction	0.61 (0.33;0.88)	<0.001	0.62 (0.32;0.93)	0.42	<0.001
	Flexion	0.60 (0.37;0.84)	<0.001	0.70 (0.44;0.95)	0.51	<0.001
	Extension	0.20 (0.09;0.31)	0.001	0.23 (0.10;0.36)	0.38	0.001

β: regression coefficients describing the difference in the independent variable expected with a 1 cm hop difference. R^2: coefficient of determination.

The composite reach from the three directions at the Y Balance Test was also statistically significantly associated with hip muscle strength in both legs (p=0.001). The regression coefficient ranged from 0.11-0.34, meaning that the Y Balance Test is expected to increase 10% for each 1.1-3.4 Nm more muscle strength a patient has (Table 10). The determination coefficient ranged from 0.24-0.44, and the association model was thus able to explain 22%-44% of the variance between the single-leg hop test and the isometric muscle strength tests. Higher isometric muscle strength was associated with better performance at the single-leg hop and Y Balance tests.

Table 10. Associations between the Y Balance test (the composite reach score) and isometric hip muscle strength in patients with hip dysplasia. The analysis was adjusted for age, sex, height and weight. The table represents Table 3 in Paper II.

		Composite reach, %				
		Crude		Adjusted		
		β (95% CI)	P-value	β (95% CI)	R^2	P-value
Muscle strength, Nm	Index leg					
	Abduction	0.25 (0.14;0.36)	<0.001	0.34 (0.22;0.46)	0.44	<0.001
	Flexion	0.16 (0.04;0.27)	0.010	0.28 (0.14;0.42)	0.31	<0.001
	Extension	0.06 (0.01;0.10)	0.019	0.11 (0.05;0.17)	0.29	<0.001
	Contralateral leg					
	Abduction	0.17 (0.03;0.30)	0.016	0.28 (0.12;0.43)	0.24	0.001
	Flexion	0.18 (0.07;0.30)	0.002	0.34 (0.22;0.47)	0.34	<0.001
	Extension	0.05 (0.00;0.11)	0.037	0.12 (0.06;0.18)	0.24	<0.001

The composite reach score was calculated and normalised this way: (the sum of the three directions)/(3x leg length) x100. β: regression coefficients describing the difference in the independent variable expected with a 1% reach difference. R^2: coefficient of determination.

Paper III – The FEAR index study

Between the 1st of January 2018 and the 31st of December 2020, 314 PAO procedures were registered in the Aarhus PAO database, of which 41 procedures had to be excluded as the patients seemed to have undergone PAO twice during the 3 years. Another 51 procedures from 51 patients were further excluded due to missing or incomplete radiographs before PAO. A total of 222 patients, with a mean age of 28.0 (SD 9.4) and 89% women (Table 6), were thus included in this paper. Of the 222 patients included in this paper, 76 (34%) had a FEAR index >2°, and 146 (66%) had a FEAR index ≤2°, before PAO. There were no differences in age, sex or educational level between the two groups. The flow chart is in Figure 2, and the patient characteristics are in Table 1, both in Paper III (appendix Paper III).

Radiographic measurements indicative of hip instability

The AI-angle, the CE-angle and the FEAR index improved after PAO (Table 11). The femoral neck-shaft angle was only measured preoperatively. In addition, a Broken Shenton's line was found in 20 patients (9%) before PAO and only six patients (3%) after PAO. All the radiographic measurements indicative of hip instability with pre- and postoperative radiographs thus improved after PAO. The number of patients with an AI-angle >10° decreased from 141 (66%) before PAO to 27 (13%) after PAO. Similar for the CE-angle, where 116 patients (54%) had a CE-angle <20° preoperative and only 20 patients (9%) postoperative. The number of patients with a FEAR index >2° and complete postoperative radiographs decreased from 69 (33%) before PAO to 15 (7%) 6 months after PAO.

Table 11. The radiographic measurements indicative of hip instability and the HOOS scores preoperative (before PAO) and postoperative (6 months after PAO) for the entire cohort. The table represents Table 2 and Table 3 in Paper III [61].

	N	Preoperative	Postoperative	Difference	P-value
Radiographic measurements					
AI-angle	214	13.0 (12.3;13.6)	4.8 (4.0;5.5)	8.2 (7.7;8.7)	<0.001
CE-angle	214	18.2 (17.4;19.0)	27.7 (26.9;28.6)	9.6 (9.0;10.1)	<0.001
FEAR index	209	-1.4 (--2.6;-0.1)	-11.5 (-12.8;-10.2)	10.1 (9.2;11.1)	<0.001
Femoral neck-shaft angle	222	135 (134;136)			
HOOS					
Pain	195	49.2 (46.5;51.9)	76.4 (73.6;79.3)	27.3 (24.4;30.1)	<0.001
Symptoms	195	46.6 (43.9;49.4)	71.0 (68.1;73.9)	24.3 (21.4;27.2)	<0.001
Activities of daily living	195	60.1 (57.1;63.0)	83.1 (80.5;85.7)	23.0 (20.4;25.5)	<0.001
Sport	195	39.5 (36.1;42.8)	67.6 (64.1;71.2)	28.2 (24.5;31.8)	<0.001
Quality of life	195	29.8 (27.7;31.9)	57.7 (54.6;60.9)	27.9 (24.8;31.1)	<0.001

Results are presented as mean with 95% confidence interval, and the radiographic measurements are in degrees. AI-angle: acetabular index of Tönnis. CE-angle: centre-edge angle of Wiberg. FEAR index: femoral-epiphyseal acetabular roof index. HOOS: Hip disability and Osteoarthritis Outcome Score. N: number of patients.

The Hip disability and Osteoarthritis Outcome Score

The HOOS scores improved statistically significantly in all five subscales from preoperative to 6 months postoperative (Table 11). The change scores were clinically relevant, exceeding twice the MCID values reported by Wasko et al. [96], and by Clohisy et al. [14]. The HOOS score also improved statistically significantly from before PAO to 6 months after PAO for both patients with a FEAR index >2° and patients with a FEAR index ≤2° (Figure 12). The change scores for both groups also exceeded twice the two MCID values [14, 96], and were thus clinically relevant. There were no differences between patients with a FEAR index >2° and patients with a FEAR index ≤2° in the HOOS subscale score before PAO, nor 6 months after PAO and thus no difference in the change scores either (Figure 12). Hip instability was, therefore, not associated with hip pain, symptoms, function, ADL or QoL among patients with hip dysplasia.

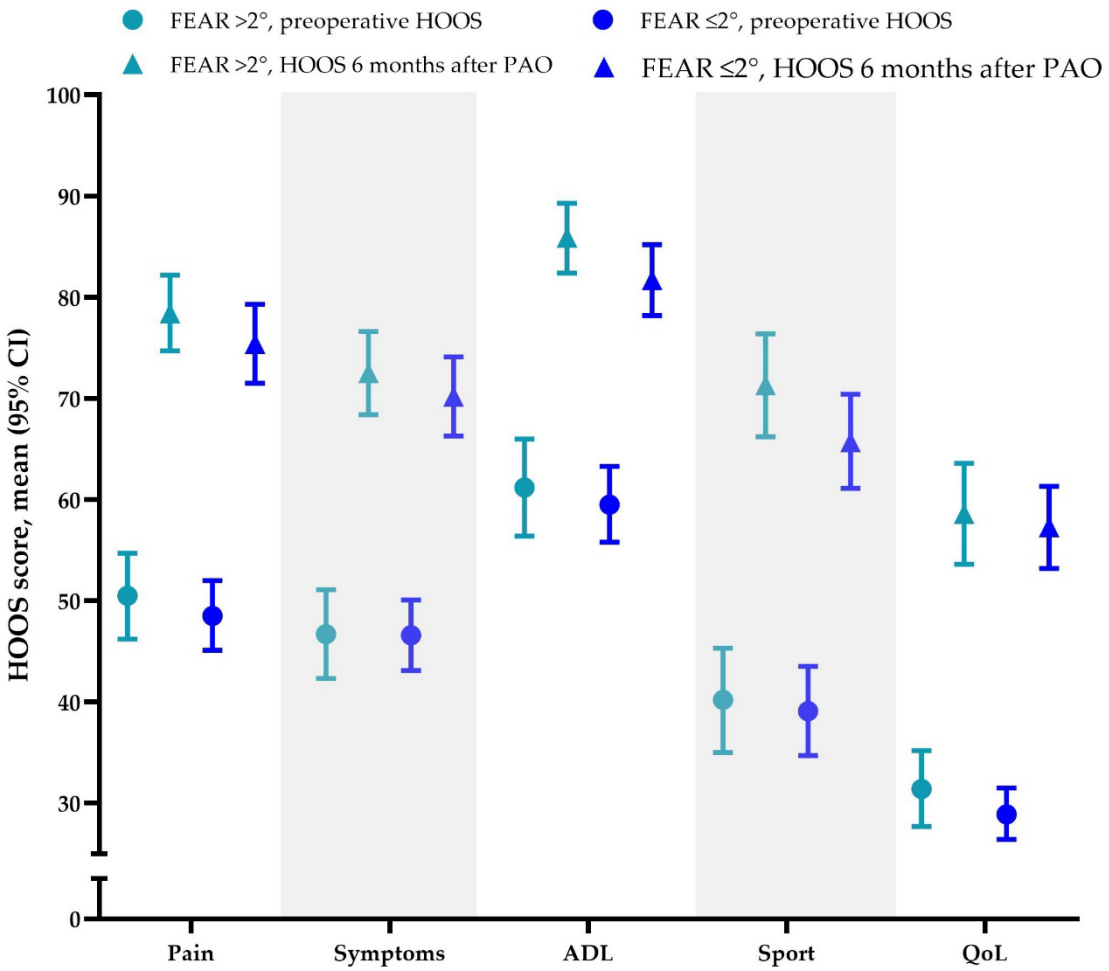

Figure 12. *The HOOS scores before and 6 months after PAO for patients with a preoperative FEAR index >2° (n = 66) and patients with a preoperative FEAR index ≤2° (n = 129). ADL: activities of daily living. HOOS: Hip disability and Osteoarthritis Outcome Scale. PAO: periacetabular osteotomy. QoL: quality of life. 95% CI: 95% confidence interval. The figure presents the data in Table 3 in Paper III.*

A sensitivity-analysis on patients with borderline hip dysplasia (defined as a CE-angle between 20°-25°) confirmed that there were no differences between patients with a FEAR index >2° and patients with a FEAR index ≤2° in any of the HOOS subscale scores (Figure 13). Hip instability was thus not associated with hip pain, symptoms, function, ADL or QoL among patients with borderline hip dysplasia. The sensitivity-analysis, however, only included 79 patients with borderline hip dysplasia, whereas only 13 patients had a FEAR index >2°, and the analysis thus may lack power. The exact estimates with 95% CI are found in Table 3 in Paper III (appendix Paper III).

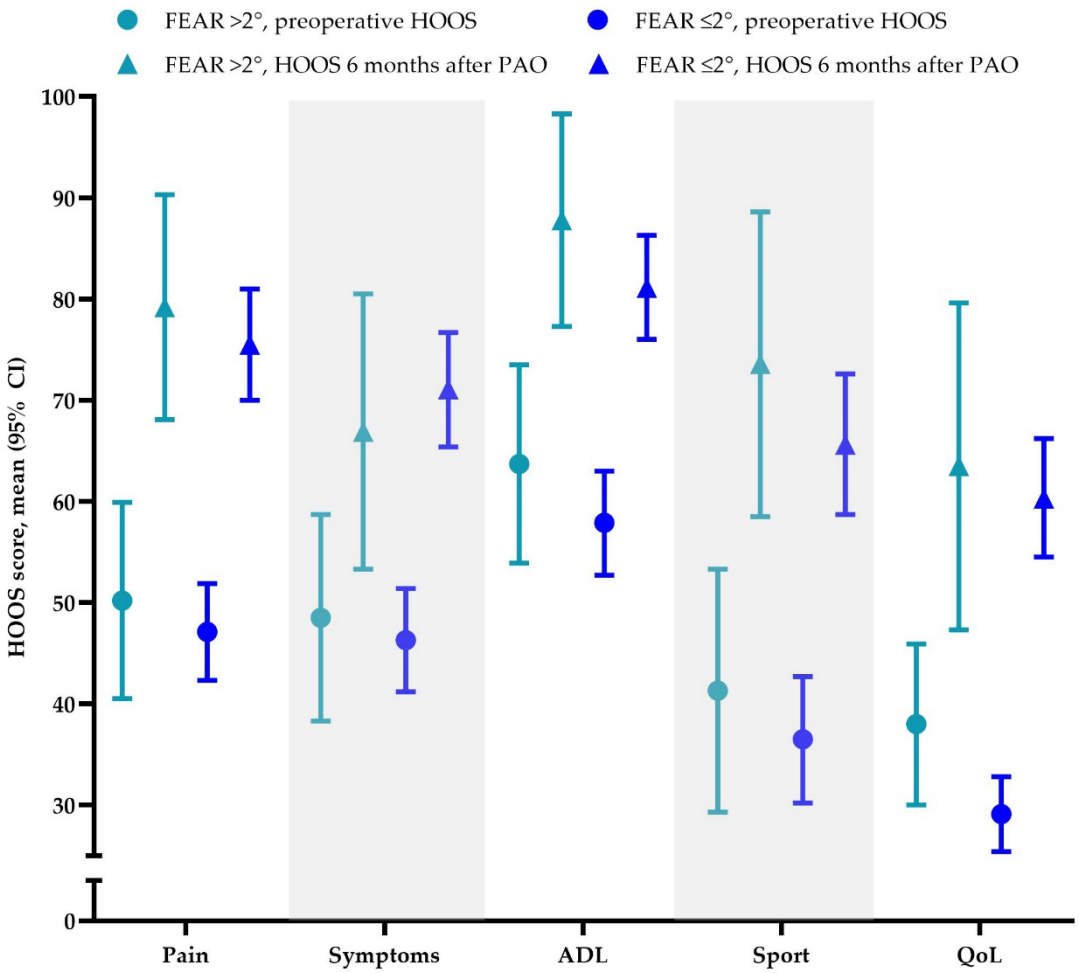

Figure 13. *The HOOS scores before and 6 months after PAO for patients with a preoperative FEAR index >2° (n = 13) and patients with a preoperative FEAR index ≤2° (n = 66), among patients with a preoperative CE-angle of 20°-25° (n = 79). ADL: activities of daily living. HOOS: Hip disability and Osteoarthritis Outcome Scale. PAO: periacetabular osteotomy. QoL: quality of life. 95% CI: 95% confidence interval. The figure presents the data in Table 3 in Paper III.*

Reliability

The ICC scores ranged from 0.80 to 0.90 for the AI-angle, the CE-angle, the FEAR index and the femoral neck-shaft angle, and the agreement between the orthopaedic surgeon and the radiologist was thus considered to be good, however, some disagreements between the raters were found (Table 12). The ICC for the AI-angle and CE-angle was very close to being excellent, defined as an ICC >0.90. In addition, Cohen's Kappa coefficient was 0.42 (95% CI: 0.12;0.71) for Shenton's line before PAO, and there was thus moderate agreement between the two raters. Postoperatively, the Cohen's Kappa coefficient for Shenton's line was 0.32 (95% CI: -0.17;0.81), and there was thus fair agreement between the orthopaedic surgeon and the radiologist.

Table 12. The inter-rater reliability for the four continuous radiographic measurements indicative of hip instability between the orthopaedic surgeon and the radiologist measured both preoperative (before PAO) and postoperative (6 months after PAO). The table represents Table 4 in Paper III [61].

	N	Preoperative	Agreement	N	Postoperative	Agreement
AI-angle	165	0.90 (0.87;0.92)	Good	165	0.85 (0.80;0.89)	Good
CE-angle	165	0.90 (0.87;0.93)	Good	165	0.86 (0.81;0.89)	Good
FEAR index	165	0.82 (0.76;0.86)	Good	162	0.80 (0.74;0.85)	Good
Femoral neck-shaft angle	165	0.88 (0.84;0.92)	Good			

Results are presented as intraclass coefficients with 95% confidence. AI-angle: acetabular index of Tönnis. CE-angle: centre-edge angle of Wiberg. FEAR index: femoral-epiphyseal acetabular roof index. N: number of patients.

Paper IV – The sports participation study

Between the 1st of January 1998 and the 31st of December 2023, 3120 procedures (hips that had undergone PAO) were registered in the Aarhus PAO-database. For the sports participation study, all second surgeries (722 procedures) and patients who had not answered the sports participation question at any time (449 patients) were excluded. Another 58 patients were excluded based on the exclusion criteria listed in Table 3. Figure 1 in Paper IV (appendix Paper IV) shows the flow chart for the total cohort.

The mean age at the time of PAO for the total cohort was 30 years (SD 10.1), and 84% were women (Table 6 and Table 13). The mean age was 22.8 years (SD 9.3) in the sub-group of elite-level athletes, and 71% were women, whereas the mean age was 28.9 years (SD 9.4) at the time of PAO and 86% were women in the sub-group of recreational-level athletes (Table 13). For those who were not sports-active before PAO, the mean age at the time of PAO was 28.3 years (SD 9.3), and 86% were women.

The responders (patients who answered the question about sports participation) did not differ from the non-responders (patients who had not answered the question about sports participation) regarding age, sex, radiographic measurements, educational level, self-reported body measurements or the five subscales of HOOS. The patient characteristics for responders and non-responders are found in Table A2 in Paper IV (appendix Paper IV).

Table 13. Demographic and preoperative data of all included patients (total cohort), as well as the subgroups of sports-active patients before PAO (divided into elite-level and recreational-level athletes) and patients who were not sports-active before PAO. The table is the same as Table 1 in Paper IV.

	Total cohort		**Sports-active before PAO**				**Not sports-active before PAO**	
			Elite-level		Recreational-level			
	Result	n	Result	n	Result	n	Result	n
Female	1588 (84)	1891	25 (71)	35	428 (86)	500	552 (86)	642
Age at the time of PAO	30.0 (10.1)	1891	22.8 (9.3)	35	28.9 (9.4)	500	28.3 (9.3)	642
Bilateral PAO	581 (31)	1891	8 (23)	35	123 (25)	500	189 (29)	642
Positive impingement test	1104 (97)	1139	33 (100)	33	428 (96)	446	559 (97)	576
Radiographic measurements								
CE-angle	18.3 (7.7)	1530	19.8 (7.1)	34	19.0 (6.5)	470	19.7 (6.6)	607
AI-angle	14.1 (7.1)	1531	12.3 (6.5)	34	13.6 (6.6)	470	13.0 (6.6)	608
Tönnis grade >0	36 (3)	1158	0 (0)	33	16 (4)	448	15 (3)	577
Level of education		1177		35		500		641
Primary[a]	205 (17)		15 (43)		57 (11)		133 (21)	
Secondary[b]	659 (56)		15 (43)		273 (55)		371 (58)	
Higher[c]	313 (27)		5 (14)		170 (34)		137 (21)	
Self-reported measurements								
Height (cm)	170.9 (7.9)	1177	171.6 (9.0)	35	170.9 (7.9)	499	170.7 (7.8)	642
Weight (kg)	66.8 (10.7)	1171	65.6 (10.8)	35	66.7 (10.4)	495	66.9 (11.0)	640
BMI (kg/m^2)	22.8 (2.9)	1171	22.2 (2.5)	35	22.8 (2.7)	495	22.9 (3.0)	640
HOOS								
Pain	50.5 (18.8)	1164	53.8 (20.2)	34	55.4 (17.0)	495	46.5 (19.3)	633
Symptoms	49.5 (19.7)	1163	52.4 (20.0)	34	53.5 (18.0)	495	46.2 (20.3)	633
ADL	61.7 (21.0)	1163	66.0 (18.9)	34	67.8 (18.4)	495	56.6 (21.7)	633
Sport	41.4 (23.7)	1163	48.5 (25.3)	34	48.2 (22.5)	495	35.7 (23.2)	633
QoL	30.8 (15.9)	1163	37.3 (17.6)	34	35.5 (14.6)	495	26.8 (15.6)	633

All continuous variables are presented as means with standard deviations, while all categorical variables are presented as numbers with percentages. [a]Primary: grade 0-10. [a]Secondary: more than primary school, but no university degree. [c]Higher: obtained university degree. ADL: activity limitations of daily living. AI: acetabular index of Tönnis. BMI: body mass index. CE: centre-edge angle of Wiberg. n: number of responses. PAO: periacetabular osteotomy. QoL: quality of life.

Descriptive results

Sports participation

Before PAO, 45% (95% CI: 43;48) reported that they participated in sports. That increased to 56% (95% CI: 53;59) 6 months after PAO, 60% (95% CI: 57;63) 2 years after PAO, 62% (95% CI: 59;65) 5 years after PAO, 62% (95% CI: 58;66) 10 years after PAO, 52% (95% CI: 45;58) 15 years after PAO and 48% (95% CI: 37;60) 20 years after PAO (Figure 14). Before PAO, 1177 (62%) answered the question about sports participation. The response rate remained around 62% for the entire period but increased to 79% 15 years after PAO (Figure 14) (appendix Paper IV). For the sub-group of (self-)categorised athletes, the number of patients who reported participating in sports ranged from 75%-76% for the first 10 years after PAO (Figure 14).

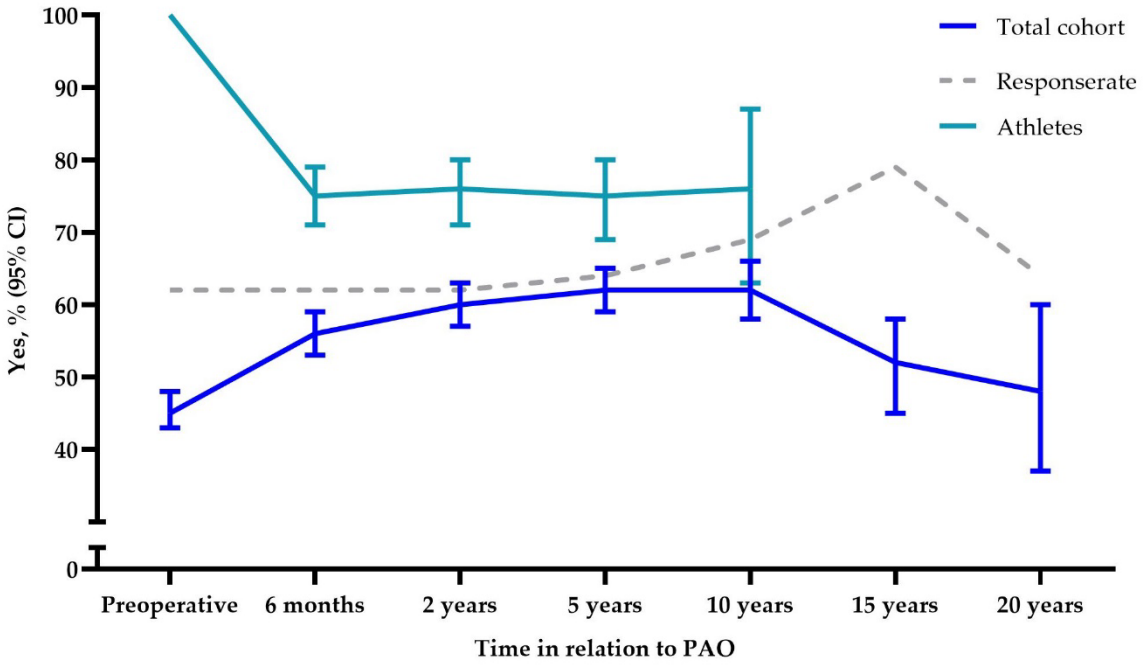

Figure 14. *The proportion of patients (the total cohort) and athletes (patients who participated in sports preoperatively) who participated in sport, defined as replying yes to the question "Are you participating in sports?" alongside the responserate (the percentage of patients who were included at the given timepoint and replied to the question) at each time point, from preoperative to 20 years after periacetabular osteotomy (PAO). Data are presented in percentages with a 95% confidence interval (95% CI) for each time point. The figure combines Figure 2 and data from Table 3, as presented in Paper IV.*

Able to perform preferred sports

Before PAO, 13% (95% CI: 10;16) reported that they were able to perform the sports activity they preferred. That increased to 41% (95% CI: 37;45) 6 months after PAO, 57% (95% CI: 53;61) 2 and 5 years after PAO, 60% (95% CI: 55;66) 10 years after PAO, 63% (95% CI: 53;72) 15 years after PAO and 55% (95% CI: 38;71) 20 years after PAO (Figure 15). All patients who answered yes to the question about sports participation also always responded to the question about their ability to perform their preferred sport (appendix Paper IV). For the sub-group of athletes, the number of patients who reported being able to participate in their preferred sports increased as well during the first 10 years after PAO and exceeded the total cohort 10 years after PAO (Figure 15).

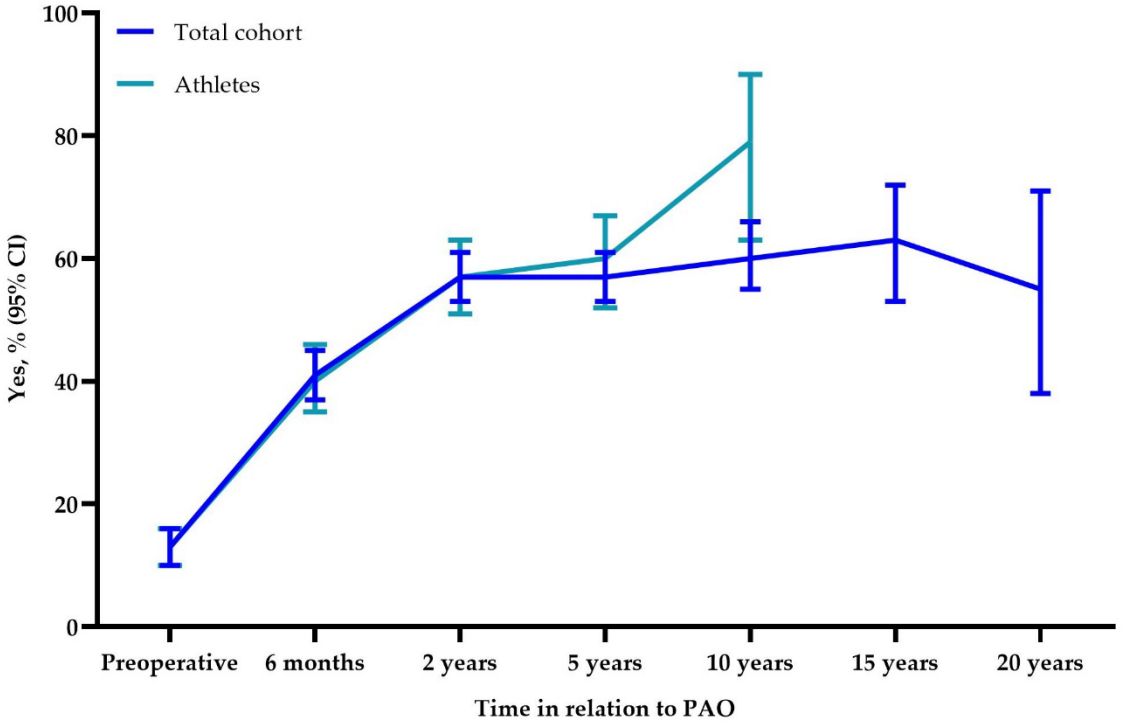

Figure 15. *The proportion of patients (the total cohort) and athletes (patients who participated in sports preoperatively) who reported that they were able to participate in their preferred sports, defined as replying yes to the question "Are you able to participate in the sports you prefer with your present hip function?" at each time point, from preoperative to 20 years after periacetabular osteotomy (PAO). Data are presented in percentages with a 95% confidence interval (95% CI) for each time point. The figure combines Figure 3 and data from Table 3, as presented in Paper IV.*

PAO improved sports performance

Six months after PAO, 56% (95% CI: 52;60) reported that PAO had improved their sports performance. The number remained the same for most of the period, increasing to 71% (95% CI: 62;79) 15 years after PAO (Figure 16). All patients who had answered yes to the question about sports participation also always responded to the question regarding improvements in sports performance following PAO (appendix Paper IV). For the sub-group of athletes, the number of patients who reported that PAO had improved their sports performance was comparable to the total cohort for the first 10 years after PAO (Figure 16).

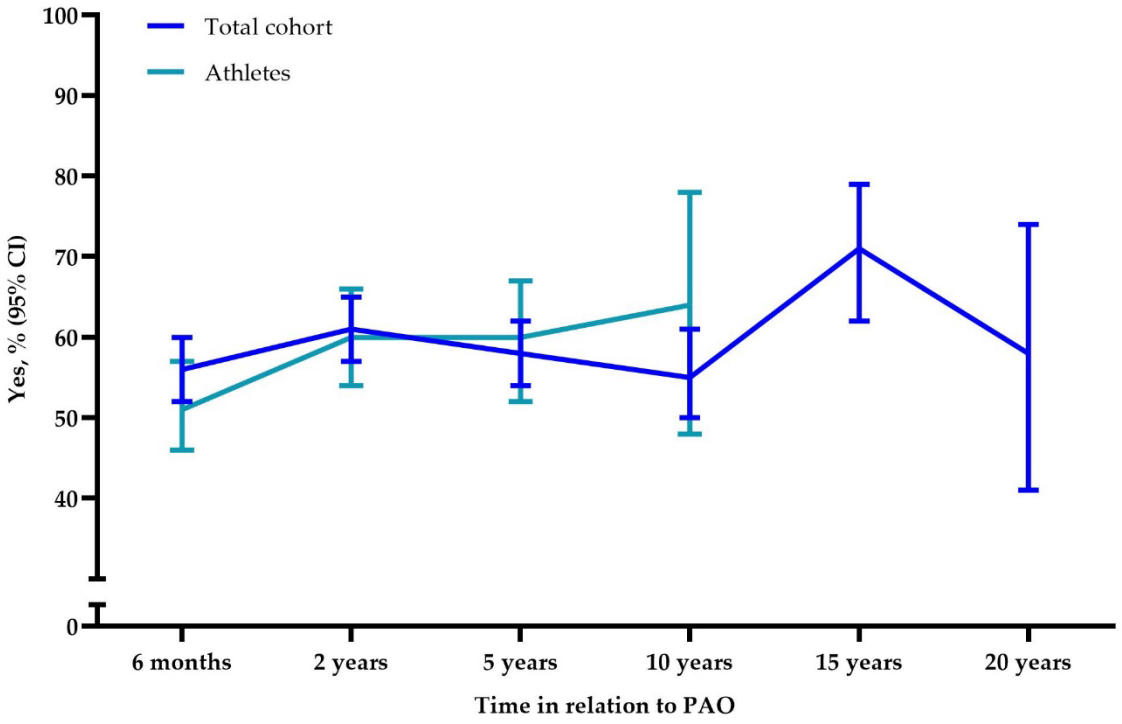

Figure 16. *The proportion of patients (the total cohort) and athletes (patients who participated in sports preoperatively) who reported that periacetabular osteotomy (PAO) had improved their sports performance, defined as replying yes to the question "Has PAO improved your sports performance?" at each time point, from preoperative to 20 years after PAO. Data are presented in percentages with a 95% confidence interval (95% CI) for each time point. The figure combines Figure 3 and data from Table 3, as presented in Paper IV.*

Lack of sports participation

Patients who reported not participating in sports were asked if that was due to a hip problem. Before PAO, 92% (95% CI: 90;94) of the patients who reported not participating in sports reported that this was due to a hip problem. The number decreased to 73% (95% CI: 69;77) 6 months after PAO, 66% (95% CI: 61;70) 2 years after PAO, 51% (95% CI: 45;56) 5 years after PAO, 51% (95% CI: 44;58) 10 years after PAO, 51% (95% CI: 42;61) 15 years after PAO and 32% 95% CI: (18;48) 20 years after PAO (Figure 17). All patients who had answered no to the question about sports participation also always responded to the question regarding the lack of sports participation (appendix Paper IV).

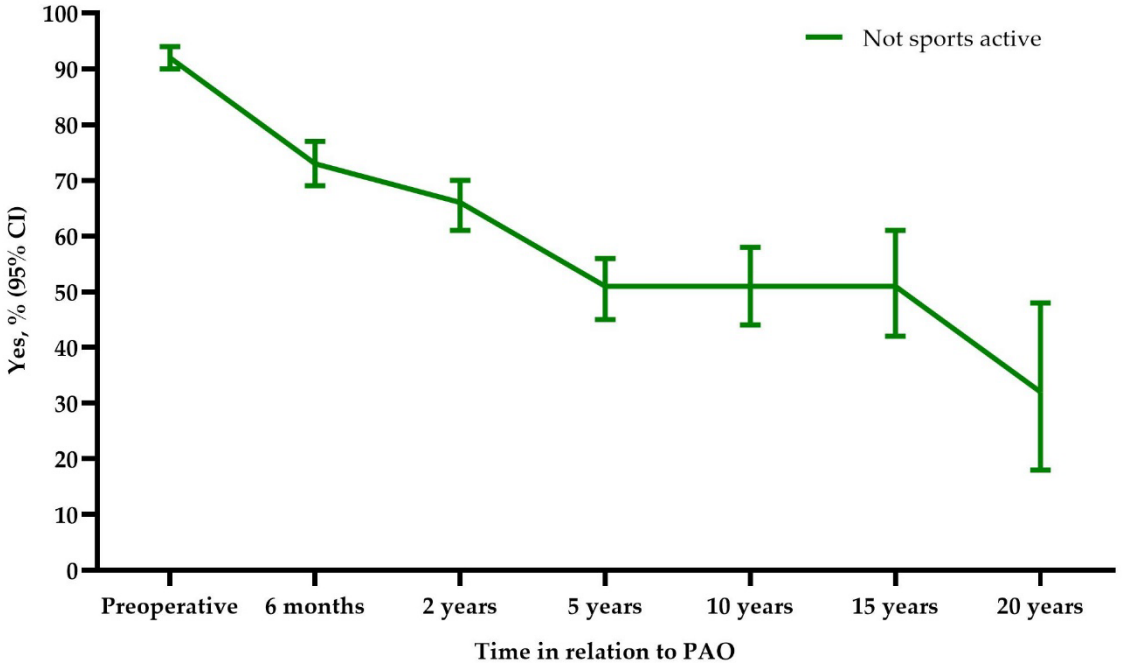

Figure 17. *The proportion of patients (the total cohort) who reported that they did not participate in sports due to a hip problem, defined as replying yes to the question "Are your lack of sports participation due to a hip problem?" at each time point, from preoperative to 20 years after PAO. Data are presented in percentages with a 95% confidence interval (95% CI) for each time point. The figure illustrates the data in Table A3 in Paper IV.*

Type of sports performed

Most patients who participated in sports participated in low-impact sports at all time points (Figure 18). The most frequently reported sport was fitness, meaning exercise in a gym and thus including resistance training, followed by running and cycling, which included road cycling and mountain biking (Table A1 in Paper IV). Therefore, the most commonly reported sports were individual activities that do not require explosive power, unlike sports involving hopping, kicking, or other high-impact movements.

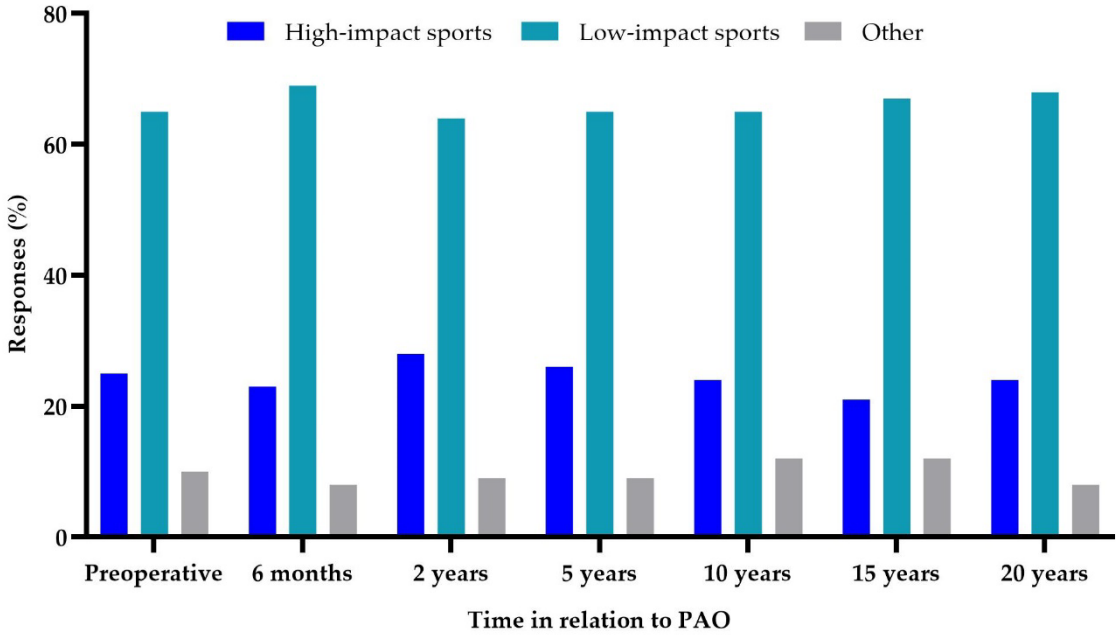

Figure 18. *High-impact, low-impact and other types of sports categorised according to Leopold et al. [101], from preoperative and up to 20 years after periacetabular osteotomy (PAO). All data are presented as percentages (%). The figure is almost identical to Figure A1 in Paper IV.*

Elite-level athletes vs. recreational-level athletes

The 535 athletes (defined as sports-active before PAO) were divided into elite- and recreational-level athletes based on their reply to the question about sports participation level before PAO. No differences were found regarding sports participation, performing preferred sports or improvements after PAO, however, there was a tendency for higher sports participation among elite-level athletes, and more elite-level athletes reported that they were able to perform their preferred sports than recreational-level athletes (Figure 19). At the first two time points (6 months and 2 years after PAO), the number of elite and recreational-level athletes that reported that PAO had improved their sports performance was similar but decreased a lot for the elite-level athletes at the 5-year follow-up point (Figure 19). Only three elite-level athletes had a longer follow-up than 5 years, and data are therefore only presented for the first three time points.

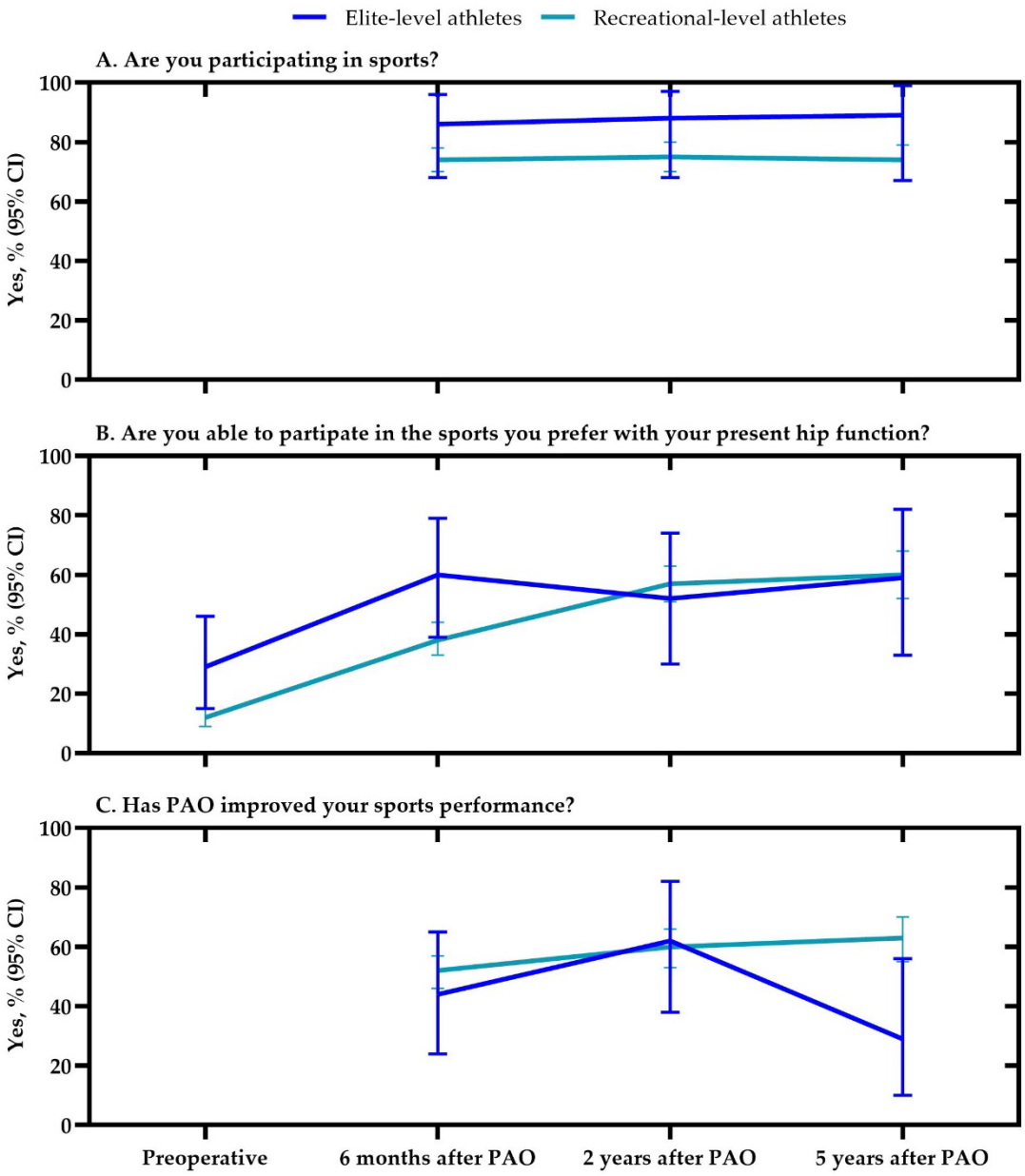

Figure 19. *The patient-reported outcomes related to sports after PAO for athletes who reported participating in sports at either the elite level (elite-level athletes) or recreational level (recreational-level athletes) before PAO. The figure presents the data in Table 3 in Paper IV.*

Prediction analysis

The prediction analysis investigating if specific patient characteristics before PAO could predict sports participation, ability to perform preferred sports and improvements in sports function after PAO revealed that age, sex, BMI, CE-angle and AI-angle were not predictors of any of the three sports outcomes. In contrast, time, being sports-active before PAO, educational level, HOOS pain and HOOS QoL were

associated with at least one of the sports-related outcomes (Table 14). The odds of being able to perform preferred sports increased by 92% (95% CI: 57%;134%) from 6 months to 2 years after PAO and 95% (95% CI: 57%;143%) from 6 months to 5 years after PAO. Time was also a predictor of improvements in sports performance after PAO, where the odds increased by 41% (95% CI: 12%;77%) from 6 months to 2 years after PAO. Being sports-active before PAO increased the odds of participating in sports after PAO by 261% (95% CI: 184%;359%) but was not associated with performing preferred sports or improvements in sports function. Higher education increased the odds of participation in sports by 97% (95% CI: 35%;188%) but lowered the odds of performing preferred sports by 55% (95% CI: 27%;72%). The HOOS pain score was also associated with sports participation with an odds ratio of 1.01 (95% CI: 1.01;1.02) but was not associated with performing preferred sports or improvements in sports function, which were associated with HOOS QoL, with odds ratios of 1.02 (95% CI: 1.01;1.04) and 0.98 (95% CI: 0.97;0.99) respectively.

Table 14. Odds ratios (OR) for predictors of sports participation, performing preferred sports and improvements in sports function, presented with 95% confidence intervals (95% CI) and marked as bold if the Bonferroni corrected p-values were <0.005. The table is the same as Table 2 in Paper IV.

	Sports participation		**Performing preferred sports**		**Improvements in sports function**	
	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Time point						
6 months	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
2 years	1.16 (1.00;1.33)	1.12 (0.94;1.33)	**1.92 (1.57;2.34)**	**2.08 (1.63;2.64)**	1.26 (1.04;1.53)	**1.41 (1.12;1.77)**
5 years	1.21 (1.04;1.42)	1.17 (0.94;1.45)	**1.95 (1.57;2.43)**	**2.25 (1.69;3.01)**	1.17 (0.96;1.44)	1.39 (1.01;1.81)
Sports-active	**4.02 (3.23;5.01)**	**3.61 (2.84;4.59)**	1.02 (0.80;1.31)	0.92 (0.69;1.21)	0.70 (0.54;0.90)	0.83 (0.62;1.12)
Age	1.01 (1.00;1.02)	1.00 (0.99;1.02)	1.00 (0.99;1.01)	0.99 (0.98;1.01)	0.99 (0.98;1.00)	0.99 (0.98;1.01)
Sex						
Woman	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Man	1.11 (0.86;1.43)	1.11 (0.80;1.55)	0.95 (0.71;1.27)	0.71 (0.48;1.06)	0.75 (0.55;1.02)	0.64 (0.43;0.97)
Education						
Primary[a]	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Secondary[b]	**1.63 (1.23;2.16)**	**1.67 (1.21;2.30)**	0.85 (0.60;1.22)	0.79 (0.51;1.24)	0.96 (0.66;1.42)	0.98 (0.62;1.53)
Higher[c]	**2.35 (1.69;3.25)**	**1.97 (1.35;2.88)**	**0.48 (0.33;0.70)**	**0.45 (0.28;0.72)**	1.01 (0.66;1.53)	0.99 (0.61;1.61)
CE-angle	1.00 (0.99;1.01)	1.01 (0.99;1.04)	0.99 (0.98;1.01)	0.99 (0.96;1.02)	1.01 (0.99;1.02)	0.99 (0.96;1.03)
AI-angle	1.00 (0.99;1.02)	1.01 (0.98;1.04)	1.01 (0.99;1.03)	0.99 (0.96;1.02)	0.99 (0.97;1.01)	0.99 (0.95;1.02)
BMI	0.95 (0.91;0.99)	0.94 (0.90;0.99)	1.00 (0.96;1.05)	1.01 (0.96;1.07)	0.97 (0.92;1.02)	0.99 (0.93;1.05)
HOOS pain	**1.02 (1.01;1.03)**	**1.01 (1.01;1.02)**	1.00 (1.00;1.01)	0.99 (0.98;1.00)	0.99 (0.99;1.00)	1.01 (1.00;1.02)
HOOS QoL	**1.02 (1.01;1.02)**	0.99 (0.98;1.00)	**1.02 (1.01;1.03)**	**1.02 (1.01;1.04)**	**0.98 (0.97;0.99)**	**0.98 (0.97;0.99)**

[a]Primary education: grade 0-10. [a]Secondary education: more than primary school, but no university degree. [c]Higher education: obtained a university degree. AI: acetabular index of Tönnis. BMI: body mass index. CE: centre-edge angle of Wiberg. CI: confidence interval. HOOS: The Hip disability and Osteoarthritis Outcome Score 2.0. N: number. OR: odds ratios. PAO: periacetabular osteotomy. Ref: reference group. QoL: quality of life.

Paper V – The validation study

From the Aarhus PAO-database, 2976 entries (hips) from 2290 individuals were identified when data was extracted on the 28th of March 2023. A total of 1832 entries had to be excluded based on the predefined exclusion criteria: missing information about the date of PAO (n=285), PAO performed before 2014 (n=1,253), PAO performed after 2021 (n=151), Legg-Calvé-Perthes disease (n=3), age <15 at the time of PAO (n=16), no Danish Civil Registration number (n=123) and double entry (n=1). Therefore, 1144 entries from 947 patients could be included from the Aarhus PAO-database. From the DNPR, 1194 entries from 999 patients were identified as having undergone PAO due to hip dysplasia in the period 2014-2021. After the exclusion of 44 entries due to the age criteria, 1150 entries from 959 patients from DNPR were included. The patients from the two registries were comparable regarding age at PAO, sex and the number of patients that had undergone surgery in the right and left hip. The flow chart is in Figure 1, and the patient characteristics are in Table 1, both in Paper V (appendix Paper V).

Completeness of registrations

In total, 1178 hips from 967 patients were included, of which 34 (2.9%) were included in DNPR but not in the Aarhus PAO-database and 28 (2.4%) were included in the Aarhus PAO-database but not in DNPR (Figure 20). The 1150 entries from DNPR all had a hospital registration, while 18 of the 1144 entries from the Aarhus PAO-database did not have a hospital registration. From the public hospital (Aarhus University Hospital), 860 (97.3%) entries were registered in both registries, whereas 20 (2.3%) were not registered in the PAO-database, and less than 5 (0.5%) were not registered in DNPR. For the private hospital (Mølholm Private Hospital), 256 (92.1%) were registered in both registries, whereas 14 (5.0%) were not registered in the PAO-database, and 8 (2.9%) were not registered in DNPR.

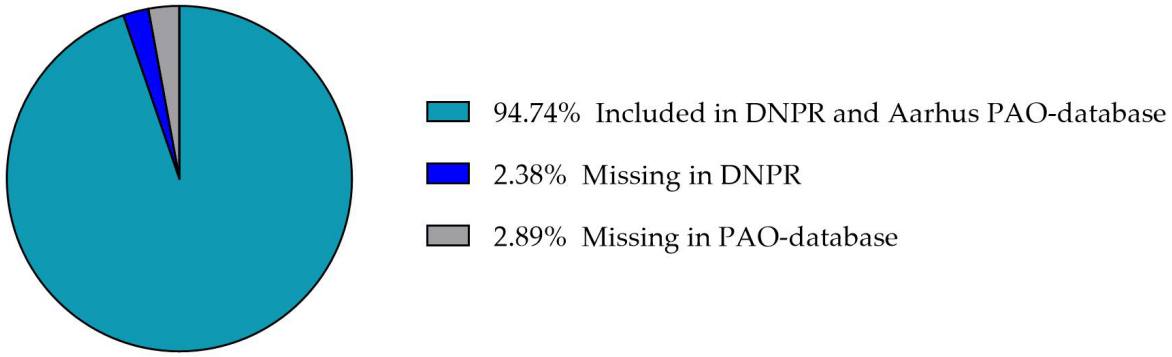

Figure 20. *The number of entries (hips that have been registered to have undergone periacetabular osteotomy (PAO) due to hip dysplasia between 2014-2021) included in both the Danish National Patient Registry (DNPR) and Aarhus PAO-database, as well as the number of entries only included in one registry. The figure presents the data in Table 2 in Paper V.*

The overall degree of completeness was 94.7% (95% CI: 93.3;95.9) and ranged from 91.6% (95% CI: 86.7;95.1) in year 2016 to 96.6% (95% CI: 90.4;99.3) in year 2021 (Figure 21). The sensitivity analysis estimated the completeness of registrations to be 87.1% (95% CI: 85.0;90.0). In the sensitivity analysis, the date of the PAO was added to the analysis, such that a difference in the date of the PAO between the two registries of more than 1 day was considered a discrepancy. The median difference in the date of the PAO for these discrepancies was 3 days (IQR: 2;99), ranging from 2 to 878 days.

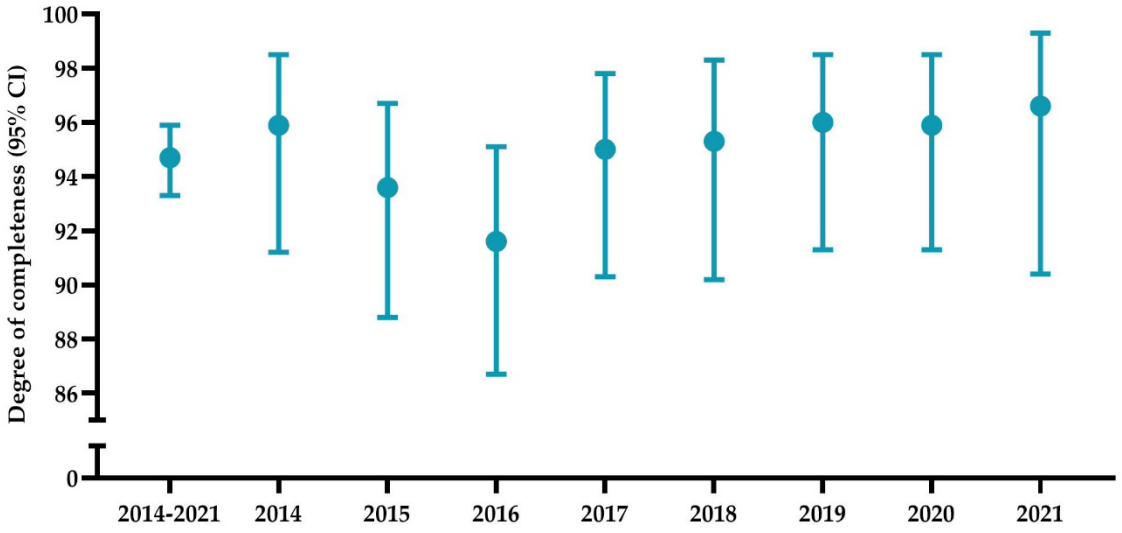

Figure 21. *The degree of registration completeness of the Aarhus-PAO database compared to the Danish National Patient Registry (DNPR) from 2014-2021 presented with a 95% confidence interval (95% CI). PAO: periacetabular osteotomy. The figure presents the data in Table 3 in Paper V.*

Verification using electronic medical records

Most of the 62 entries only registered in one of the registries could be verified as having undergone PAO due to hip dysplasia between 2014 and 2021 by the medical records. The medical records could not confirm the diagnosis or surgery in less than five entries, which, surprisingly, were all registered in DNPR. The PPV for the verification was thus 0.95 (9% CI: 0.82;0.99) for DNPR and 0.97 (95% CI: 0.89;1.00) overall. In addition, the electronic medical records confirmed that all the randomly selected entries had undergone PAO between 2014-2021 due to hip dysplasia. The hospital registered in DNPR matched the hospital registered in the PAO-database for 318 of the 320 patients, and the PPV for the hospital was thus 0.99 (95% CI: 0.98;1.00). The date of PAO varied between the two registries for 67 entries with a median difference of 1 day (IQR: 1;2), ranging from 1- 930 days, and the PPV was thus 0.79 (95% CI: 0.74;0.83) for the date of PAO.

7. Discussion

Key findings

Paper I – The systematic review

Paper I combined the results from 29 studies to assess the harms and benefits following PAO. The risk of a major adverse event following PAO was 4.3% (95% CI: 3.7;4.9), and the risk of a minor adverse event was 14% (95% CI: 13.0;15.1). Based on the patient-reported outcomes, the benefits of PAO were clinically relevant improvements in hip-related pain and function for at least 5 years after PAO. PAO had a low-medium rate of adverse events and improved hip-related pain and function, but the results were based on studies with a serious risk of bias.

Paper II – The cross-sectional study

Baseline test results from the ongoing PreserveHip trial were compared between the legs of 59 patients with hip dysplasia, and the legs considered a candidate for PAO were compared with a group of 39 healthy subjects. Comparing the patients' legs, no clinically relevant differences were found in the single-leg hop test, the Y Balance test or isometric muscle strength. Compared to the healthy subjects' leg, the leg that was considered a candidate for PAO had worse results in the single-leg hop test, with a mean difference of 19.3 cm/m (95% CI: 13.1;25.4), corresponding to a clinically relevant mean difference of 37.4%. For the Y Balance test, the patients had a worse score in both the posteromedial direction, the posterolateral direction and the composite score, which were clinically relevant, with a mean difference of 18.6% (95% CI: 12.6;24.5), 16.9% (95% CI: 10.8;22.9), and 15.2% (95% CI: 10.3;20.1), respectively. The patients had a 14.9 Nm (95% CI: 3.9;26.4) lower isometric hip flexion strength than the healthy subjects, corresponding to a mean difference of 21.2% which is considered clinically relevant. There were no clinically relevant differences in isometric hip abduction or

hip extension strength between the patients and the healthy subjects. Therefore, PAO candidates exhibited clinically relevant physical impairments across several tests.

Paper III – The FEAR index study

The radiographic measurements of hip instability significantly improved from before to 6 months after PAO. The five subscales of HOOS also improved statistically significantly from before to 6 months after PAO at a clinically relevant level for the total cohort. Differentiating the total cohort into stable and unstable hips based on the patients' FEAR index showed the same results, and no differences in the HOOS scores were found between patients with a FEAR index >2° and patients with a FEAR index ≤2° before PAO or 6 months after PAO. There were also no differences in the change scores between the two groups. The assessment of inter-rater reliability between the radiologist and the orthopaedic surgeons revealed that the agreement for the FEAR index was good, with an ICC score of 0.82 (95% CI: 0.76;0.86) before PAO and 0.80 (95% CI: 0.74;0.85) 6 months after PAO. Paper III thus demonstrated significant improvements in hip instability and HOOS, but no association were found between the FEAR index and patient-reported outcomes.

Paper IV – The sports participation study

The rate of patients participating in sports increased from 45% (95% CI: 43;48) before PAO to 56% (95% CI: 53;59) 6 months after PAO and a further 60% (95% CI: 57;63) 2 years after PAO. Being sports-active before PAO, having a higher education or having less pain increased the odds of participating in sports after PAO. The rate of patients being able to participate in their preferred sports increased from 13% (95% CI: 10;16) before PAO to 41% (95% CI: 37;45) 6 months after PAO and a further 57% (95% CI: 55;66) 2 years after PAO. Time and higher QoL were associated with higher odds of being able to participate in preferred sports, while higher education was associated with lower odds of being able to participate in preferred sports. The rate of patients

reporting an improvement in sports function after PAO remained the same for most of the study period despite time being associated with higher odds of improving sports function after PAO. A higher QoL score was also associated with lower odds of improving sports function. Age, sex, BMI, the CE-angle and the AI-angle were not associated with any of the 3 sports outcomes. The sub-analysis of athletes, defined as patients reporting being sports-active before PAO, showed no difference between elite- and recreational-level athletes. However, the athletes were generally more sport-active than the total population. Paper IV, therefore, reports that sports increased after PAO, with various preoperative characteristics influencing sports-related outcomes.

Paper V – The validation study

The validation study investigating the completeness of the Aarhus PAO-database revealed that 1116 of the 1178 registered hips were registered in both registries. Of the 62 hips registered in one registry, 34 hips (2.9%) were only registered in DNPR, while 28 hips (2.4%) were only registered in the Aarhus PAO-database. The overall registration completeness was 94.7% (95% CI: 93.3;95.9), meaning that 94.7% of hips undergoing PAO at Aarhus University Hospital or Mølholm Private Hospital were registered in both the Aarhus PAO-database and DNPR. The patients' electronic medical records verified the diagnosis and PAO procedure for all randomly selected hips. For the 62 hips with a discrepancy, fewer than five hips from DNPR could not be verified using the electronic medical records, as these hips had been diagnosed with a different condition or had undergone a different surgical procedure.

Results in context of existing evidence

Paper I – The systematic review

Harms

Besides Paper I, three other systematic reviews have reported on adverse events following PAO and found rates of adverse events of 9.8% based on five studies, 14.1% based on 47 studies and 23.5% based on 24 studies, respectively [48]. The adverse event rates were thus consistent with those found in Paper I (4.3% for a major adverse event and 14.0% minor adverse event) since the adverse event rates reported in the three systematic reviews combined major, minor, and other adverse events. The most frequently reported adverse events were neuropathy and other nerve damage [135, 136], which was also the case for the studies included in Paper I [47]. The differences in the number of included studies were explained by different inclusion and exclusion criteria as a consequence of different aims. Furthermore, none of the three systematic reviews had an inclusion criterion regarding patient-reported outcome measures, as in Paper I. One of the systematic reviews compared overall and major adverse events following PAO to THA in four studies [137]. Of these four studies, two were included in the meta-analysis in Paper I, which compared adverse events between PAO and THA, while the other two were not included in Paper I as they did not include a patient-reported outcome measure.

Benefits

Patient-reported outcomes before and after surgery were combined across the 26 included studies. In the systematic review by O'Brien et al., changes in patient-reported outcomes from before to after PAO were only compared between the nine studies that had reported a change [38]. The meta-analysis of these nine studies revealed that the patients' pain scores were improved for up to 7 years after PAO [38]. Despite the substantial difference in the included studies, the changes were comparable to those in Paper I.

Paper II – The cross-sectional study

The single-leg hop test

In a feasibility study, Jacobsen et al. investigated a 6-month exercise and patient education intervention at Aarhus University Hospital among patients with hip dysplasia who were either not eligible for PAO, as defined in Table 2 or had declined to have a PAO. Hip function was evaluated using the single-leg hop test, and hip balance was assessed using the Y Balance test [43]. Before the intervention, the patients had a normalised median single-leg hop test at 37 cm/m (IQR: 30;44), corresponding to a mean test result of 37 cm/m (95% CI: 33.3;40.7), which increased to 52 cm/m (IQR: 45;58), corresponding to a mean test result of 52 cm/m (95% CI: 48.1;55.9), after the 6 months of intervention [43]. In comparison, the normalised mean single-leg hop test for the patients in Paper II was 41.9 cm/m (95% CI: 37.7;46.1) for the index leg. The patients in the study by Jacobsen et al., therefore, had a worse hop test before the intervention, which was most likely a result of the differences in the populations due to the contraindications for PAO. Despite the improvement, the patients in the study by Jacobsen et al. did not reach the level of the healthy subjects in Paper II, as the normalised mean for the healthy subjects was 61.2 cm/m (95% CI: 57.0;65.4).

In addition, Mortensen et al. investigated the feasibility of an 8-week exercise intervention among 17 Danish patients with hip dysplasia using the single-leg hop test in both the index and contralateral leg before and after the intervention [41]. The index leg improved significantly from 93.7 cm (95% CI: 77.7;109.8) before the intervention to 102 cm (95% CI: 88.3;115.7) after the intervention, and the contralateral leg improved significantly from 91.4 cm (95% CI: 73.6;109.1) to 100.7 cm (95% CI: 84.1;117.3) after the intervention [41]. The results were not normalised to height, but the absolute distances were higher for both the index and contralateral leg compared to patients in Paper II. The difference might be explained by Mortensen et al. allowing the patients to have their arms free, while the arms had to be held behind the back in the study by Jacobsen et al. and Paper II. Ageberg et al. found poor agreement between the two procedures and concluded that they should not be compared, as having the arm behind the back

was more demanding than having the arms free but also more sensitive in detecting deficiencies in muscle function among patients with lower limb injuries [103]. After the 8-week exercise intervention, the patients had single-leg hop scores that were comparable to the results of healthy subjects reported in Paper II.

O'Brien et al. also used the single-leg hop test, where patients had their arms behind their backs, to assess hip function among 101 symptomatic football players, divided into those with hip dysplasia defined as a CE-angle >25° (n=50) and those without hip dysplasia [39]. The mean absolute hop distance was 135 cm (95% CI: 128;141) for the athletes with hip dysplasia and a comparable 136 cm (95% CI: 130;142) for the athletes without hip dysplasia [39]. The hop distance was thus better than the patients and the healthy volunteers included in Paper II. This was most likely due to differences in sports participation. Despite being non-professionals, the athletes competed at a sub-elite level and probably had greater muscle strength than the healthy controls and, thereby, better hip function according to the associations found between the single-leg hop test and muscle strength in Paper II. In addition, there were more men in the cohort of football players, and they were younger than the patients and healthy subjects included in Paper II.

The Y Balance test

The Y Balance test is a relatively new measurement of balance and hip function, developed from the star excursion test in 2009 [104]. Only the previously mentioned feasibility study by Jacobsen et al. [43] has previously used the Y Balance test among patients with hip dysplasia. The two groups of dysplasia patients had comparable scores in the posteromedial and posterolateral test directions, but the patients included in the study by Jacobsen et al. had a significantly better score in the anterior direction before the 6-month exercise intervention than patients in Paper II. After the exercise intervention, patients in the study by Jacobsen et al. improved to a level comparable to healthy subjects in Paper II (Figure 22). Foldager et al. investigated the reliability of the Y Balance test in a group of healthy subjects, using similar inclusion criteria as per

Paper II [108]. The normalised mean reaches were significantly lower among the healthy subjects in the study by Foldager et al. than the healthy subjects in Paper II (Figure 22), indicating that the healthy subjects in Paper II had a better hip function than the healthy subjects in the study by Foldager et al. [108]. The differences could be explained by differences in the amount of included women, as there were fewer women and a larger variation in age in the study by Foldager et al. [108] (42% women) than in Paper II (74% women).

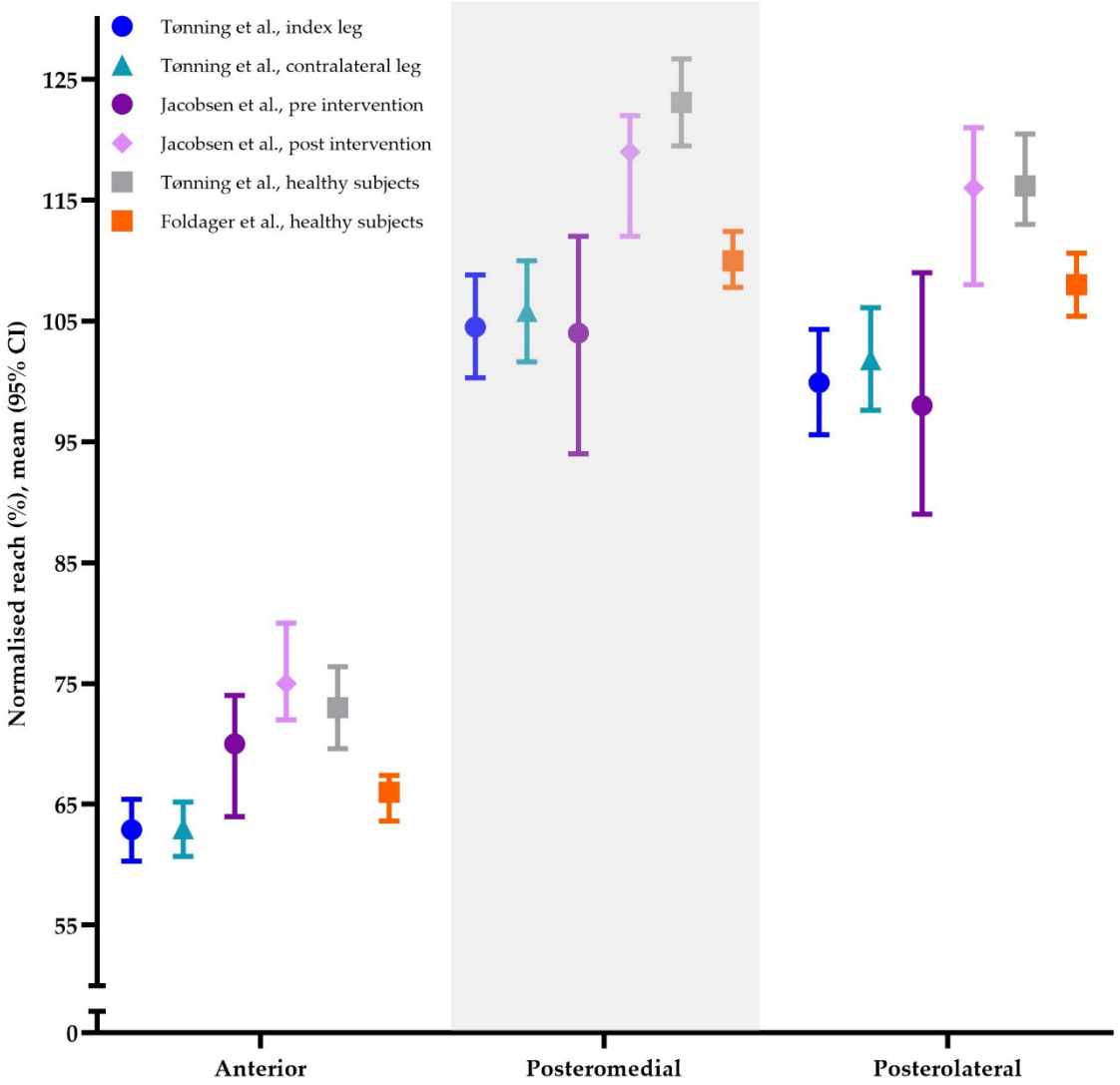

Figure 22. *Y Balance Test results from paper II compared with the results from the studies by Jacobsen et al. [43] and Foldager et al. [108]. Normalised mean scores in the anterior, posteromedial and posterolateral directions are marked with a circle for the index legs, a triangle for the contralateral legs, and a square for healthy subjects, alongside the 95% confidence interval (95% CI).*

The isometric muscle strength test

The previously mentioned systematic review by O'Brien et al. from 2022 investigating physical impairments in patients with hip dysplasia undergoing PAO found that hip abduction and hip flexion strength did not change from before to after PAO [57]. The conclusion was based on 3 studies that measured muscle strength using isokinetic motor-driven dynamometers. Mortensen et al. also measured isometric hip flexion and extension strength in the index and contralateral leg before and after the intervention in the above-mentioned feasibility study [41]. There were no differences between the legs nor any differences in hip extension following the exercise program. The results for hip extension were comparable to those of both the patients and the healthy subjects in Paper II. Isometric hip flexion was increased significantly following the 8 weeks of exercise intervention for the contralateral leg but not for the index leg [41]. The results for hip flexion were significantly higher for the patients in the study by Mortensen et al. than the patients and the healthy subjects in Paper II (Figure 23). The difference in hip flexion was surprising, as the inclusion criteria for the two groups of hip dysplasia patients were similar. In addition, the groups had comparable baseline characteristics regarding BMI, sex, and age, and they were tested in the exact location using the same equipment.

De La Roche et al. compared hip flexion and abduction strength between 13 patients who had received pelvis surgery before PAO and 13 patients who had not received pelvic surgery before PAO [138]. To account for multiple comparisons, De La Roche et al. used a Bonferroni corrected p-value of 0.013 and concluded that there were no differences in the change scores between the groups from before to 6 months and 1 year after PAO [138]. Isometric hip abduction was comparable to the patients and healthy volunteers in Paper II, while isometric hip flexion seemed higher for the group that had not received previous pelvis surgery than the index and contralateral leg for patients in Paper II (Figure 23). The difference could be explained by the patients in the study by De La Roche et al. being younger, with a mean age of 16.3 years (ranging

from 11.5-25.1 years), compared to 27.5 years (ranging from 18-38 years) among patients in Paper II.

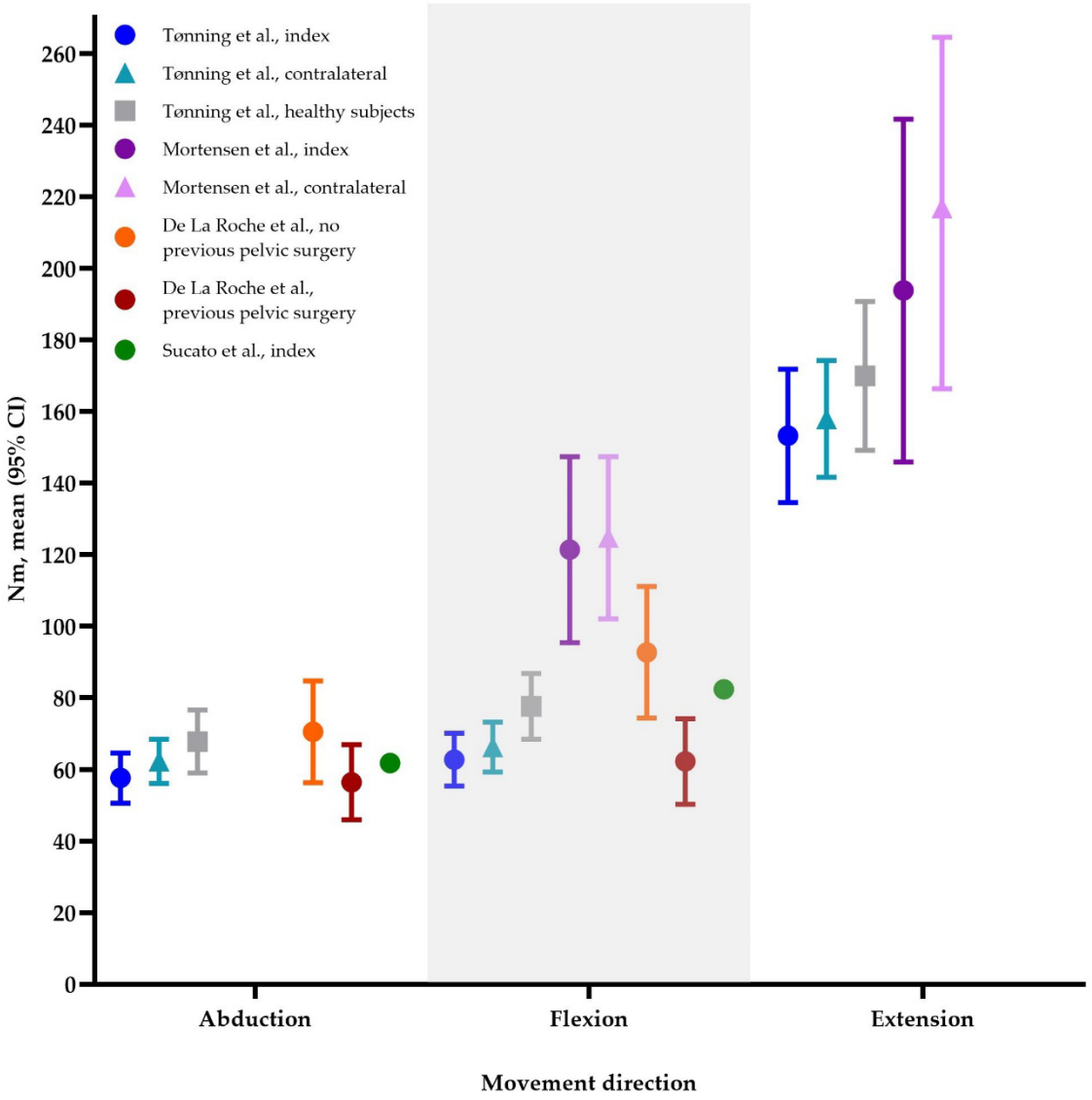

***Figure 23**. Hip muscle strength results from Paper II compared with the results from the studies by Mortensen et al. [41], De La Roche et al. [138] and Sucato et al. [45]. Mean hip abduction, flexion and extension muscle strength are marked with a circle for the index legs, a triangle for the contralateral legs, and a square for healthy subjects, alongside the 95% confidence interval (95% CI).*

The last study (Sucato et al.) that assessed isokinetic muscle strength in patients with hip dysplasia aimed at investigating the effect of PAO from before surgery to one year after surgery among 23 patients with a mean age of 16.2 years (SD 3.5) at the time of PAO [45]. Sucato et al. stated that isokinetic hip abduction decreased from 62 Nm/kg before PAO to 58 Nm/kg 6 months after PAO and improved to 64 Nm/kg 1 year after

PAO. Isokinetic hip flexion decreased from 82.4 Nm/kg to 57.7 Nm/kg 6 months after PAO and improved to 69.0 Nm/kg 1 year after PAO [45]. No variations or confidence intervals were published, and the results should therefore be interpreted with caution. As seen in Figure 23, the baseline isokinetic hip abduction was comparable to the isometric hip abduction found among the patients with hip dysplasia in Paper II. In contrast, isokinetic hip flexion was higher than the isometric hip flexion found among the patients with hip dysplasia in Paper II.

The studies mentioned above all used motor-driven dynamometers to measure isokinetic muscle strength, which is the golden standard for assessing muscle strength. However, these dynamometers are expensive, and the measurement process is time-consuming. Other studies have thus measured hip muscle strength in patients with hip dysplasia using handheld isokinetic dynamometers [43, 139-141], which is an appropriate method to measure muscle strength with good to excellent intra and inter-rater reliability [141], despite not being the golden standard. In addition, handheld dynamometers are likely more straightforward to implement in clinical practice compared to motor-driven dynamometers [141].

Paper III – The FEAR index study

Reliability

Despite being a relatively new radiographic measurement, a recent systematic review from 2023 found 11 studies on the FEAR index using the search databases EMBASE, MEDLINE and PubMed [74]. Of the 11 studies, five included patients with hip dysplasia, four included patients with FAIS, and two included patients with hip dysplasia and patients with FAIS. The inter-rater reliability of the FEAR index was reported in eight studies [74]. The ICC scores ranged from 0.78 to 1.00 across the eight studies, meaning a good to an excellent agreement using the Koo and Li categorisation [120]. The inter-rater reliability found in Paper III thus corresponds to the reliability found in similar studies. The FEAR index was measured by orthopaedic surgeons,

research assistants, a medical student and a radiologist, indicating that the level of experience did not influence the reliability [74]. Paper III was the only study comparing the radiographic measurements between an orthopaedic surgeon and a radiologist.

Patient-reported outcomes

Besides Paper III, three other studies have correlated the FEAR index with patient-reported outcome measures. Marland et al. included 249 female patients with hip dysplasia (defined as a CE-angle ≤25°) who had undergone hip arthroscopy and found a statistically significant lower iHOT-12 score 2-4 years after hip arthroscopy among patients with a preoperative FEAR index >0° compared to patients with a preoperative FEAR index ≤0° [142]. In addition, the patients with a FEAR index >0° were less likely to reach an acceptable symptom state, defined as having a Patient Acceptable Symptom State of ≥75 points 2-4 years after hip arthroscopy (p=0.001) [142]. The iHOT-12 score was also assessed before surgery, and the differences from before to 2-4 years after hip arthroscopy were clinically relevant for both groups, however, the difference between the change score for patients with a FEAR index >0° and the change score for patients with a FEAR index ≤0° was not statistically significant, nor clinically relevant [142]. Thus, the results were consistent with those in Paper III despite using a cutoff on the FEAR index of 0°, whereas the cutoff in Paper III was 2°.

Wong et al. found a statistically significant change among 140 patients with FAIS who underwent hip arthroscopy, measured with the Hip Outcome Score and the modified Harris Hip Score, before and 2 years after hip arthroscopy [143]. There were no differences in the change between patients with a FEAR index ≥2° and patients with a FEAR index <2°. There were also no differences in the number of patients that achieved an MCID between the two FEAR index groups [143]. The results were thus consistent with those found in Paper III despite the different orthopaedic patient groups.

Zimmerer et al. found a statistically significant and clinically relevant change from before to after hip arthroscopy for 36 patients with FAIS on the iHOT-12 (mean follow-

up of 43.8 months) [144]. The patients were divided into four clusters based on the FEAR index and the anterior and posterior wall indexes. Cluster 1 (eight patients with a preoperative FEAR index >2° and an anterior wall index of <0.35), Cluster 2 (seven patients with a preoperative FEAR index <2° and an anterior wall index of <0.35) and Cluster 3 (six patients with a preoperative FEAR index >2° and a normal anterior and posterior wall indexes) all had a clinically relevant improvement on iHOT-12 ranging from 30-64 points on the iHOT-12 score [144]. Cluster 4 (15 patients with a preoperative FEAR index <2° and a posterior wall index of <0.85) improved by 10 points on iHOT-12, which was neither clinically relevant nor statistically significant. The results by Zimmerer et al. indicate that the FEAR index, in combination with the anterior and posterior wall indexes, could be a valuable tool to predict which patients with FAIS would benefit most from hip arthroscopy. However, the very few patients in the four clusters introduce some uncertainty.

Based on Paper III and the studies by Marland et al., Wong et al., and Zimmerer et al., the FEAR index alone cannot predict patient-reported outcomes among patients with hip dysplasia or FAIS undergoing surgery.

Paper IV – The sports participation study

Descriptive sports results

The increase in patients participating in sports from preoperative to 2 years after PAO has also been shown by Novais et al., who investigated the number of patients returning to sport using the University of California Los Angeles Activity Scale (Figure 24) [132]. Novais et al. included 51 patients with hip dysplasia who had undergone PAO and defined being sport-active as equal to a score of eight or higher on the University of California Los Angeles Activity Scale. The number of patients participating in sports increased from 39% preoperative to 61% 2 years after PAO and were thus comparable to the results found in Paper IV. On the contrary, Leopold et al. reported that 38% of 111 patients with hip dysplasia who underwent PAO reported being sports-active 6

months after PAO, which only increased to 42% >6 months after PAO [101]. The marked difference between the findings of Paper IV and the study by Leopold et al. was the number of included patients, with almost 10 times more patients in Paper IV. In addition, a slight difference was found in BMI, as the patients in Paper IV had a mean self-reported BMI of 22.8 kg/m² (SD 2.9) and the patients in the study by Leopold et al. had a mean BMI of 24.3 kg/m² (SD 4.7). There were no differences in surgical indications, age or sex distribution between the two studies.

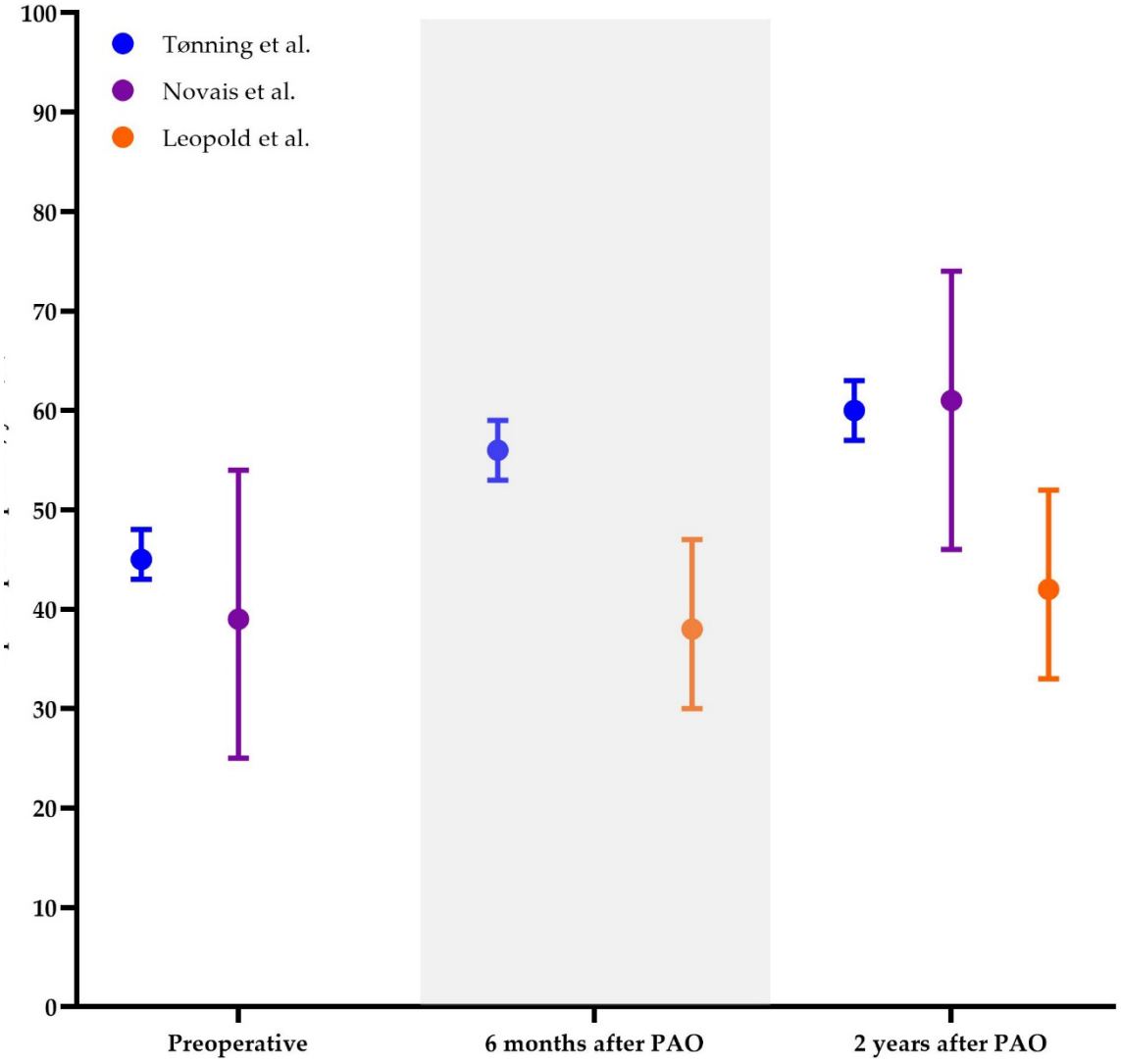

Figure 24. *The proportion and 95% confidence interval (95% CI) of patients reporting being sports-active before and 2 years after periacetabular osteotomy (PAO) from Paper IV compared to the results from the studies by Novais et al.* [132] *and Leopold et al.* [101].

Leopold et al. also asked if the PAO had improved their sports ability, and 58.1% reported that PAO had improved their sports ability, while 18.8% reported that PAO had decreased their sports ability, and 23.1% reported that PAO had not affected their sports ability, at a mean follow-up of 63 months (SD 10) after PAO [101]. The sports ability results were thus comparable to the improvement in sports performance results reported in Paper IV, where 58% (95% CI: 54;62) reported that PAO had improved their sports performance 5 years after PAO.

Prediction analysis

Novais et al. found that younger age and higher preoperative activity levels were associated with higher physical activity levels 1 and 2 years after PAO among 51 patients with hip dysplasia [132]. In addition, Novais et al. found that age, sex, BMI, radiographic measurements, adverse events and self-reported pain, measured with the pain subscale on WOMAC, were not associated with physical activity level 1 or 2 years after PAO [132]. In Paper IV, participating in sports before PAO, low education and low pain were associated with sports participation after PAO, while self-reported BMI, radiographic measurements and HOOS QoL were not. Contrasting to Paper IV, Novais et al. did not include education in their prediction model, and the pain level measured with the WOMAC approached significance (p-value = 0.050). The difference likely results from differences in sample size, with Paper IV being based on a patient group more than 30 times larger than Novais et al.

Type of sports

The proportion of patients participating in low-impact sports was consistently more than double that of patients participating in high-impact sports at all time points, remaining stable throughout the 20-year follow-up period (ranging from 64%-69%). The finding contrasts with the results by Leopold et al., who found an increase in low-impact sports participation and a decrease in high-impact sports participation [101]. As previously suggested, the difference is most likely due to differences in sample size. Heyworth et al. also found that individual sports were more common than team sports

among 41 elite-level athletes [145], suggesting that patients with hip dysplasia may avoid sports requiring explosive power, favouring low-impact sports.

Elite-level athletes

Of the 535 patients who reported being sports-active before PAO, 35 reported participating in sports at an elite level. Of the elite-level athletes, 86% (95% CI: 68;96) participated in sports 6 months after PAO and 89% (95% CI: 67;99) 5 years after PAO. Heyworth et al. reported that 80% (95% CI: 66;91) of 46 hips from 41 elite-level athletes were participating in sports at an average of 9 months after PAO (95% CI: 7;11) [145]. Bogunovic et al. reported that 71% (95% CI: 54;85) of 35 patients maintained or increased their activity level at an average of 33 months (ranging from 18-59 months) after PAO [146]. The results are thus comparable, but the small sample of elite-level athletes in the three studies introduces considerable uncertainty.

Paper V – The validation study

The registration completeness of PAO due to hip dysplasia in the Aarhus PAO-database was validated using DNPR. The registration completeness was 94.7% (95% CI: 93.3;95.9). Two other studies have assessed the registration completeness by comparing the registrations in DNPR to 2 national Danish registries, the Danish Hip Arthroplasty Register [147] and the Danish Knee Ligament Reconstruction Register [148]. Pedersen et al. estimated the registration completeness of primary THA found in the Danish Hip Arthroplasty Register to be 94.1% (95% CI: 93.9;94.4) [147]. The Danish Hip Arthroplasty collects data on THA from all 48 orthopaedic departments in Denmark located in 44 public and four private hospitals. Despite the large differences in sites and patients and the fact that Pedersen et al. did not include private hospitals in the assessment of the Danish Hip Arthroplasty, the registration completeness was comparable, and both were very high. Rahr-Wagner et al. estimated the registration completeness of anterior cruciate ligament reconstructions in the Danish Knee Ligament Reconstruction Register to be 78.5% (95% CI: 77.9;79.1) [148]. The difference

could be a result of registration experience, as Rahr-Wagner included all anterior cruciate ligament reconstructions registered since the registry was established, thus including the start-up period where the orthopaedic surgeons were not familiar with the registration task, while the first 4 years of registration in the Aarhus PAO-database was excluded in Paper V.

Mechanism of change – behavioural and functional factors

Sports participation and hip function

Throughout the 20-year follow-up period in Paper IV, low-impact sports were more frequently performed than high-impact sports and individual sports that do not require explosive power were the most reported. Patients with hip dysplasia may avoid team sports and sports requiring explosive power, muscle strength and good hip function. The significant difference observed in the single-leg hop test between patients with hip dysplasia and healthy subjects in Paper II highlights the reduced hip function in these patients. This impairment likely contributes to lower participation in high-impact sports both before and after PAO. O'Brien et al. found no differences in muscle strength or hip function among 50 sub-elite football players with hip dysplasia (defined as having a CE-angle <25° and hip/groin pain) and 51 sub-elite football players without hip dysplasia (defined as having a CE-angle 25°-40° and no hip/groin pain) [39]. The authors suggest that participation in football promotes a high level of hip function and muscle strength and that physical activity may influence hip function more than the acetabular morphology or pain level among people with hip dysplasia [39]. In addition, the authors speculate that reduced hip function may become evident when physical activity is reduced [39]. For some patients, adverse events following PAO may further prevent participation in high-impact sports. Other factors not investigated in this thesis, such as fear of injury, exacerbation of symptoms or behavioural changes due to inactivity following surgery, may also contribute to avoiding high-impact sports.

Patient-reported outcomes and hip function

This thesis did not investigate the possible association between hip function and patient-reported outcomes. However, Alrashdi et al. found that lower hip muscle strength before PAO was not associated with HOOS pain 6 months after PAO, despite a correlation between lower hip muscle strength 6 months after PAO and HOOS pain 6 months after PAO [149]. Additionally, O'Brien et al. found a concave relationship between eccentric hip adduction and the sport subscale on HAGOS [139]. However, there was no association between eccentric hip adduction and the sport subscale on iHOT [139]. Hip abduction, flexion and extension strength were not associated with the two patient-reported outcomes. A linear relationship was found between hip function measured with the on-leg-rise test and the iHOT sport subscale, however, the single-leg hop and the side bridge tests were not associated with the sports subscales on the iHOT score or HAGOS [139]. Therefore, whether the patients' physical function is associated with their experiences expressed through the patient-reported outcome remains unknown.

Radiographic measurements and patient-reported outcomes

No differences were found in the HOOS subscale scores between patients with hip dysplasia and a FEAR index >2° (indicative of hip instability) and patients with hip dysplasia and a FEAR index ≤2° (not indicative of hip instability), despite a significant and clinically relevant improvement in both groups [61]. This suggests that neither microinstability nor the FEAR index is not associated with patient-reported outcomes in patients with hip dysplasia. Birch et al. found that the CE- and AI-angles were not associated with QoL measured with the Short Form Health Survey 36 questionnaire among patients with hip dysplasia [35], which suggests that the radiographic measurements do not correlate with the patients' experiences. Treatment decisions should thus be based on both the radiographic parameters, the clinical examination and the patients' experiences [150].

Methodological considerations

Paper I – The systematic review

The systematic review did not follow the usual strict methods. Instead, the search strategy and screening process focused on patient-reported outcomes and physical impairments rather than adverse events. The idea for a third review came from our desire to investigate harms and benefits in a systematic review based on studies that had reported both. Instead of doing the systematic search again, we used the studies included in the previous systematic review on patient-reported outcomes, and then took a step back and excluded studies that did not report or mentioned harms. Reporting both harms and benefits comprehensively evaluates PAO, highlighting effectiveness and safety. On the contrary, excluding studies without a patient-reported outcome measure probably influenced the rates of adverse events. If studies had not been excluded due to missing or incorrect patient-reported outcome measures, the estimate of the adverse events rates and the meta-analysis would have been more extensive due to more data.

Adverse events were categorised according to Biedermann et al. However, 10 studies used a modified Clavien-Dindo score to classify adverse events [151, 152]. In the modified Clavien-Dindo Classification system, an adverse event is given a grade ranging from 1-5 ("no treatment required" to "death") depending on the severity of the adverse event [152]. The modified Clavien-Dindo score has the benefit of being widely recognised and used in various surgical procedures, not only limited to studies on PAO procedures and has been validated among 302 patients who had undergone hip preservation surgery due to FAIS [152]. The categorisation by Biedermann et al. has the advantage of being developed specifically for PAO procedures, however, not all adverse events reported in the studies on PAO were included in the adverse events defined by Biedermann et al. and some adverse events were therefore not possible to classify. Categorising adverse events based on the predefined events by Biedermann et al. could have caused some misclassifications in Paper I, as a clear description of

each adverse event in the studies was required, which was not always the case. The reviewers (MO and the PhD candidate) and the senior researcher (IM) thus had to categorise the adverse events based on their judgment, which could have led to misclassification.

If the systematic review were ever to be repeated, it could benefit from focusing solely on studies reporting harms and categorising them using the modified Clavien-Dindo score.

Paper II – The cross-sectional study

The cross-sectional study design is classified as level 3b according to OCEBM Levels of Evidence [65]. In cross-sectional studies, there are no time difference between exposure and outcome, and assumptions regarding causality cannot be made. Consequently, it cannot be determined whether the observed association between hip function and muscle strength is caused by hip muscle strength affecting hip function or the reverse.

Studies that recruit healthy volunteers through advertisements have the potential problem of self-selection bias, also known as volunteer bias [153]. In Paper II, the differences observed between patients and healthy volunteers are likely overestimated because the healthy volunteers represent a selective group who are more conscious and aware of having a healthy and active lifestyle than the general population. If the healthy volunteers had been recruited solely from the patients' network, the risk of overestimation would have been reduced. Similarly, matching the patients and the healthy volunteers on participant characteristics such as age and sex would have further reduced the risk of bias and overestimation.

Like the healthy volunteers, the patients included in Paper II were also a selected group, as they were all participating in the ongoing randomised controlled trial,

PreserveHip. Both groups thus volunteered for this research project, dedicating their time and commitment. The healthy volunteers did so without any personal gain, and the patients risked being assigned to a treatment different from their preference by their commitment to the trial. Additionally, the time-consuming intervention could have contributed to some patients declining participation. Those who declined might have had lower socioeconomic status, making it financially unfeasible for them to commit to the trial [153].

Paper II might suffer from type II error, meaning that the patient sample was too small to detect all functional differences between the index and contralateral legs. All functional performance measures were higher for the contralateral leg than the index leg, indicating an overall trend. However, the differences were too small to be significant and did generally not exceed thresholds for clinically relevant differences, except for the single-leg hop test.

Paper III – The FEAR index study

Wyatt et al. developed the FEAR index to identify whether hips are stable or unstable in patients with borderline hip dysplasia, defined as having a CE-angle between 20°-25° [72]. Paper III measured the FEAR index on all patients who had undergone PAO due to hip dysplasia from 2018-2020 and were registered in the Aarhus PAO-database, regardless of their CE-angle. Thus, The FEAR index was used on a slightly different population than the one it was developed for. Therefore, a sensitivity-analysis only including the 79 patients with a CE-angle between 20°-25° was conducted, and the sensitivity-analysis found the same result as the primary analysis: no differences in any of the change scores on the HOOS from before to 6 months after PAO. The sensitivity-analysis, however, was based on a relatively small number of patients, as only 13 patients with borderline hip dysplasia had a FEAR index >2° and 66 patients with borderline hip dysplasia had a FEAR index ≤2°.

No sample size calculation was possible, and the population thus consisted of a convenience sample of 222 patients who had undergone PAO due to hip dysplasia within 3 years. For comparison, the seven other studies that reported the inter-rater reliability of the FEAR index included between 59 and 267 patients with hip dysplasia or FAIS [74]. The sample size of 222 patients for the inter-rater reliability analysis thus seems relevant and comparable despite the relatively high number of 51 (19%) patients that had to be excluded due to incomplete or missing preoperative radiographs. In addition, the sample size for the investigation of an association between the FEAR index and patient-reported outcomes had to further exclude 27 patients due to missing pre- or postoperative HOOS scores. For comparison, the three other studies that investigated this association included the following patient groups: 249 female patients with hip dysplasia [142], 140 patients with FAIS [143] and 36 patients with FAIS [144], respectively. The sample size of 195 patients for the association analysis thus also seems relevant and comparable despite the relatively high number of missing patients (35%).

Despite the retrospective measurement of the FEAR index where both assessors knew the purpose of the study, recall bias was not a problem in Paper III, as none of the assessors were involved with the patient's treatment and were not aware of the study design, including the use of the 2° cutoff value. However, a prospective approach would have been preferable, as the assessors would have been blinded to the treatment when assessing the preoperative radiograph, and the number of missing and incomplete radiographs could have been avoided.

Paper IV – The sports participation study

The sports participation study was based on information collected from questionnaires that were not validated. The orthopaedic surgeon who initiated the database formulated the sports-related questions, which were neither validated nor tested among patients, but were based on his professional experience. The term "sport" was

not defined, and the patients had to answer the sports participation question before being introduced to different types of sports. Consequently, the sports construct relied on the patient's perception, which could have introduced bias due to uncertainty of the construct. This could have been avoided if validated questionnaires had been used instead. Novais et al. [132] and Heyworth et al. [145] used the University of California Los Angeles Activity Scale to investigate sports participation and return to sports among patients undergoing PAO. The University of California Los Angeles Activity Scale was, however, not translated and validated into Danish until 2021 [154] and, unfortunately, not available when the PAO database was established, despite being published in 1998 [155].

The extended follow-up allowed for a detailed understanding of the long-term effects but also introduced the potential for confounding variables in the patients' lives, which may have influenced changes in sports behaviour substantially. For instance, life events such as having children could have resulted in changes regarding sports participation that are unrelated to PAO, and the change in patients participating in sports 10 years after PAO may not necessarily be the result of the surgical procedure.

The amount of missing data in Paper IV is worth mentioning, as 19% of the patients had not answered the question about sports participation at any time and were thus excluded. In the quality assessment in Paper I, moderate risk of bias due to missing data was defined as missing 10-19%, while major risk of bias was defined as missing ≥20%. Paper IV thus had moderate but very close to major risk of bias due to missing data, thereby possibly introducing selection bias.

Besides selection bias and confounding, recall bias was also a limitation of Paper IV. Patients were asked whether the PAO had improved their sports performance at all time points. At the 20-year follow-up point, patients thus had to evaluate if the PAO surgery done 20 years ago had improved their sports performance, which obviously introduced recall bias. The improvement question is the only question relying on the

patient's memory, and recall bias was thus not a problem with the other sports-related questions.

Although there were certain limitations, this study represented the most extensive investigation into sports participation before and after PAO conducted to date. The large and diverse sample of patients provided a broad and novel perspective on the sports outcomes following PAO.

Paper V – The validation study

The number of hips registered in the Aarhus PAO-database as having undergone PAO due to hip dysplasia was validated using the DNPR and the patients' electronic medical journals. Validating research resources like the Aarhus PAO-database is crucial for ensuring the accuracy and reliability of clinical data, so conclusions based on this data can enable improvements in treatments. Using the electronic medical journal for validation is the gold standard, but this approach is very time-consuming and was thus not feasible [156]. Validating the Aarhus PAO-database against the DNPR was the next best approach, as the DNPR collects data from the patients' electronic medical records. The validation of the two random samples of patients from DNPR and the Aarhus PAO-database confirmed the high registration completeness.

The registration completeness is an estimate of the sensitivity [156]. The sensitivity is the rate of true positives, which in Paper V is the number of patients with hip dysplasia who have undergone PAO and could be validated. Usually, both the sensitivity and the specificity must be estimated, but the comparison of two registries does not allow for an estimation of the specificity [156]. The specificity is the rates of true negatives, which in Paper V is the number of patients without hip dysplasia who have not undergone PAO and could be validated. The specificity was thus not possible to estimate. According to Sørensen et al., it can be assumed that the specificity will be close to one if the disease is rare [156]. The prevalence of hip dysplasia in Danish adults

has been estimated to range from 5.4 to 12.6% [10], but only few patients with hip dysplasia undergo PAO, and the combination of the disease and treatment could, therefore, be considered rare, and thereby the specificity high.

The validation study was restricted to 2014-2021, despite the registry being established in 2010 and the data being extracted from DNPR and the Aarhus PAO-database in September 2023. The ethical approval was limited to 2021 because obtaining the necessary approval began in 2022. The starting point was chosen to be January 1st 2014, due to changes in hospital structures in 2011, when the three hospitals in Aarhus were merged into one hospital and thus one hospital code (SHAK code). The old hospital codes for the three previous hospitals remained active until the end of 2013. When ethical approval for Paper V was finally granted, it only covered the SHAK code for the combined hospital, making data from before 2014 inaccurate and thus excluded. If this study is ever redone, including all data from 2010 and onwards would be preferable, using all relevant hospital codes.

Generalisability

The generalisability of systematic reviews and meta-analyses depends on the studies included. In Paper I, the included studies were all cohort studies with comparable study populations in terms of age, sex and BMI [47]. The use of different PAO techniques increases the generalisability of the results. However, only one of 29 studies was conducted outside a Western country, so the results predominantly represent Western populations. Therefore, the results of Paper I are primarily generalisable to hip dysplasia patients undergoing PAO in Western countries.

Paper II was based on data from a highly selected patient population, and the results are thus generalisable to patients willing to be allocated to a treatment that might be different from their preference and being willing to participate in a 12-month exercise trial. As described, the time-consuming intervention could have resulted in patients

with lower socioeconomic status declining participation. Despite these limitations, Denmark is a wealthy country with a health and social system that allows most patients to participate in trials like the PreserveHip trial, making the results generally applicable to Danish patients with hip dysplasia [157].

The data in Papers III, IV and V was collected from the Aarhus PAO-database. The registry collects data from two out of four hospitals performing PAO in Denmark, including the only private hospital performing PAO. Both hospitals are located in the Central Denmark Region but treat patients nationwide. The Private Hospital Mølholm performs PAO on Danish patients and patients from other countries, however, the ethical approvals only included Danish patients, so foreign patients were excluded. The results from Papers III, IV and V thus represent Danish patients but are generalisable to other Western countries, as the study populations were comparable to those found in the 29 studies included in Paper I in terms of age, sex and BMI. Additionally, the high registration completeness of the Aarhus PAO-database found in Paper V increases the generalisability and indicates a low risk of selection bias in the inclusion process. However, Papers III and IV were missing patient-reported outcomes from 12% and 19% of their populations, which limits their generalisability.

8. Conclusion

Paper I – The systematic review

The systematic review revealed that patients undergoing PAO experience clinically relevant improvements in hip-related pain and function that persist for at least 5 years after the procedure. However, the surgery carries a 4% risk of a major and a 14% risk of a minor adverse event. No randomised controlled trials were found, and these results are based solely on cohort studies. Of the 29 included cohort studies, 83% had a serious risk of bias, and the certainty in the evidence is thus very low.

Paper II – The cross-sectional study

The cross-sectional study demonstrated that patients with hip dysplasia scheduled for PAO are significantly impaired compared to healthy subjects. Patients had poorer functional performance in the single-leg hop and Y Balance tests and a significant deficit in isometric hip flexion strength. However, their isometric muscle strength in hip abduction and extension was comparable to that of healthy subjects. Additionally, muscle strength in hip abduction, flexion, and extension was associated with functional performance in both legs of the patients.

Paper III – The FEAR index study

The radiographic study demonstrated significant improvements in hip instability measurements from before to 6 months after PAO. Additionally, all five subscales of the HOOS showed statistically significant and clinically relevant improvements for the entire cohort. When differentiating between stable and unstable hips based on the FEAR index, no differences were found in HOOS scores before or 6 months after PAO, nor in the change scores between the two groups. The inter-rater reliability for the FEAR index was good, with ICC scores of 0.82 before PAO and 0.80 6 months after

PAO. These findings indicate significant improvements in hip instability and HOOS but no association between the FEAR index and patient-reported outcomes.

Paper IV – The sports participation study

The sports participation study revealed that patients have a 56% chance of participating in sports 6 months after PAO, increasing to 60% 2 years after PAO. The likelihood of participating in preferred sports rose from 13% before PAO to 41% 6 months after and to 57% 2 years after PAO. Preoperative characteristics such as being sports-active, having higher education, and better HOOS pain scores increased the odds of sports participation. However, age, sex, BMI, CE-angle, and AI-angle were not associated with sports outcomes. These findings indicate that sports participation improves after PAO, influenced by various preoperative factors.

Paper V – The validation study

The validation study revealed that the registration completeness between the Aarhus PAO-database and DNPR was 95%, with 1116 out of 1178 registered hips recorded in both registries. This indicates that nearly all patients who underwent PAO for hip dysplasia from 2014 to 2021 were included in the Aarhus PAO-database. The diagnosis and PAO procedure were verified for all randomly selected hips using patients' electronic medical records. However, for the hips that were only recorded in one registry, the diagnosis and PAO procedure could not be verified in fewer than five patients. The unverified hips were only included in DNPR and not the Aarhus PAO-database. These findings, therefore, suggest that the PAO-database is a valid resource for future research projects and the quality assurance of PAO for patients with hip dysplasia.

9. Perspectives and future research

The effect of PAO

The systematic review (Paper I) revealed that no randomised controlled trials investigating the effect of PAO in patients with hip dysplasia >15 years old were published before January 2021. In addition, only three randomised controlled trials are registered at ClinicalTrials.gov, the PreserveHip trial and MoveTheHip trial from Aarhus University Hospital and a trial from the Mayo Clinic in Rochester, Minnesota.

The ongoing trial from the Mayo Clinic investigates the effect of adding concomitant hip arthroscopy to PAO (registration number: NCT03181048). In Paper I, the risk of a major adverse event was estimated to be 29% lower for patients undergoing PAO concomitant with hip arthroscopy or arthrotomy. The results were, however, not statistically significant and were based on two cohort studies with a high risk of bias. In addition, the patient-reported outcome was not compared between the two groups in Paper I, which is the primary analysis in the trial from the Mayo Clinic. The randomised controlled trial from the Mayo Clinic thus has the potential to determine if concomitant hip arthroscopy results in better outcomes in patients with hip dysplasia undergoing PAO, based on high-level evidence.

The PreserveHip trial, where the patients in Paper II are enrolled, investigates if PAO followed by progressive resistance training is more efficient than exercise alone (registration number: NCT03941171) [42]. The PhD candidate is the primary investigator on the trial, which started in July 2019 and is expected to end in August 2025. In this trial, the patients are randomised to either (1) The intervention, which consists of a PAO followed by 4 months of usual care and a further 8 months of progressive resistance training, or (2) The control, which consists of 12 months of progressive resistance training. The PreserveHip trial will be the first randomised controlled trial

to allocate patients to PAO or another treatment and, thereby, the best estimate of the true effect of PAO. The results will hopefully help orthopaedic surgeons, physiotherapists, and patients in shared decision-making when managing symptoms and deciding on treatments. In Paper II, an association between muscle strength and hip function was found, indicating that exercise treatment could be a potential treatment pathway for patients with hip dysplasia. Based on this finding, it seems possible that progressive resistance training could increase muscle strength and, thereby, the physical function of patients with hip dysplasia who are candidates for a PAO.

The effect of exercise and patient education as a treatment option for patients with hip dysplasia who are not candidates for PAO is currently being investigated in the MoveTheHip trial (registration number: NCT04795843). In this trial, the patients with hip dysplasia who are not candidates for PAO, based on the contraindications presented in Table 2, are allocated to either exercise and patient education or usual care [44]. If exercise and patient education are superior to usual care, as expected, a new treatment path for patients with hip dysplasia who are not candidates for PAO (due to their age, BMI or hip osteoarthritis), or do not wish to undergo surgery can be established.

All three randomised controlled trials investigate the effect of PAO using self-reported hip pain. However, the effect of PAO extends beyond pain level and should also involve the patient's lived experience and the economic aspects of PAO. Fortunately, two systematic reviews focusing on this have been registered on Prospero. Hibbert et al. will investigate the lived experiences and healthcare perspectives of people with hip dysplasia by including only qualitative studies on the patients' lived experiences and beliefs (registration number: CRD42024581726). In addition, Lukas et al. will investigate the costs for the patients and the healthcare system related to PAO (registration number CRD42022378731). Both systematic reviews have not yet started

extracting data but will contribute to further understanding of the effect of PAO when finished.

Ongoing systematic reviews

In addition to the studies mentioned above, other interesting research is currently being conducted on hip dysplasia and PAO. According to Prospero, four systematic reviews involving patients with hip dysplasia are currently being conducted.

MacLeod et al. have registered a similar systematic review as Paper I on Prospero, including harms and benefits in terms of adverse events and patient-reported outcomes in patients with hip dysplasia undergoing PAO (registration number: CRD42024530108). The systematic review is currently under review, and the results are therefore unknown. The major difference will be the adverse events, where MacLeod et al. have not stated which adverse events they will extract and how they will analyse them. In addition, the patient-reported outcomes of interest by MacLeod et al. are not completely identical to the patient-reported outcomes in Paper I, as MacLeod et al. have extracted the NAHS, the University of California Los Angeles Activity Scale, VAS, iHOT, HOOS and Harris Hip Score.

Costa et al. have registered a systematic review focusing on biomechanical changes following surgical or non-surgical interventions in patients with hip-related pain on Prospero (registration number: CRD42025649096). They have not finished screening studies yet, but according to their protocol, studies that include patients with hip dysplasia are eligible for inclusion. They will extract data on biomechanics during activities before and after treatment.

In addition, two systematic reviews investigating the effect of concomitant arthroscopy in hip dysplasia patients undergoing PAO are registered at Prospero (registration numbers: CRD42023444815 and CRD42023438314). The protocols state

that adverse events and patient-reported outcomes will be extracted. Both studies were supposed to be finished in 2023, but according to Prospero, the screening process has not yet started, which could indicate that the author group has decided not to perform the systematic reviews. Only two studies with harms and benefits following PAO with concomitant hip arthroscopy or arthrotomy were found in Paper I, and the small number of studies could be a reason for not fulfilling these systematic reviews.

Future research

Based on the findings of this PhD thesis, it is evident that patients with hip dysplasia experience reduced hip function and that hip function is associated with hip muscle strength. The research has identified the risks and benefits associated with the PAO procedure, as well as the preoperative factors that affect sports participation after surgery. Furthermore, it has been determined that the FEAR index does not affect patient-reported outcomes following PAO. Despite the substantial evidence on hip dysplasia and the outcomes of PAO, several questions remain regarding the optimal treatment strategies for hip dysplasia and the long-term effects of PAO. The research questions range from establishing whether hip dysplasia causes hip osteoarthritis to defining the best rehabilitation after PAO. In Paper IV, 38% of the patients did not participate in sports 5 years after PAO. Of these, 49% reported that a hip problem was not the reason for not participating in sports, which leaves the question of why they stopped participating in sports open for future research.

The effect of PAO could be further established by using the data from the Aarhus PAO-database. The hypotheses that the radiological findings correlate with patient-reported outcomes could be investigated using the Aarhus PAO-database. Another hypothesis that is possible to investigate is if markers for mental health are associated with self-reported hip pain and function after PAO. The Aarhus PAO-database could also be used to develop a prediction model, identifying patients that likely will have a good outcome of PAO based on preoperative characteristics. A prediction model could help

the orthopaedic surgeon and patient decide if PAO is the best treatment for the patient. According to clinicaltrials.gov, Cheng et al. are developing a similar model that focuses on conservative treatment for patients with hip-related problems (registration number: NCT04069507). They are investigating predictors for conservative treatment in a cohort study of patients with hip problems, including patients with hip dysplasia, to develop a clinical prediction model to identify patients who would benefit from conservative treatment. Future studies using data from the Aarhus PAO-database should preferably use data from 2014 and onwards, as the registration completeness was established as high in Paper V.

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11. Appendices

Paper I – The systematic review

Periacetabular osteotomy to treat hip dysplasia: a systematic review of harms and benefits

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HIP ARTHROPLASTY

Periacetabular osteotomy to treat hip dysplasia: a systematic review of harms and benefits

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Abstract

Introduction Periacetabular osteotomy (PAO) is often performed in patients with hip dysplasia. The aim of this systematic review and meta-analysis was to evaluate the harms and benefits of PAO in patients with hip dysplasia in studies reporting both adverse events and patient-reported hip pain and function.

Materials and methods A systematic search combing PAO and patient-reported outcomes was performed in the databases MEDLINE, CINAHL, EMBASE, Sports Discuss and PsychINFO. Studies including both harms and benefits defined as adverse events and patient-reported hip pain and function were included. Risk of bias was assessed using The Cochrane Risk of Bias In Non-Randomized Studies – of Interventions.

Results Twenty-nine cohort studies were included, of which six studies included a comparison group. The majority of studies had serious risk of bias and the certainty of evidence was very low. The proportion of adverse events was 4.3 (95% CI 3.7; 4.9) for major adverse events and 14.0 (95% CI 13.0; 15.1) for minor adverse events. Peroneal nerve dysfunction was the most frequent adverse event among the major adverse events, followed by acetabular necrosis and delayed union or non-union. All patient-reported hip pain and function scores improved and exceeded the minimal clinically important differences after PAO. After 5 years, scores were still higher than the preoperative scores.

Conclusion PAO surgery has a 4% risk of major, and 14% risk of minor adverse events and a positive effect on patient-reported hip pain and function among patients with hip dysplasia.

Keywords Hip dysplasia · Patient-reported outcomes · Adverse events · Harms · Benefits

Introduction

Hip dysplasia is characterized by a shallow and/or oblique acetabulum, and can also involve abnormalities of the proximal part of femur. The result is insufficient coverage of the femoral head [1–3] anteriorly, laterally, and less frequently posteriorly [4]. This results in a smaller load-bearing area [3], which is believed to result in higher contact pressure on the cartilage causing degenerative changes and potentially osteoarthritis of the hip joint [3, 5, 6]. The periacetabular osteotomy (PAO) procedure, which aims to reorientate the acetabulum to increase coverage of the femoral head without compromising blood perfusion to the acetabular fragment, is the a common surgical treatment for hip dysplasia [6–8]. Besides improving the femoral head coverage, the aim of PAO is to redistribute high compressive loads from the acetabular edge to the entire acetabular surface and to preserve the cartilage [9, 10].

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Patients with hip dysplasia experience hip- and groin-related pain [2, 11, 12], altered gait patterns [13, 14] and often muscle–tendon pain [15]. PAO has been shown to relieve pain [2, 12, 16], improve hip function [17], gait [18] and quality of life [12, 16] although reported pain and quality of life remain worse compared with aged-matched controls [19]. Moreover, minor and major adverse events following PAO have been reported [20]. A systematic review from 2009 found that major adverse events were present in 6–37% of the hips after PAO [8]. The most commonly reported major adverse events were symptomatic heterotopic ossification, wound hematomas, nerve palsies, intra-articular osteotomies, loss of fixation and undercorrections [8]. Since the review from 2009 was published, several studies regarding adverse events after PAO have been published. In addition, the use of patient-reported outcome measures have become more prevalent as a way to assess the effectiveness of surgical treatments [21, 22]. The aim of this systematic review was thus to evaluate the harms and benefits of PAO in patients with hip dysplasia using studies reporting both adverse events and patient-reported hip-related pain and function in the same study population.

Methods

Search strategy

This systematic review was reported according to the PRISMA harms checklist for systematic reviews reporting harms [23] and registered on the Prospero registration site for systematic reviews (registration number:CRD42021253438), before study selection was performed. A systematic literature search was conducted based on the search strategy from the review by O'Brien et al. [24] regarding patient-reported outcomes after PAO. In short, a systematic search combining PAO and patient-reported outcomes was performed in the databases MEDLINE, CINAHL, EMBASE, Sports Discuss and PsychINFO. The search ended on 5 January 2021. Studies were included if PAO was the primary intervention for hip dysplasia and patients were aged 15 years or older. In addition, one of the following hip-specific patient-reported outcome tools was used: The Western Ontario and McMaster Universities Arthritis Index (WOMAC), the Hip disability and Osteoarthritis Outcome Score (HOOS), the International Hip Outcome Tool 12 and 33 (iHOT), The Copenhagen Hip and Groin Outcome Score (HAGOS), the Non-Arthritic Hip Score (NAHS) or the Oxford Hip Score (OHS). Studies only applying the Harris hip Score, the Merle d'Aubigne Score, or non-hip-specific patient-reported outcomes (e.g., visual analog scales, the University of California Los Angeles activity scale and Short Form 36) were excluded. Studies including patients with cerebral palsy, Down syndrome or Charcot–Marie–Tooth disease were also excluded. In addition, studies reporting on a rotational or curved PAO, case studies and animal studies were excluded.

A modified version of the Downs and Black checklist was used to assess quality of the included studies in the review by O'Brien et al. [24]. The eighth item in the checklist involves adverse events. The item formulation is, "Have all important adverse events that may be a consequence of the intervention been reported?" and response catagories include high, low or unclear risk of bias. Studies with a low or unclear risk of bias score in the specific item were included in the present systematic review and studies with a high risk of bias score were excluded. Furthermore, preoperative studies and studies without any of the adverse events defined by Biedermann et al. were excluded [20].

Quality assessment

The Cochrane Risk of Bias In Non-Randomized Studies – of Interventions (ROBINS-I) was used to individually assess the methodological quality of the included studies [25]. Two independent reviewers (LT and MO) performed quality assessment and data extraction. Disagreements between reviewers were solved by consulting a third reviewer (*IM*). In the assessment of risk of bias due to confounding, multiple surgeons, multiple previous surgeries, and multiple surgical centers were considered independent confounders of the harms and benefits outcome. In the assessment of deviations from the intended intervention, co-interventions such as concomitant procedures were a priori defined as a moderate risk of bias. In addition, it was decided that missing data in $\geq 20\%$ of the patients constituted a major risk of bias and a moderate risk if data were missing in 10–19%. Regarding bias in the selection of reported results, no specification of primary aim was considered a major risk of bias. Overall, bias was assessed as the worst score given across the study domains in accordance with Sterne et al. [25].

Data extraction

We used a priori defined decision rules for data extraction: Harms reported in patients after PAO were predefined as major and minor in accordance with Biedermann et al. [20] and benefits were predefined as patient-reported hip pain and hip function. As patient-reported outcomes had already been extracted independently by the two reviewers (*LT* and *MO*), only data on harms (adverse events) were extracted for this review. Data extraction was managed using a customized excel worksheet (Microsoft Excel version 2108). In case of doubt regarding categorisation of an adverse event, a third reviewer (*IM*) was consulted; if doubt persisted, the authors of the relevant study were contacted. In case of no response from the authors or inability to categorize the adverse event,

the case was categorized as "other adverse events". In case of missing data or clarification issues, one author (*LT*) contacted the corresponding author.

The patient-reported outcomes used in this study were retrieved from the HOOS, the WOMAC, the iHOT, the HAGOS,the NAHS and the OHS tools. The subscales Pain and Activities of Daily Living were extracted from the HOOS, the subscales Pain and Physical Function from the WOMAC and the subscales Pain and Activities of Daily Living from the HAGOS. All six questionnaires cover hip-specific patient-reported outcomes with focus on pain and function. The six questionnaires have all been described in detail in the systematic review by *O'Brien et al.* [24]. The minimal clinically important difference has been reported to be 6 for the iHOT [26], 7.5 for the NAHS [27], 10.3 for the HOOS Pain and 10.8 for the HOOS Activities of Daily Living, the WOMAC Pain and the WOMAC Physical Function [28]. The minimal important change has been reported to be 9.8 for the HAGOS Pain and 11.9 for Activities of Daily Living in a group of patients with femoroacetabular impingement syndrome [29]. For the OHS, the minimal important change has been reported to be 10.6 for patients undergoing hip replacement [30].

Certainty assessment

Two reviewers (*LT* and *MO*) rated the certainty of the evidence for each metaanalysis using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) [31]. The GRADE approach specifies four levels of certainty, high, moderate, low, and very low, reflecting the extent of confidence in the estimates presented in Table 4. The overall certainty of evidence was based on the lowest rating for the critical outcome.

Statistical analysis

All adverse events were reported as categorical data and thus presented as number and proportion of events with 95% confidence intervals (95% CI). Meta-analysis was performed on adverse events from studies with more than one group and adverse events were reported separately for the groups, using risk ratios (RR) with 95% CI. Zero events were handled by adding 0.5 to every cell in the 2 × 2 table as suggested in the PRISMA checklist for reporting harms in systematic reviews [23]. A random-effect model was used as large heterogeneity was expected due to difference in outcome measures and PAO procedures. We assessed the heterogeneity of results and quantified it as I^2 values and an I^2 value above 50% was considered indicative of substantial heterogeneity. All patient-reported outcomes were normalized to a scale of 0–100, where 0 indicates the worst possible outcome and 100 indicates the best possible outcome. For each of the patient-reported outcomes, weighted mean scores were calculated at each time point reported in the included studies, with number of patients as the weighted component. All statistical analyses were performed in Stata version 16.0 (StataCorp LLC, College Station, TX, USA).

Results

Of the 62 studies in the systematic review on patient-reported outcomes by *O'Brien et al.* [24], 28 did not report on adverse events and were thus excluded from this systematic review (Fig. 1). Another two studies were excluded because they were pre-surgical studies and three studies were excluded as they did not include any of the adverse events defined by Biedermann et al. [20]. Thus, 29 studies with information on adverse events after PAO were included and six were included in the quantitative synthesis in this systematic review.

Twelve studies used a classification system to describe adverse events. Of these, ten studies used a modified Clavien-Dindo score [32–41], one study used the WOMAC score categories poor, good and very good [42] and one study used five grades based on required treatment and long-term morbidity ranging from no change in postoperative care to death [43]. Overall, the studies had comparable study populations regarding sex, age and body mass index. The type of PAO procedure varied, however, and the number of patients and hips included in the studies ranged from 17 to 1385 (Table 1).

Quality assessment

The overall assessment of the methodological quality across the studies showed that the majority of studies had a serious risk of bias (Fig. 2). Bias in measurement of outcomes was the most predominant, as most of the studies had patient-reported outcomes as the primary outcome and the assessor could obviously not be blinded to the intervention. In addition, almost half of the studies had a serious risk of bias regarding selection of the reported results. This was due to not reporting the primary outcome of interest and performing multiple analyses on similar outcomes. Almost all studies had a low or moderate risk of bias regarding confounding, selection of patients, classification of interventions and deviations from intended interventions.

Adverse events after PAO according to Biedermann et al.

Overall, 182 major adverse events and 598 minor adverse events in 4260 PAO procedures were reported, and the proportion was 4.3% (95% CI 3.7; 4.9) for major adverse

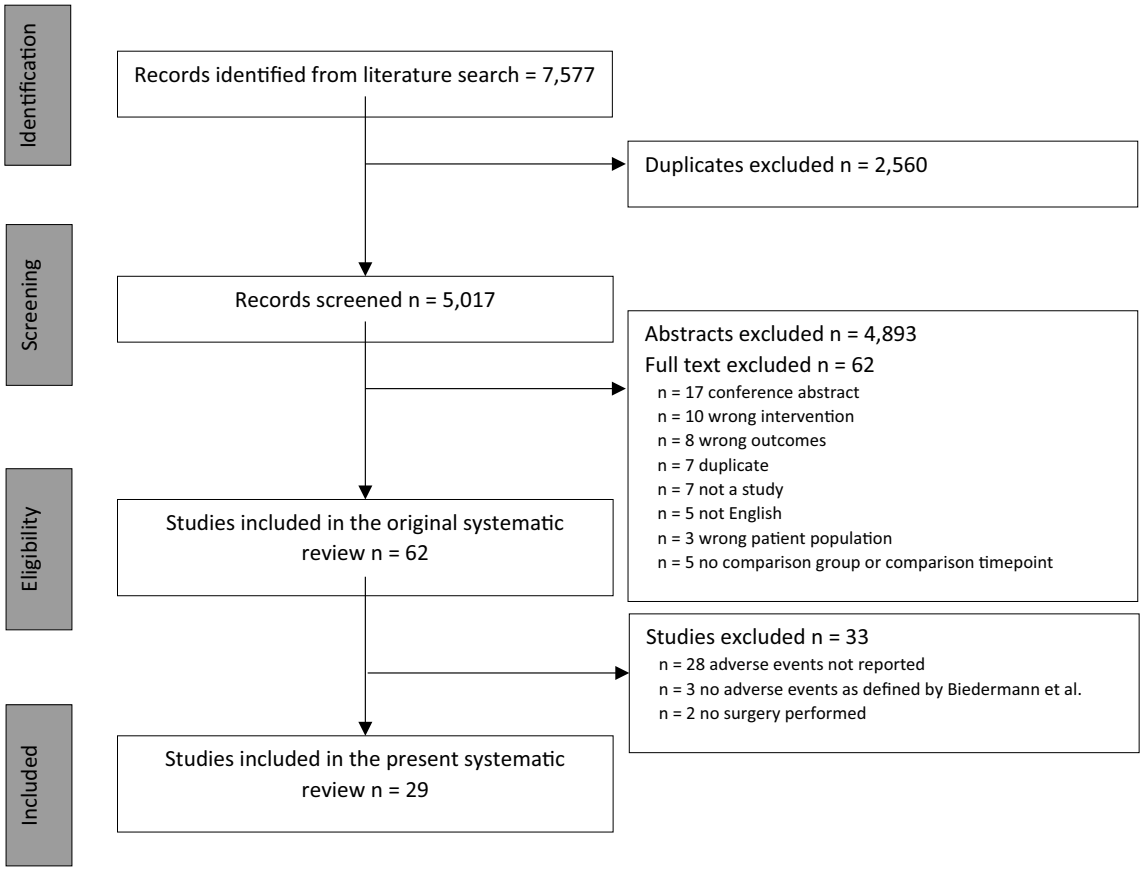

Fig. 1 Flow diagram on selection of studies

events and 14.0% (95% CI 13.0; 15.1) for minor adverse events. Peroneal nerve dysfunction was the most frequent adverse event among those experiencing major adverse events, followed by acetabular necrosis and delayed union or non-union (Table 2). Delayed union or non-union was the major complication reported in most studies (17 studies) and the proportion was 2.0% (95% CI 1.5; 2.5) across studies. Ectopic bone formation Brooker I–II was the most frequent adverse event among those experiencing minor adverse events, followed by postoperative fever and symptomatic hardware removal. Dysaesthesia of the lateral femoral cutaneous nerve was the most frequently reported minor complication in most studies (15 studies) and the proportion was 9.6% (95% CI 8.2; 11.1) across studies. Other adverse events not described by Biedermann et al. are presented in Table 3.

Meta-analysis of major and minor adverse events

Six studies included a comparison group and reported adverse events separately for the two groups. As the aim of these six studies was not the same, three meta-analyses were performed based on type of intervention or severity of hip dysplasia. Garbuz et al. and Hsieh et al. reported seven major adverse events and seven minor adverse events among patients treated with PAO, and one major and one minor adverse event among patients treated with a total hip arthroplasty (THA) [44, 45]. The RR for major adverse events was 4.30 (95% CI 0.70; 26.57) for patients undergoing PAO compared to THA (Fig. 3) and 5.70 (95% CI 1.03; 31.60) for minor adverse events (Fig. 4). Grammatopoulos et al. and Riccardi et al. reported adverse events among patients with severe and mild dysplasia [34, 37]. The overall RR for a major adverse event was 1.10 (95% CI 0.23; 5.25) for patients with severe dysplasia compared to patients with mild dysplasia (Fig. 3). In addition, the RR for a minor adverse event was 0.66 (0.09; 4.99) for patients with severe dysplasia compared to patients with mild dysplasia (Fig. 4). Riccardi et al. and Thanacharoenpanich et al. reported adverse events among patients treated with PAO and patients treated with PAO and arthroscopy or arthrotomy [38, 39] The overall RR for a major adverse event was 0.71 (95% CI 0.21; 2.42) in favor of PAO compared to PAO and arthroscopy or arthrotomy (Fig. 3). The overall RR for a minor adverse event was 0.53 (95% CI 0.13; 2.16) in favor of PAO compared to PAO and arthroscopy or arthrotomy (Fig. 4). The GRADE assessment of major and minor adverse events

Table 1 Summary of included studies with patient characteristics and type of periacetabular osteotomy (PAO)

Author, year	Patients	Hips	Females	Age (y)[a]	BMI (kg/m^2)	PAO intervention type
Beaulé, 2015	67	72	69%	32 (14–54)	26	Smith-Peterson
Biedermann, 2008	50	60	72%	27 (12–44)	–	Smith-Peterson
Clohisy, 2017	391	391	79%	25 < 810)	25	Ganz, no further specification
Dahl, 2014	82	116	–	–	–	Minimally invasive transartorial
Domb, 2015	17	–	82%	24 (7)	24 (5)	Abductor-sparing
Edelstein, 2020	67	70	93%	29 (10)	24 (4)	Ganz, no further specification
Garbuz, 2008	PAO: 28 THA: 34	–	90% 88%	45 47	–	Smith-Peterson
Grammatopoulos, 2018	Mild: 61 Severe: 183	61 320	84%	26 (10)	24 (4)	Ganz, no further specification
Grammatopoulos, 2016	57	68	86%	25 (7)	24 (3)	Smith-Peterson
Hartig-Andreasen, 2015	90	95	88%	34 (15–59)	–	Minimally invasive transartorial
Heyworth, 2016	41	46	88%	26 (13–41)	–	Abductor-sparing
Hsieh, 2009	PAO: 31 THA: 31	31 31	84% 84%	32 (29–52) 32 (29–52)	– –	Transtrochanteric approach
Khan, 2017	151	166	90%	32 (15–66)	–	Modified Smith-Peterson Minimal Invasive
Kralj, 2005	26	26	85%	30 (18–50)	–	Bernese PAO, no further specification
Larsen, 2020	1112	1385	85%	32 (13–59)	–	Minimally invasive transartorial
Maldonado, 2019	16	16	81%	24 (7)	24 (6)	Modified iliofemoral approach with no rectus femoris-sparing
Matheney, 2009	109	135	70%	27 (9)	–	Abductor-sparing
McClincy, 2019	49	49	94%	27 (8)	24 (5)	Rectus femoris-sparing
Millis, 2009	70	87	-	44 (40–51)	–	Abductor-sparing
Møse, 2019	99	104	92%	34 (14–59)	–	Minimally invasive transartorial
Novais, 2013	51	51	92%	27 (11)	24 (4)	Ganz, no further specification
Ramirez-Nunez, 2020	118	131	78%	32 (10)	–	Minimally invasive transartorial
Riccardi, 2017a	93	110	92%	25 (12–43)	23 (3)	Rectus sparing
Riccardi, 2017b	Mild: 27 Severe: 50	28 54	100% 88%	25 (15–43) 23 (12–41)	22 (18–36) 23 (17–30)	Rectus sparing
Riccardi, 2016	PAO + A: 21 PAO: 52	24 58	100% 89%	27 (12–41) 23 (12–43)	22 (3) 23 (3)	Rectus sparing
Thanacharoenpanich, 2018	PAO: – PAO + A: –	47 60	87% 92%	25 (10) 31 (9)	25 (4) 25 (4)	Smith-Peterson
Wells, 2019	129	154	86%	26	24 (17–34)	Abductor-sparing
Wells, 2018	129	154	86%	26	24 (17–34)	Abductor-sparing
Ziebarth, 2011	38	46	0%	24 (10)	–	Abductor-sparing

BMI Body mass index, *THA* Total hip arthroplasty

[a]Age presented with standard deviation or range, depending on available information in the included study. PAO + A: Periacetabular osteotomy combined with arthroscopy [38, 39] or arthrotomy [39]

revealed a very low certainty of evidence in all six meta-analyses, primarily due to study design and risk of bias in the included studies (Table 4).

Patient-reported outcomes

Preoperative and postoperative weighted mean score for HOOS pain, HOOS function, WOMAC pain, WOMAC function, iHOT and NAHS indicated that patients had benefited from PAO, as all included studies reported improved outcome after PAO (Fig. 5). The improvements were clinically relevant as they exceeded the minimal clinically important difference for all included patient-reported outcomes [26–28]. After 5 years, the weighted mean score across the studies was still higher than the preoperative mean scores and clinically relevant for all the included patient-reported outcomes. Two studies were excluded from this analysis as one study only presented the patient-reported outcomes graphically in a figure [43]; the other study only presented the total score of HOOS with no subscale scores [34]. No included studies used the HAGOS or the OHS as patient-reported outcomes.

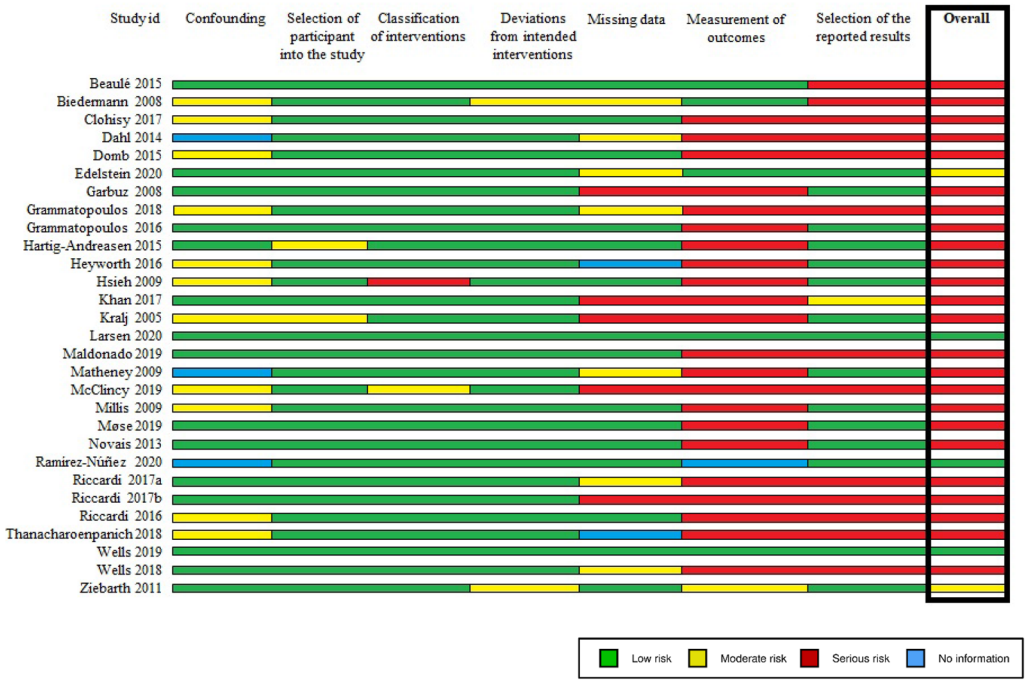

Fig. 2 The results of the risk of bias assessment performed with The Cochrane Risk of Bias In Non-Randomized Studies – of Interventions (ROBINS-I) for each of the included study

Discussion

This systematic review included 29 studies with information on both adverse events and patient-reported outcomes; six studies were further included in meta-analyses. We showed that PAO has a low-medium rate of adverse events and a positive effect on patient-reported hip pain and function among patients with hip dysplasia. All of the included studies were cohort studies, and at least one group of the included patients had undergone PAO. Most included studies had a serious risk of bias related to measurement of outcomes. The certainty of the evidence was very low due to the study design and the serious risk of bias.

The overall proportion of adverse events was 4.3% for major adverse events and 14.0% for minor adverse events. Clohisy et al. found that major adverse events were more common and occurred in 6–37% of the procedures [8]. Even though adverse event categories used by Clohisy et al. are different from those used in the present systematic review, most of the adverse events defined as major by Clohisy et al. have also been defined as major adverse events in the present systematic review. The most frequent major adverse events were peroneal nerve dysfunction, acetabular necrosis, and delayed union or non-union. Among the minor adverse events, ectopic bone formation Brooker I–II, postoperative fever and symptomatic hardware removal were the most frequent. Due to serious risk of bias, interpretation of the results of this systematic review should be cautious. Clohisy et al. found that symptomatic heterotopic ossification, wound hematomas, nerve palsies, intra-articular osteotomies, loss of fixation and undercorrections were the most common major adverse event and symptomatic hardware removal was the most common moderate adverse event [8]. The differences in our findings and those previously reported are probably due to the results from several studies published after the systematic review by Clohisy et al., as well as differences in search strategy and exclusion criteria. Even though Clohisy et al. only included studies with both clinical and radiographic outcomes, some of the included clinical outcomes were clinician-reported and not patient-reported (e.g., the Merle d'Aubigné score).

In our meta-analysis comparing patients who had undergone PAO with patients who had undergone THA, the number of adverse events in the THA group is probably underestimated due to the pre-defined adverse events related to PAO and not THA. This may in part explain that patients

Table 2 Adverse events reported in the included studies on patients undergoing periacetabular osteotomy

	Number of studies	Number of procedures	Number of adverse events	Proportions, % (95% CI)
Major complications				
Femoral head necrosis	1	60	1	1.7 (0.04; 8.9)
Acetabular necrosis	1	60	2	3.3 (4.1; 11.5)
Femoral nerve dysfunction	2	226	2	0.9 (0.1; 3.2)
Sciatic nerve dysfunction	8	539	8	1.5 (0.6; 2.9)
Peroneal nerve dysfunction	5	469	23	4.9 (3.1; 7.3)
Major blood loss	3	1611	8	0.5 (0.2; 1.0)
Post. column discontinuity	7	595	10	1.7 (0.8; 3.1)
Intra-articular osteotomy or fracture	3	567	8	1.4 (0.6; 2.8)
Ischial fracture	–	–	–	–
Delayed union or non-union	17	3140	62	2.0 (1.5; 2.5)
Reflex sympathetic dystrophy	2	247	2	0.8 (0.1; 2.9)
Deep vein thrombosis and/or embolism	11	2626	20	0.8 (0.5; 1.2)
Arterial thrombosis	–	–	–	–
Overcorrection	1	110	1	0.9 (0.02; 4.9)
Undercorrection	3	319	4	1.3 (0.3; 3.2)
Resubluxation	–	–	–	–
Acetabuar fragment migration or displacement	–	–	–	–
Ectopic bone formation Brooker III–IV or excision	15	3219	31	1.0 (0.7; 1.3)
Minor complications				
Dysaesthesia of lateral femoral cutaneous nerve	15	1687	162	9.6 (8.2; 11.1)
Ectopic bone formation Brooker I–II	7	641	123	19.2 (16.2; 22.5)
Haematoma	9	803	21	2.6 (1.6; 4.0)
Symptomatic hardware removal	7	1738	243	14.0 (12.4; 15.7)
Secondary wound closure or wound infection	11	2702	28	1.0 (0.7; 1.5)
Urinary tract infection	2	176	10	5.7 (2.8; 10.2)
Fever post-operatively	1	60	11	18.3 (9.5; 30.4)
Avulsion of iliac crest	–	–	–	–

who had undergone PAO had a four times higher risk of major adverse event compared to patients who had undergone THA. In addition, conversion to THA was not a part of the adverse events described by Biedermann et al. Thus, data on patients who received a THA after PAO were not extracted for this systematic review, indicating that the true rate of major adverse events after PAO may be higher than reported in this systematic review.

Adverse events were a priori defined as the adverse events described by Biedermann et al., but there are multiple other ways to report adverse events, e.g., using a classification system. The modified Clavien–Dindo score was the classification system used in most of the included studies. However, the modified Clavien–Dindo is a general classification system for surgically related adverse events [46] and thus not specific for patients undergoing PAO as is the case in Biedermann et al.

To the best of our knowledge, this is the first systematic review with meta-analysis, using GRADE to include both harms and benefits in patients undergoing PAO. We only included studies reporting both adverse events and patient-reported outcomes because we intended the results on harms and benefits to originate from comparable identical study populations. This means that the results on harms and benefits in patients undergoing PAO reflect outcomes from identical PAO procedures, identical surgical circumstances and learnings curves. The decision to include only studies reporting both harms and benefits is probably the reason why only two studies could be included in each meta-analysis. We acknowledge the limitation due to the low number of

Table 3 Other adverse events reported in the included studies on patients undergoing periacetabular osteotomy

Adverse events—other	Number of studies	Number of procedures	Number of adverse events
THA	5	1870	115
Hip arthroscopy	3	1228	159
Revision PAO	3	936	5
Nerve injury	3	262	6
Extraarticular fracture	5	1763	20
Additional surgery			
Surgery performed on bones	2	264	2
Surgery performed on tendons	2	1503	9
Surgery performed on muscles	1	70	1
Lateral hip pain	3	372	3
Dislocation requiring closed reduction	1	391	1
Open exploration of soft tissue	1	1112	1
Soft tissue biopsy	1	1112	1
Tumour excision	1	1112	1
Intrapelvic abscess	1	135	1
Spinal headache	1	60	1
Broken and retained instrument	1	60	1

PAO Periacetabular osteotomy, *THA* Total hip arthroplasty

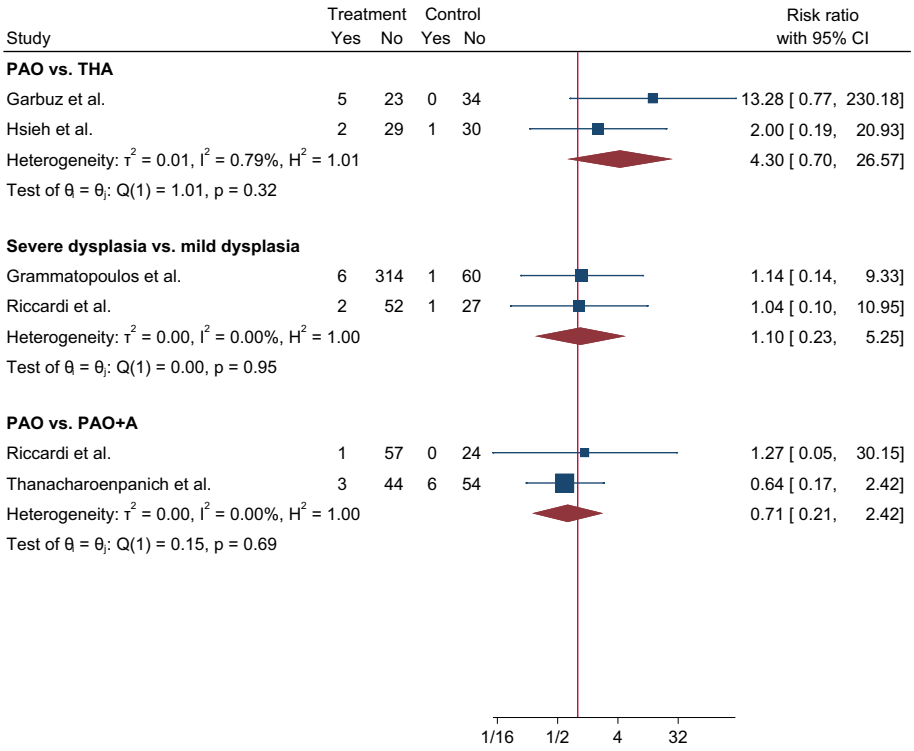

Fig. 3 Meta-analysis on risk ratio of major adverse event after periacetabular osteotomy (PAO), compared to total hip arthroplasty (THA) and PAO combined with arthroscopy or arthrotomy (PAO + A), as well as between severe and mild dysplasia

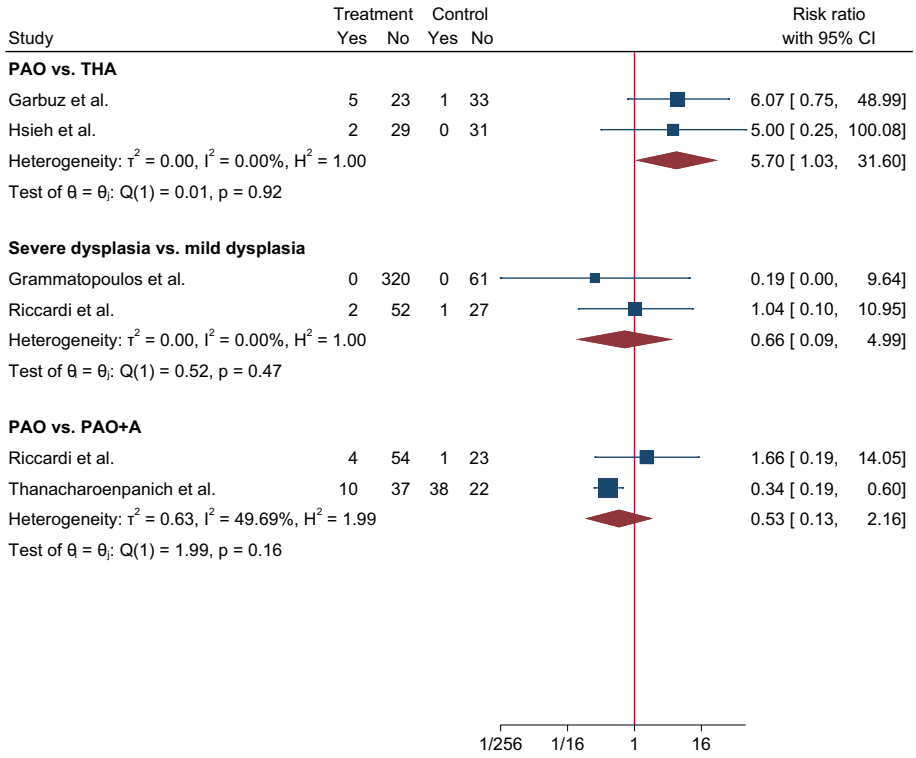

Fig. 4 Meta-analysis on risk ratio of minor adverse event after periacetabular osteotomy (PAO), compared to total hip arthroplasty (THA) and PAO combined with arthroscopy or arthrotomy (PAO + A), as well as between severe and mild dysplasia

Table 4 Summary of findings

Outcome	Patients and controls	Number of studies	Number of patients	Risk ratio (95% CI)	Quality of the evidence (GRADE)
Major adverse events	PAO vs. THA	2	124	4.30 (0.70; 26.57)	⊕⊖⊖⊖
Major adverse events	Severe dysplasia vs. mild dysplasia	2	463	1.10 (0.23; 5.25)	⊕⊖⊖⊖
Major adverse events	PAO vs. PAO + A	2	189	0.71 (0.21; 2.42)	⊕⊖⊖⊖
Minor adverse events	PAO vs. THA	2	124	5.70 (1.03; 31.60)	⊕⊖⊖⊖
Minor adverse events	Severe dysplasia vs. mild dysplasia	2	463	0.66 (0.09; 4.99)	⊕⊖⊖⊖
Minor adverse events	PAO vs. PAO + A	2	189	0.53 (0.13; 2.16)	⊕⊖⊖⊖

95% CI 95% Confidence Interval, *GRADE* Grading of Recommendations, Assessment, Development and Evaluations, *PAO + A* Periacetabular osteotomy combined with arthroscopy [38, 39] or arthrotomy [39], *THA* Total hip arthroplasty

studies in the meta-analyses. A systematic review that only focused on harms would probably be able to include more studies in the meta-analyses, but would not be advantaged from the inclusion of data on benefits of PAO.

The categorisation of adverse events into predefined adverse events, required a clear description of each adverse event in the included studies and is thus a limitation in this study. As this was not always the case, there is a risk that some adverse events may have been misclassified when data were extracted. Since data extraction was performed by two independent reviewers assisted by a senior researcher, attempts to minimize this problem were made, but we acknowledge the potential risk of misclassification of adverse events.

Conclusion

All the studies included in this systematic review were cohort studies and most of the studies had a serious risk of bias, due to bias in the measurement of outcomes and the certainty of the evidence was thus very low. This systematic review and meta-analysis found that PAO surgery has a 4% risk of major and 14% risk of minor adverse

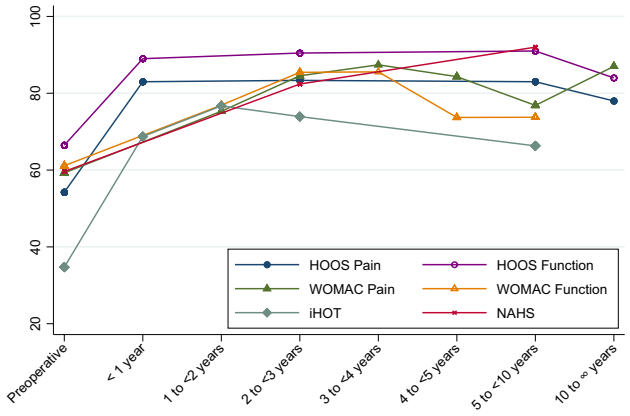

Fig. 5 Weighted mean scores of patient-reported hip pain and function where 0 indicates the worst scores and 100 indicates the best possible score. The patient-reported outcomes presented is; Hip Dysfunction and Osteoarthritis Outcome Score (HOOS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), International Hip Outcome Tool 12 and 33 (iHOT) and Non-Arthritic Hip Score (NAHS)

events and a positive effect on patient-reported hip pain and function among patients with hip dysplasia. Despite the high number of studies on patients undergoing PAO, only few studies included a comparison group. This should be a priority in future prospective cohort studies. There are no existing studies conducted in a randomized controlled design; thus, future studies investigating PAO are warranted using this design focusing on both harms and benefits.

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Author contributions All authors contributed to the study conception and design. Risk of bias assessment and data extraction were performed by LT and MO, with support from IM. Data analysis was performed by LT. The first draft of the manuscript was written by LT and IM after which all authors made comments. All authors approved the final manuscript.

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Declarations

Conflict of interest None of the authors has a conflict of interest for this project.

Ethical approval This systematic review was registered on the Prospero registration site for systematic reviews, registration number: CRD42021253438.

Informed consent Not applicable.

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Paper II – The cross-sectional study

Functional performance and muscle strength in patients with hip dysplasia compared to healthy subjects – a cross-sectional study

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Lower body functional performance and isometric muscle strength in adults with hip dysplasia compared to healthy subjects – a cross-sectional study

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Abstract

Objectives: The aim was to compare functional performance and isometric maximum voluntary contraction (MVC) during hip flexion, extension and abduction between patients with hip dysplasia scheduled for periacetabular osteotomy (PAO) and healthy subjects.

Design: Cross-sectional study.

Method: The single-leg hop for distance, Y Balance Test and MVC tests in an isokinetic dynamometer were compared between patients and healthy subjects. The statistical methods applied were t-tests and regression analysis.

Results: 59 patients (mean age 28 years, 86% women) and 39 healthy subjects (mean age 27 years, 74% women) participated. The single-leg hop test showed a 4.2 cm (95% CI: 0.3;8.0) difference between the index and contralateral leg for patients. Healthy subjects hopped 34.3 cm (95% CI: 23.2;45.4) longer than patients. The Y Balance Test indicated a difference in the posterolateral direction between patients hips, while healthy subjects performed better in all directions. Muscle strength were comparable between patients index and contralateral hip. Hip abduction and extension were comparable between groups, but hip flexion was 14.9 Nm (95% CI: 3.9;26.4) lower in patients.

Conclusions: Patients with hip dysplasia had significantly worse functional performance in single-leg hop and Y Balance Test, and significant deficit in hip flexion strength compared to healthy subjects.

Keywords: Hip dysplasia, [Hip Dislocation/pathology], [Healthy Subjects], [Exercise Test/methods*], [Muscle Strength*/physiology]

Introduction

Hip dysplasia is a developmental joint condition characterised by a shallow, oblique acetabulum, laxity of ligamentous structures, and abnormalities in the proximal femur, resulting in insufficient coverage of the femoral head [8, 19, 32]. The prevalence of hip dysplasia in Danish adults ranges from 5.4-12.6%, depending on

the radiographic index applied [10]. Symptomatic cases are up to four times more common in women than in men [11]. Treatment often involves periacetabular osteotomy (PAO), to increase coverage of the femoral head [28]. Candidates for PAO typically have a Centre Edge angle of Wiberg (CE-angle) below 25° and experience persistent hip pain over an extended period [30].

A recent systematic review revealed that patients with hip dysplasia eligible for PAO had a lower peak hip extension angle and a lower peak hip extension and flexion moment during walking, compared to healthy subjects [22]. Furthermore, patients with hip dysplasia showed reduced performance in functional tests compared to healthy subjects, who were faster in timed stair ascent, five sit-to-stands and four-square step test [26]. The included studies were mostly retrospective cohort studies, and only four studies provided comparisons to healthy subjects [22]. None of the studies used isokinetic dynamometry, the golden standard for assessing muscle strength [20].

In recent years microinstability in the hip has been suggested as a possible cause of pain among patients with hip dysplasia [12, 31], and muscle strengthening has been proposed as the treatment [15]. A recent Delphi study among 15 physiotherapists specialized in non-operative rehabilitation of hip dysplasia patients found that initial evaluations should include measurements of hip muscle strength (i.e. hip abductors, hip extensors, deep rotators and core muscles) and physical performance in single-leg activities (i.e. single-leg stance, single-leg squat and single-leg step down) [4].

The primary aim of this study was to compare functional performance and isometric maximum voluntary contraction (MVC) during hip flexion, extension and abduction between patients with hip dysplasia scheduled for PAO and a group of healthy subjects. The secondary aim was to investigate associations between hip muscle strength and functional performance. The hypotheses were that patients with hip dysplasia would have lower functional performance and muscle strength compared to healthy subjects without hip problems, and that muscle strength would be associated with functional performance.

Method

The present study is a cross-sectional comparative study, assessing functional performance and MVC strength in a group of patients with hip dysplasia, enrolled in an ongoing randomised controlled trial [24] and a group of healthy subjects. The study was approved by the Central Denmark Region Committee on Biomedical Research Ethics (j. no. 1-10-72-234-18) and registered at the Central Denmark Region's internal list of research projects (j. no. 1-16-02-120-19). Before inclusion, all participants gave written consent in accordance with the Declaration of Helsinki II.

Patients

All patients were recruited at two University Hospitals as part of the PreserveHip trial [24]. To be included the patients had to be eligible for PAO, defined as having a CE-angle below 25°, an Acetabular Index angle of more than 10°, persistent groin pain and a range of motion of more than 110° of hip flexion and 15° internal- and external hip rotation. Patients with hip osteoarthritis of more than 0 on the Tönnis Classification [29], a CE-angle below 10°, Legg-Calve-Perthes or epiphysiolysis diagnosis, a neurological or rheumatoid disease affecting the hip, or unable to read written Danish, were excluded. In addition, patients who had previously undergone hip or pelvic surgery in the affected hip as well as surgery for herniated disc, spondylosis or arthroplasty of the hip, knee or ankle were excluded. The patients' index leg was defined as the hip scheduled for PAO while the opposite hip was defined as the contralateral leg, regardless of bilateral hip dysplasia.

Healthy subjects

The healthy subjects were recruited via advertisements at Aarhus University Hospital, Aarhus University, VIA University College, social media, and patients' network. The healthy subjects were not matched to the patients with hip dysplasia. The healthy subjects were ineligible if they had experienced hip-related pain or problems within the past year, had a history of major surgery of the hip, knee, ankle or back, or had a

neurological or rheumatoid disease. As they were not surgery candidates, the right leg was defined as the index leg and the left leg as the contralateral leg.

Test procedure

Participants were tested by one of two physiotherapists (LT and LM) or by an exercise physiologist (TK) in a laboratory setting. Before the assessment, the participants completed a questionnaire on education and employment, and the Danish version of the Forgotten Joint Score [(2)]. They rated their pain level over the past four weeks at rest and during physical activity on a 100-mm Visual Analogue Scale [(7)]. Weight was measured using a Tanita weight (SC-330MA, Tanita Corporation of America, Illinois, USA) and height was measured using a telescopic height measuring device from ADE (MZ10023, DES Germany Gmbh, Hamburg, Germany). Participants' limb length was measured using the Y Balance Test procedure from the anterior superior iliac spine to the distal edge of the medial malleolus, while lying supine on an examiner table [(23)]. The participants then performed a 10-minute warm-up on an ergometer-bicycle before performing the isometric MVC test.

Isometric muscle strength

MVC was tested during hip abduction, flexion and extension using a Humac Norm isokinetic dynamometer (CSMi, Stoughton, Massachusetts, USA). Isokinetic dynamometry has been described as the golden standard for assessing muscle strength [(20)]. Testing began with isometric hip abduction, starting with the right hip, followed by the left hip. This was followed by isometric hip flexion and extension, starting with the right leg. To correct for gravity, the weight of the measured leg was recorded for each test setup. Participants performed two familiarisation trials, followed by three MVC trials for each leg, with 30 seconds rest periods between each trial. They were instructed to push as hard and fast against the dynamometer pad as possible for approximately four seconds.

119 The procedure for hip abduction followed Meyer et al. [20]. The participant was placed in a supine position
120 with the test leg on top of the non-tested leg. The dynamometer rotation axis was aligned with the greater
121 trochanter on the leg being tested and the length of the dynamometer arm was adjusted so the edge of the pad
122 was aligned with the superior border of the patella (Figure 1a). The non-test leg was kept in a 45º hip flexion.

123 The procedures for hip flexion and extension followed Kierkegaard et al. [16]. The participant was placed in a
124 side-lying position with a 15º inclined backrest to reduce lumbar curve and increase comfort. The
125 dynamometer axis was aligned with the greater trochanter, and the pad was placed five centimetres proximal
126 to the lateral femoral condyle. The test was performed at 45º hip flexion from the chair surface (Figure 1b).
127 Participants crossed their arms over their chest, with the non-test leg flexed and the foot placed on the chair.
128 A shoe was worn on the foot of the non-test leg to enhance traction with the chair surface.

129

130 *Functional performance*

131 Functional performance was assessed by the single-leg hop for distance test [1, 13] and the Y Balance Test [6, 23]
132 both requiring strength, flexibility, neuromuscular control, stability, and balance. The single-leg hop test was
133 performed barefooted with the arms held behind the back (Figure 1). The right leg was tested first followed
134 by the left leg. Participants stood with the toe behind a marked starting line and hopped the farthest possible
135 distance on one leg while still maintaining balance for two seconds after landing. The distance from the line
136 to the heel was measured. Two familiarisation trials were followed by three maximal trials. If the third trial
137 exceeded the second by more than 10 cm, additional trials were performed until the increase was less than 10
138 cm [1]. Only the longest distance was recorded and normalised for height by dividing the longest hop distance
139 by the participant's height [13].

140 After the single-leg hop test, participants were introduced to the Y Balance Test using the Y Balance Test
141 Kit™ (Perform Better, West Warwick, Rhode Island). Participants were tested barefoot (Figure 1) [6]. The
142 assessor demonstrated the test and participants performed six familiarisation trials per leg and direction.
143 They stood with their toe behind the line on the platform and pushed the moveable indicator as far as

possible with the other foot, while maintaining single-leg stance [6]. A trial was approved if the foot returned to the platform without losing balance. A trial was repeated if the participant lost balance, lifted the heel, failed to maintain contact with the distance indicator, or used it for support. Participants performed three trials in the anterior, posteromedial and posterolateral directions, starting with the right leg. Only the maximal reach distance in each direction was recorded and summed to a composite reach distance, normalised to limb length [6]. The Y Balance Test has good to excellent intra-rater and inter-rater reliability [5, 23].

Statistical analysis

Before the statistical analysis was performed, all continuous variables were assessed for normal distribution using q-q plots and histograms. Continuous variables were presented as mean and standard deviation (SD) when normally distributed and as median with interquartile range (IQR) when non-normally distributed. The Y Balance Test was normalised to limb length by dividing with the limb length and multiplying with 100 [5]. The composite score was calculated by summing the three directions and normalised by dividing with 3 times the limb length and multiplying with 100 [5]. Comparison between the patients index and contralateral leg, as well as the patients index and the volunteer's right leg were performed using student t-tests. Additionally, a sensitivity analysis was conducted comparing the patients' index and contralateral legs, stratified by unilateral or bilateral hip dysplasia. The differences were considered statistically significant if the p-value <0.05 and clinically relevant if they were >15% in hip muscle strength [17], ≥15% for the single-leg hop test [14] and ≥15% for the Y Balance Test [18]. Multiple linear regression analyses were used to investigate the association between muscle strength and functional performance. The model was adjusted for age, sex, height and weight, and the adjusted R^2 was reported as a measure of model fit. All statistical analysis was performed in Stata version 18.0 (StataCorp LLC, College Station, TX, USA).

Results

This study included 59 patients, and 39 healthy subjects. The two groups were comparable in age and sex, whereas weight tended to be higher in patients (Table 1). The healthy subjects had significantly lower BMI and had better pain and hip scores. For the patients, 58% had hip dysplasia in both hips.

Functional performance

The normalised single-leg hop test showed a statistically significant difference of 2.4 cm/m (95% CI: 0.2;4.7) between the index and contralateral leg for patients with hip dysplasia (p =0.04) (Table 2). However, the difference was 5.8% and thus not clinically relevant. The sensitivity analysis revealed that the difference seemed larger for patients with unilateral hip dysplasia than patients with bilateral hip dysplasia, however the results were neither statistically nor clinically significant (Table 3). The single-leg hop test was clinically significantly higher for healthy subjects than patients with hip dysplasia, with a normalised mean difference of 19.3 cm/m (95% CI: 13.1;25.4) corresponding to 37.4% (Table 2).

The normalised Y Balance Test was comparable for the index and contralateral leg for patients with hip dysplasia in all directions (mean differences; anterior 0.1% (95% CI: -1.3;1.5), posteromedial 1.3% (95% CI: -0.4;3.0), posterolateral 1.9% (95% CI: -0.1;3.9) and composite reach -0.1% (95% CI: -0.4;0.2)) (Table 2). The sensitivity analysis revealed that the index leg was significantly impaired in the posteromedial and posterolateral directions, but the differences were not of clinically relevance (Table 3). Performance was in all directions in favour of the healthy subjects when compared to hip dysplasia patients (p <0.001), with a mean difference of 10.1% (95% CI: 6.0;14.2) in the anterior direction, 18.6% (95% CI: 12.6;24.5) in the posteromedial direction, 16.9% (95% CI:10.8;22.9) in the posterolateral direction and 15.2% (95% CI: 10.3;20.1) in the composite reach (Table 2). The point estimate exceeded the threshold for being clinically relevant for all directions, except for the anterior direction, however the lower limit of the 95% CI was below the thresholds for all directions.

Isometric muscle strength

The mean differences in isometric muscle strength between the index and contralateral legs of hip dysplasia patients were small (hip abduction 4.7 Nm (95% CI: 0.1;9.3), hip flexion 3.5 Nm (95% CI: -0.8;7.8), and hip extension 4.7 Nm (95% CI:-5.5;15.0)) and not statistically significant (Table 2). These differences (7.8%, 5-6% and 3.0%, respectively) were not clinically relevant either. The sensitivity analysis revealed that patients with unilateral hip dysplasia had significantly lower isometric hip abduction and hip flexion strength of their index leg compared to their contralateral leg (Table 3). However, only hip abduction strength exceeds the threshold for clinical relevance.

Isometric hip flexion was significantly higher in healthy subjects compared to patients with hip dysplasia, with a mean difference of 14.9 Nm (95% CI: 3.9;26.4) (p =0.01), indicating a clinically relevant difference as the healthy subjects had a 21.2% higher hip flexion strength than patients with hip dysplasia (Table 2). There were no significant group differences in hip abduction or hip extension, however the difference in mean hip abduction was clinically relevant in favour of healthy subjects, as their hip abduction strength was 16.3% higher than patients with hip dysplasia. The difference in hip extension was not clinically relevant, as the difference to the healthy subjects was only 10.3%.

Associations between functional performance and isometric muscle strength

The single-leg hop test was significantly associated with hip abduction, flexion and extension strength for both the index and contralateral leg in patients with hip dysplasia (Table 4). When adjusted for age, sex, height and weight, higher isometric muscle strength was associated with better performance at the single-leg hop test (adjusted R^2: 0.36-0.51, p <0.001). The composite reach score from the Y Balance Test was also significantly associated with hip abduction, flexion and extension (adjusted R^2: 0.29-0.44, p <0.001). Thus, greater isometric hip muscle strength was associated with greater hip function.

Discussion

This is the first study to compare functional performance and muscle strength between patients with hip dysplasia scheduled for PAO and healthy subjects. Functional performance, assessed by the single-leg hop test and Y Balance Test, was significantly reduced in patients with hip dysplasia compared to healthy subjects. The differences observed between groups were all clinically relevant, except for the anterior direction on the Y Balance Test. Isometric muscle strength did not differ between groups for hip abduction and hip extension but was significantly higher in hip flexion for healthy subjects. Differences in both isometric hip flexion and abduction were clinically relevant. Furthermore, hip abduction, flexion and extension muscle strength were all associated with functional performance tests in both legs for patients with hip dysplasia. There were no differences in any of the three directions of the normalised Y Balance Test, nor in the composite reach score, between the index and contralateral leg in patients with hip dysplasia. The same was found for isometric hip abduction, flexion and extension muscle strength. A small significant difference (4.2 cm (95% CI: 0.3;8.0)) was found in the single-leg hop test, but it was not considered clinically relevant. However, across performance and strength tests, the contralateral leg performed slightly better than the index leg. The stratified sensitivity analysis revealed that patients with unilateral hip dysplasia had significantly worse results for the index leg than for the contralateral leg in the posteromedial and posterolateral directions on the Y Balance Test, as well as significantly lower muscle strength in hip abduction and hip flexion. The differences were, however, not clinically relevant.

The cross-sectional design of the study prevents us from determining whether greater functional performance leads to greater muscle strength or vice versa. Two feasibility studies have investigated the effect of exercise in patients with hip dysplasia [9, 21]. Mortensen et al. found that 8 weeks of progressive resistance training improved functional performance measured with the standing distance jump and counter movement jump test [21]. Isometric hip flexion and extension in the affected leg, did not improve, nor did isokinetic hip extension. However, isokinetic hip flexion improved in the concentric phase with a mean difference at 15.8 Nm (95% CI: 5.9;25.8) after the resistance training intervention period [21]. Isometric hip flexion was 121.4 Nm (95% CI 95.4;147.4) in the index leg and 124.7 Nm (95% CI 102.0;147.4) in the contralateral leg before

the exercise intervention, nearly twice as high as the flexion strength measured in our study. De La Roche et al. studied muscle strength in 13 patients with hip dysplasia without previous pelvic surgery and 13 with previous pelvic surgery [3]. They found isometric hip abduction strength was 70.5 Nm (SD 26.1) for the patients without previous pelvic surgery and 56.4 Nm (SD 19.3) for the patients with previous pelvic surgery. Isometric hip flexion strength was 92.7 Nm (SD 33.9) for the patients without previous pelvic surgery and 62.2 Nm (SD 22.1) for the patients with previous pelvic surgery, measured with a isokinetic dynamometer [3]. Interestingly, patients in our study had hip flexion and abduction strength comparable to patients that had received previous pelvic surgery. In addition, Sucato et al. found that isometric hip abduction strength was 61.8 Nm while hip flexion strength was 82.4 Nm in a sample of 23 patients with hip dysplasia measured with a isokinetic muscle dynamometer [27]. Patients in our study therefore appear to have lower muscle strength than those in comparable studies, indicating more severe hip dysplasia in our sample.

Jacobsen et al. investigated the effects of 6 months of home-based exercise and patient education for hip dysplasia patients, finding improvements in functional performance (Y Balance Test and the single-leg hop), and isometric muscle strength (handheld dynamometer) [9]. The normalised single-leg hop test was 37 (IQR: 30;44) before the intervention, which corresponds well to the 42 (95% CI: 38;46) we found. The Y Balance Test scores were 8-14 cm better than the scores in our study, indicating a possible difference in disease severity. Foldager et al. investigated the reliability of the Y Balance Test among 51 healthy, active participants and found absolute reach scores of 62 cm (95% CI: 60;65) in the anterior direction, 105 cm (95% CI: 102;108) in the posteromedial direction, and 103 cm (95% CI: 101;106) in the posterolateral direction [5]. These results correspond with those of the healthy subjects in our study.

Limitations

The study has several limitations. Firstly, the study was a cross-sectional study so assumptions regarding causality cannot be made. Secondly, no matching was done between patients and healthy subjects. Thirdly, patients with hip dysplasia were enrolled in an ongoing randomised controlled trial, receiving either surgery

followed by progressive resistance training or progressive resistance training alone. Thus, the results are only generalisable to patients willing to participate in a 12-month exercise trial. Fourthly, the healthy subjects had a lower BMI, suggesting a healthier lifestyle, possibly due to volunteer bias, were participation associated with health consciousness and a more active lifestyle than the general population. This could lead to an overestimation of the differences between patients and healthy subjects. In addition, BMI could be a confounder for the associations presented. Fifth, the absence of information on leg dominance and pain severity may have influenced the results.

Conclusion

Patients with hip dysplasia had significantly worse functional performance, measured with the single-leg hop test and Y Balance Test, compared to healthy subjects. While isometric muscle strength in hip abduction and extension was comparable between the groups, a significant deficit in hip flexion strength was observed in the hip dysplasia patients. Additionally, muscle strength in hip abduction, flexion, and extension was significantly associated with functional performance in both legs of patients with hip dysplasia. These results indicate that targeted interventions to improve muscle strength and overall functional performance may be warranted in this patient population.

Key points

We found that patients with hip dysplasia have impaired functional performance and hip muscle strength compared to healthy subjects. Therefore, healthcare professionals should consider including specific exercises to improve functional performance and muscle strength in hip dysplasia rehabilitation. Furthermore, muscle strength was associated with functional performance. A such, strengthening the hip muscles, may potentially lead to improvements in functional performance. The most important limitations of the study was the cross-sectional study design and the lack of matching between patients and healthy subjects.

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Ethics: The study was approved by the Central Denmark Region Committee on Biomedical Research Ethics (j. no. 1-10-72-234-18) and registered at the Central Denmark Region's internal list of research projects (j. no. 1-16-02-120-19). Before inclusion, all participants gave written consent in accordance with the Declaration of Helsinki II.

Trial registration: The study was a part of a randomised controlled trial registered at ClinicalTrials.gov with ID number NCT03941171

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Author's Contribution statement: LT, SJ, UD and IM designed the study and performed the approval applications. LT, SJ, OO and MH included all patients and LT and LM included all healthy subjects. LT, TK and LM performed all the functional tests. LT conducted the data analysis and drafted the manuscript, while IM revised it several times. All authors revised the manuscript and approved the final version.

Conflict of interest: None of the authors has any conflict of interest.

Patient and Public Involvement: Before initiating the randomised controlled trial, which this project was a part of, a group of patients with hip dysplasia were interviewed to gaining knowledge on the patients thoughts on the trial design and and thoughts related to participating in a clinical trial with the purpose of investigating efficacy of PAO compared with resistance training. The PPI has been reported elsewhere [25].

Data sharing statement: All data are available upon reasonably request, however not until the original trial has been published. Please contact the corresponding author by e-mail.

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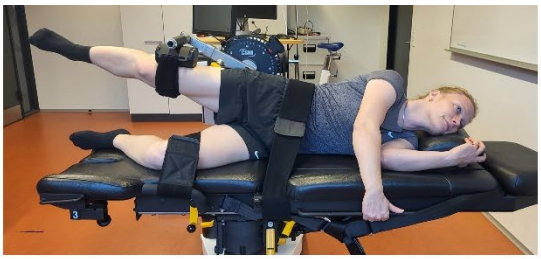
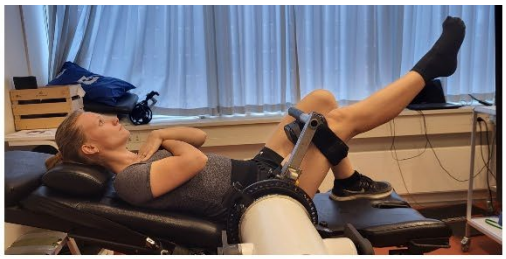
Figure 1. Test setup for isometric muscle strength in (A) hip abduction and (B) hip flexion and extension using a Humac Norm isokinetic dynamometer and the starting position (C) and end position (D) for the single-leg hop for distance test, as well as the end position for the Y Balance Test in (E) anterior direction, (F) posteromedial direction and (G) posterolateral direction using the Y Balance Test Kit.

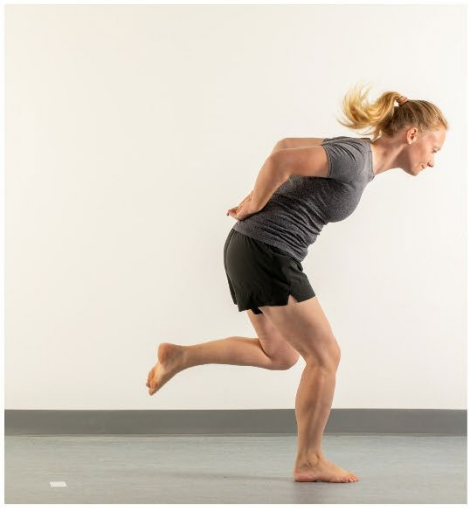


A: isometric hip abduction



B: isometric hip flexion/extension

C: starting position for the single-leg hop test



D: end position for the single-leg hop test

E: anterior direction for the Y Balance Test

F: posteromedial direction for the Y Balance Test

G: posterolateral direction for the Y Balance Test

436 **Table 1.** Participant characteristics

437

	Hip dysplasia patients n = 59	**Healthy subjects** n = 39	**P**
Women, n (%)	51 (86.4)	29 (74.4)	0.13
Age (years), mean (SD)	27.5 (5.6)	26.6 (4.9)	0.45
Height (m), mean (SD)	1.71 (0.1)	1.73 (0.1)	0.26
Weight (kg), mean (SD)	70.6 (11.0)	66.5 (9.8)	0.06
BMI kg/m^2, mean (SD)	24.2 (3.1)	22.2 (1.8)	<0.001
The Forgotten Joint Score, median (IQR)	20.8 (12.5;35.4)	100 (100;100)	<0.001
The Visual Analogue Scale (mm), median (IQR)			
In rest	55 (30;68)	0 (0;0)	<0.001
In activity	65 (50;73)	0 (0;0)	<0.001
Hip affected, n (%)			
Right hip	16 (27.1)	NA	
Left hip	9 (15.3)		
Bilateral	34 (57.6)		

438 [a]Highest completed educational level. One healthy subject lacked information on both Visual Analogue Scale
439 measurements, another was missing the Forgotten Joint Score, and one had not filled out the question regarding alcohol
440 consumption. BMI: Body Mass Index. IQR: Interquartile Range. n: number. SD: Standard Deviation.

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Table 2. Functional performance and isometric muscle strength in patients with hip dysplasia and in healthy subjects.

	Hip dysplasia patients				Healthy subjects		
	Index	Contralateral	Difference[b]	P	Right	Difference[c]	P
Single-leg hop for distance							
Absolute, cm	71.7 (64.4;79.0)	75.9 (68.5;83.4)	4.2 (0.3;8.0)	0.03	106.0 (97.7;114.4)	34.3 (23.2;45.4)	<0.001
Normalised to height, cm/m	41.9 (37.7;46.1)	44.4 (40.1;48.6)	2.4 (0.2;4.7)	0.04	61.2 (57.0;65.4)	19.3 (13.1;25.4)	<0.001
Y Balance Test							
Absolute reach							
Anterior, cm	56.4 (54.2;58.6)	56.5 (54.5;58.5)	0.1 (-1.1;1.3)	0.86	63.8 (60.9;66.7)	7.4 (3.8;10.9)	<0.001
Posteromedial, cm	93.8 (89.9;97.7)	95.0 (91.2;98.8)	1.2 (-0.3;2.7)	0.12	107.6 (104.3;110.9)	13.8 (8.3;19.2)	<0.001
Posterolateral, cm	89.6 (85.8;93.4)	91.4 (87.6;95.2)	1.8 (0.1;3.5)	0.04	101.9 (98.9;105.0)	12.3 (7.1;17.6)	<0.001
Composite reach, cm	239.8 (230.6;249.1)	242.9 (234.1;251.8)	3.1 (-0.4;6.7)	0.08	273.3 (265.2;281.3)	33.4 (20.4;46.4)	<0.001
Normalised reach[a]							
Anterior, %	62.9 (60.3;65.4)	63.0 (60.7;65.2)	0.1 (-1.3;1.5)	0.91	73.0 (69.6;76.4)	10.1 (6.0;14.2)	<0.001
Posteromedial, %	104.5 (100.3;108.8)	105.8 (101.6;110.0)	1.3 (-0.4;3.0)	0.14	123.1 (119.5;126.7)	18.6 (12.6;24.5)	<0.001
Posterolateral, %	99.9 (95.6;104.3)	101.8 (97.6;106.1)	1.9 (-0.1;3.9)	0.06	116.8 (113.0;120.5)	16.9 (10.8;22.9)	<0.001
Composite reach, %	89.1 (85.6;92.6)	89.0 (85.6;92.4)	-0.1 (-0.4;0.2)	0.56	104.3 (101.1;107.4)	15.2 (10.3;20.1)	<0.001
Isometric muscle strength							
Hip abductor, Nm	57.6 (50.5;64.6)	62.3 (56.1;68.4)	4.7 (0.1;9.3)	0.05	67.8 (59.0;76.6)	10.2 (-0.9;21.3)	0.07
Hip flexor, Nm	62.7 (55.4;70.1)	66.3 (59.3;73.2)	3.5 (-0.8;7.8)	0.11	77.6 (68.4;86.8)	14.9 (3.9;26.4)	0.01
Hip extensor, Nm	153.2 (134.6;171.8)	157.9 (141.6;174.2)	4.7 (-5.5;15.0)	0.36	169.9 (149.2;190.7)	16.8 (-11.3;44.9)	0.24

[a]Normalised for limb length, by dividing with the leg length and multiplying with 100. [b]The difference between the index- and contralateral leg for hip dysplasia patients. [c]The difference between the healthy subjects right leg and the index leg for hip dysplasia patients. The composite reach score was calculated as the sum of the three directions and normalised this way: (the sum of the three directions) / (3 x leg length) x 100. Data is presented as mean with 95% confidence interval (95% CI). Diff: Difference. SD: Standard Deviation.

Table 3. Functional performance and isometric muscle strength in patients with unilateral hip dysplasia and patients with bilateral hip dysplasia.

	Hip dysplasia patients with unilateral hip dysplasia (n=25)				Hip dysplasia patients with bilateral hip dysplasia (n=34)			
	Index	Contralateral	Difference	P	Index	Contralateral	Difference	P
Single-leg hop for distance								
Absolute, cm	71.2 (62.6;85.9)	79.4 (67.2;91.6)	5.2 (0.2;10.1)	0.04	69.9 (60.1;79.7)	73.4 (63.6;83.2)	3.5 (-2.3;9.3)	0.23
Normalised to height, cm/m	43.3 (36.6;50.0)	46.3 (39.4;53.2)	3.0 (0.1;5.9)	0.05	40.9 (35.3;46.6)	42.9 (37.3;48.6)	2.0 (-1.4;5.5)	0.24
Y Balance Test								
Absolute reach, cm								
Anterior	55.4 (52.1;58.8)	56.2 (53.1;59.3)	0.8 (-0.9;2.4)	0.35	57.1 (54.0;60.2)	56.8 (54.0;59.5)	-0.4 (-2.2;1.5)	0.68
Posteromedial	95.4 (89.7;101.1)	93.6 (87.2;100.0)	1.8 (-0.2;3.8)	0.08	94.0 (88.9;99.1)	94.7 (89.4;100.0)	0.7 (-1.5;2.9)	0.50
Posterolateral	93.4 (88.2;98.7)	89.8 (83.9;95.8)	3.6 (1.7;5.5)	<0.001	89.5 (84.2;94.7)	90.0 (84.5;95.5)	0.5 (-2.1;3.1)	0.70
Composite reach	245.0 (232.0;258.1)	238.9 (223.9;253.8)	6.2 (1.9;10.4)	0.006	240.6 (228.9;253.0)	241.4 (228.9;253.9)	0.9 (-4.5;6.2)	0.74
Normalised reach[a], %								
Anterior	61.7 (58.2;65.2)	62.8 (59.4;66.2)	1.1 (-0.7;2.8)	0.23	63.7 (60.1;67.4)	63.1 (60.0;66.2)	-0.7 (-2.7;1.4)	0.53
Posteromedial	106.6 (100.4;112.8)	104.2 (97.4;110.9)	2.4 (0.1;4.6)	0.04	104.8 (99.0;110.5)	105.2 (99.4;111.1)	0.5 (-2.0;2.9)	0.71
Posterolateral	104.4 (98.7;110.0)	100.0 (93.7;106.3)	4.3 (2.3;6.4)	<0.001	99.9 (93.6;106.1)	100.0 (93.8;106.2)	0.1 (-2.9;3.2)	0.93
Composite reach	88.9 (83.7;94.1)	88.6 (83.4;93.9)	0.2 (-0.02;0.5)	0.07	89.5 (84.6;94.3)	89.1 (84.4;93.8)	-0.3 (-0.8;0.1)	0.16
Isometric muscle strength, Nm								
Hip abductor	62.8 (52.1;73.5)	53.6 (42.3;64.9)	9.2 (1.5;16.8)	0.02	60.5 (51.1;69.9)	61.9 (54.1;69.7)	1.4 (-4.4;7.1)	0.63
Hip flexor	71.2 (59.8;82.6)	63.9 (52.5;75.3)	7.3 (1.4;13.2)	0.02	61.9 (51.7;72.0)	62.6 (53.5;71.7)	0.7 (-5.4;6.9)	0.81
Hip extensor	161.8 (135.1;188.5)	151.2 (121.5;181.0)	10.6 (-3.7;24.8)	0.14	154.6 (129.5;179.7)	155.1 (133.5;176.6)	0.5 (-14.3;15.2)	0.95

[a]Normalised for limb length, by dividing with the leg length and multiplying with 100.

Table 4. Associations between functional performance (the single-leg hop test and the Y Balance Test), and isometric muscle strength in patients with hip dysplasia.

	Single-leg hop for distance, cm					Composite reach[a], %				
Muscle strength, Nm	Crude β (95% CI)	P	Adjusted β (95% CI)	R^2	P	Crude β (95% CI)	P	Adjusted β (95% CI)	R^2	P
Index leg										
Abduction	0.51 (0.27;0.75)	<0.001	0.47 (0.20;0.74)	0.36	0.001	0.25 (0.14;0.36)	<0.001	0.34 (0.22;0.46)	0.44	<0.001
Flexion	0.46 (0.22;0.69)	<0.001	0.49 (0.21;0.76)	0.36	0.001	0.16 (0.04;0.27)	0.010	0.28 (0.14;0.42)	0.31	<0.001
Extension	0.19 (0.10;0.28)	<0.001	0.22 (0.11;0.33)	0.40	<0.001	0.06 (0.01;0.10)	0.019	0.11 (0.05;0.17)	0.29	<0.001
Contralateral leg										
Abduction	0.61 (0.33;0.88)	<0.001	0.62 (0.32;0.93)	0.42	<0.001	0.17 (0.03;0.30)	0.016	0.28 (0.12;0.43)	0.24	0.001
Flexion	0.60 (0.37;0.84)	<0.001	0.70 (0.44;0.95)	0.51	<0.001	0.18 (0.07;0.30)	0.002	0.34 (0.22;0.47)	0.34	<0.001
Extension	0.20 (0.09;0.31)	0.001	0.23 (0.10;0.36)	0.38	0.001	0.05 (0.00;0.11)	0.037	0.12 (0.06;0.18)	0.24	<0.001

[a]Normalised for limb length. The composite reach score was calculated and normalised this way: (the sum of the three directions a) / (3 x leg length) x 100. Adjusted for age, sex, height and weight. β: regression coefficients describing the difference in the dependent variable expected with a 1 cm hop difference. R^2: coefficient of determination.

Paper III – The FEAR index study

Is the Femoral-Epiphyseal Acetabular Roof (FEAR) index associated with hip pain in patients with hip dysplasia?

Lisa Urup Tønning, Markus Schmid, João Barroso, Benedicte Hovind, Dunia Hessain, Marie Balling, Stig Storgaard Jakobsen & Inger Mechlenburg

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Abstract

Background: Micro instability of the hip joint has been suggested to cause pain in patients with hip dysplasia. Recently, the Femoral-Epiphyseal Acetabular Roof (FEAR) index has been developed to evaluate hip instability in patients with dysplasia.

Purpose: To investigate associations between the FEAR index and patient-reported outcomes before and six months after periacetabular osteotomy (PAO).

Material and Methods: Radiographs of patients with hip dysplasia who underwent PAO between 2018 and 2020 were retrospectively assessed by a radiologist and an orthopedic surgeon. Radiographic measurements indicative of hip instability (Shenton's line, FEAR index, center-edge angle of Wiberg, acetabular index of Tönnis, and the femoral neck-shaft angle) were measured. Data on hip pain, function, and quality of life were collected prospectively using the Hip dysfunction and Osteoarthritis Outcome Score (HOOS).

Results: A total of 222 patients were included in the study. All radiographic measurements and patient-reported outcomes improved significantly from preoperative to six months postoperative ($P < 0.001$). There were no differences in the change score of patient-reported outcomes between patients with a FEAR index >2° (indicative of hip instability) and patients with a FEAR index ≤2°.

Conclusion: The FEAR index was not associated with hip pain, function, and quality of life among patients with hip dysplasia. This study did not find evidence supporting that instability defined by the FEAR index caused pain in patients with hip dysplasia.

Keywords

Hip dysplasia, Femoral-Epiphyseal Acetabular Roof index, patient-reported outcomes, Hip dysfunction and Osteoarthritis Outcome Score, hip instability

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Introduction

Hip dysplasia is a developmental joint disease characterized by a shallow and oblique acetabulum, laxity of ligamentous structures, and anteverted femur, leading to insufficient coverage of the femoral head (1–3). The main radiographic measures used to assess hip dysplasia are the center-edge angle of Wiberg (CE angle) and the acetabular index of Tönnis (AI angle). According to Wiberg, a normal hip has a CE angle >25°, while a dysplastic hip has a CE angle of <20° (4); a hip with a CE angle in the range of 20°–50° is considered borderline dysplastic (5).

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Patients with hip dysplasia experience pain (6), altered gait pattern (7,8), and often muscle-tendon pain (9). Micro instability, defined as extra physiologic hip motion due to the reduced acetabular coverage of the femoral head, has been suggested to be a cause of pain among patients with hip dysplasia (10,11). Periacetabular osteotomy (PAO) is the surgical treatment of choice for patients with hip dysplasia (12). In short, the osteotomized acetabular fragment is reoriented in an adducted, extended, and rotated position, and fixated with screws (13).

Recently, a new radiographic measurement, the Femoral-Epiphyseal Acetabular Roof (FEAR) index, has been developed to identify if a hip joint is unstable among patients with borderline hip dysplasia (14). The FEAR index has been found to be associated with instability and may guide the surgeon to decide on the correct treatment (14).

The primary aim of the present study was to investigate associations between the FEAR index and patient-reported outcomes before and six months after PAO. We hypothesized that patients with a FEAR index >2° indicative of hip instability would have a worse patient-reported outcome score before PAO than patients with a FEAR index ≤2° not indicative of hip instability, and thus a better improvement six months after PAO. The secondary aim was to investigate radiographic measurements indicative of hip instability before and six months after PAO and report inter-rater reliability of measurements.

Material and Methods

This was a retrospective cohort study with prospectively collected data on patient-reported outcomes. According to Danish law, ethics approval was not required. The study was registered at Central Denmark Region's internal list of research projects (j. no. 713207).

Patients

Information on patient characteristics and patient-reported outcomes used in this study has been collected from an institutional database with data on all patients undergoing PAO at either **Aarhus University Hospital** or **Mølholm Private Hospital** in **Denmark** since 2004 . In this study, all patients undergoing PAO at one of the two hospitals between 1 January 2018 and 31 December 2020 were included. If a patient had undergone PAO of both hips within the specified period, only data on the second surgery was included. If a patient had two identical entries, the first entry was included as the second entry might be a double entry. If the preoperative radiographs were missing, or if measurements were not possible due to incomplete radiographs, the patient was excluded. PAO was performed using the minimally invasive transsartorial approach in all included patients (13). The indications for PAO were as follows: (i) clinically verified symptomatic hip dysplasia with persistent hip pain and reduced function; (ii) a CE angle <25° and an AI angle >10°; (iii) hip congruence (if in doubt a 25° abduction radiograph was obtained); (iv) pelvic bone maturity; (v) range of motion >15° internal and external rotation and >110° hip flexion; (vi) absence of osteoarthritis defined as having a Tönnis grade of 0 or a joint space width ≥3 mm; (vii) body mass index ≤25 kg/m^2; (viii) age ≤45 years; (ix) reduced range of motion indicating joint degeneration; and (x) lack of hip congruence (15).

Radiographic measurements

A radiologist (**MS**) performed all the radiographic measurements on pre- and postoperative anteroposterior digital radiographs. In addition, an orthopedic surgeon (**JB**) performed the same measurements to investigate the inter-rater reliability in the latest 200 patients. In daily clinical practice, the orthopedic surgeon often performs these measurements. The two raters where blinded to the results of the other as well as to patient-reported outcomes. All radiographic measurements were performed using the digital measurement tool IMPAX client 6.5 (AGFA HealthCare, Mortsel, Belgium). To address hip instability, the following radiographic measurements indicative of hip instability were used: Shenton's line; the FEAR index; the CE angle; the AI angle; and the femoral neck-shaft angle (NSA) (Fig. 1) (16). According to Wyatt and Beck, the estimated predictive value of the radiographic measurement to detect instability is 100% if the Shenton's line is broken, 92% if the FEAR index is >2°, 70% if the CE angle is <20°, 70% if the AI angle is >10°, and 55% if the NSA is >135°.

The Shenton's line is an arc drawn from the inferior border of the femoral neck to the superior border of the obturator foramen (17). The CE angle is the angle between a line drawn through the femoral head and perpendicular to a horizontal line drawn between the center of the two femoral heads, and a line drawn from the lateral edge of the acetabular roof and through the center of the femoral head (18). The AI angle is the angle between the horizontal inter-teardrop line and a line from the lateral to the medial point of the weight-bearing part of the acetabulum (18). The NSA is the angle between a line drawn along the axis of the femoral neck to the center of the femoral head and the axis of the femoral shaft (19).

The FEAR index is formed by the angle between the acetabular roof and the central third of the femoral growth plate (14). It is measured between a line connecting the most medial and lateral point of the sourcil and a line connecting the medial and lateral end of the straight part of the physeal scar of the femoral head. The angle is positive when the vertex is medial and negative when the vertex is lateral. Initially, a cutoff of 5° was introduced to differentiate

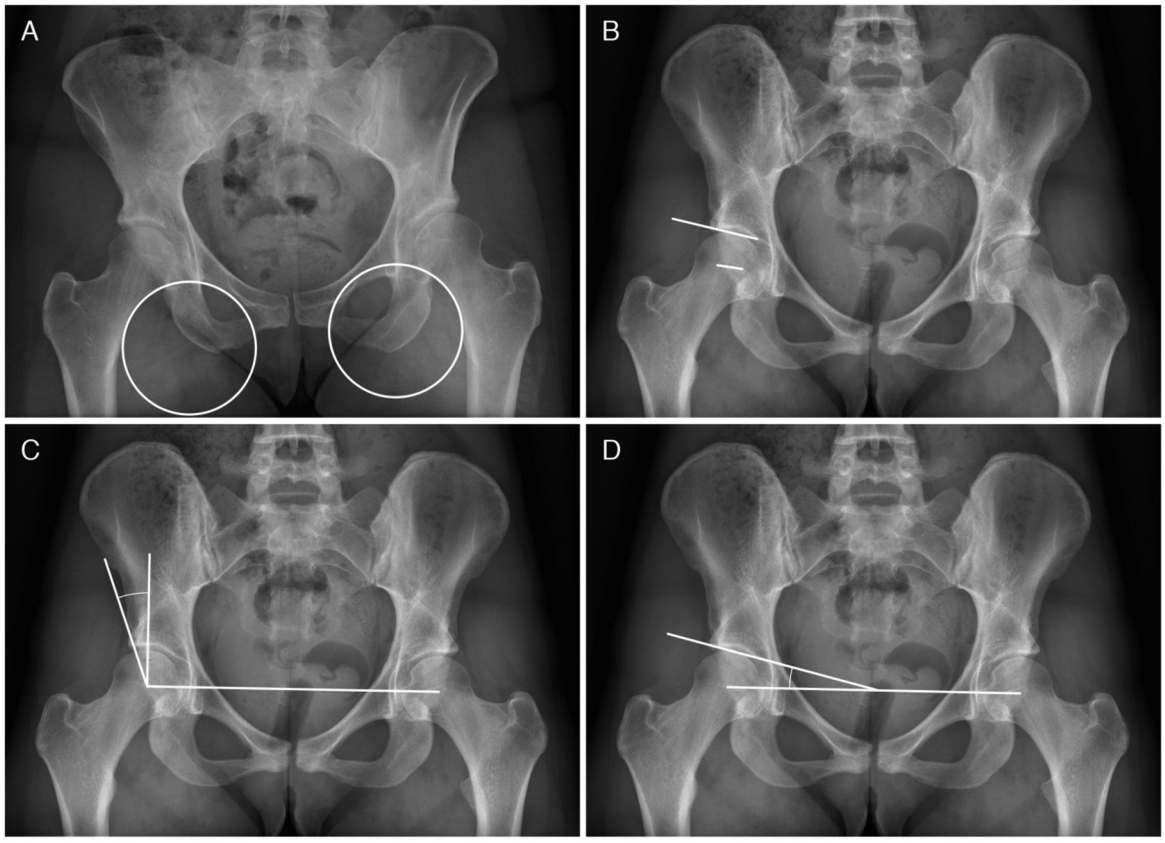

Fig. 1. Radiographic measurement of (a) a broken Shenton's line on the left hip, (b) the FEAR index, (c) the CE angle, and (d) the AI angle. AI, acetabular index; CE, center-edge; FEAR, Femoral-Epiphyseal Acetabular Roof.

between a stable and unstable hip among patients with borderline hip dysplasia (14). However, a cutoff of 2° has been found to be more precise, predicting hip instability with a 90% probability (20). Thus, a hip with a FEAR index ≤2° should be considered stable and a hip with a FEAR index >2° should be considered unstable (16). The FEAR index has been found to be highly reliable with excellent intra-rater and inter-rater agreement (14).

Patient-reported outcomes

One of the patient-reported questionnaires providing prospectively collected data to the institutional database is the Hip dysfunction and Osteoarthritis Outcome Score (HOOS) version 2.0 (21). The HOOS has five separate subscales: pain; symptoms; activity limitations of daily living; activity limitations in sport and recreation; and hip-related quality of life (22,23). A score is calculated for each subscale and transformed to a score of 0–100, where 0 indicates extreme problem and 100 indicates no problem. The HOOS version 2.0 has been validated in a group of patients undergoing total hip replacement due to osteoarthritis (22) and has been found sensitive to measure changes over time (24). In addition, the HOOS has shown adequate internal consistency and external validity among patients with hip dysplasia undergoing PAO (25). The minimal clinically important difference for HOOS in a group of patients with hip dysplasia undergoing PAO has been reported to be 9 for pain and 6–11 for the other subscales (26).

Statistical analysis

Descriptive statistics are presented as means with 95% confidence intervals (95% CI) for all normally distributed continuous variables and as numbers with percentages for all categorical variables. Proportions for categorical variables were compared with the chi-square test and continuous radiographic measures were compared with the Student's *t*-test. Changes in HOOS scores from preoperative to postoperative for the entire cohort, as well as between patients with a FEAR index >2° and patients with a FEAR index ≤2° were also compared with the Student's *t*-test. Since the FEAR index was originally intended for patients with borderline hip dysplasia (defined as having a preoperative CE angle in the range of 20°–25°), a sub-analysis within this group was performed. For the inter-rater reliability analysis, the intraclass coefficient (ICC) and Cohen's Kappa statistics were applied. The ICC was interpreted as

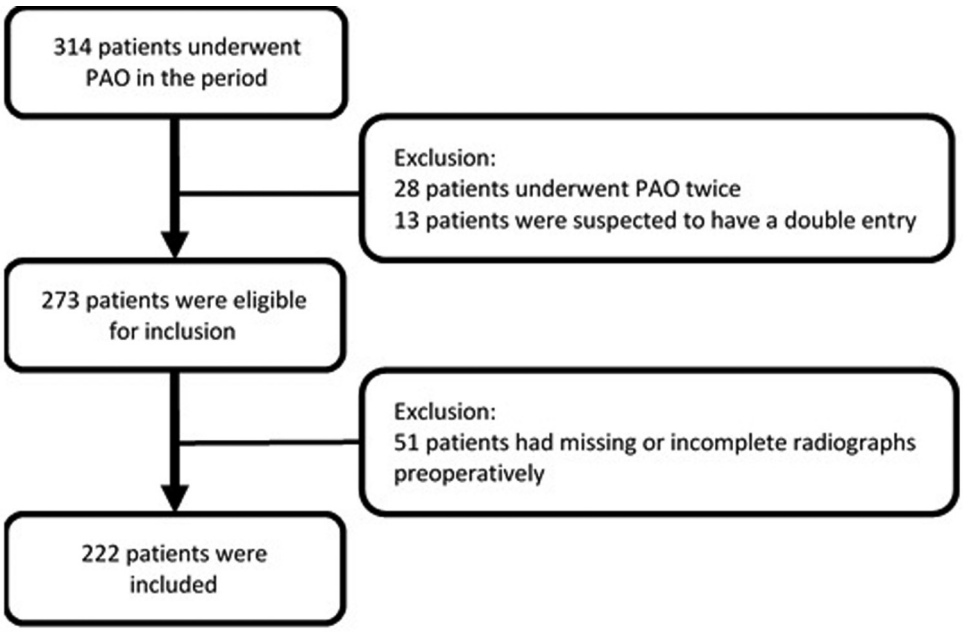

Fig. 2. Flow chart of included patients treated with PAO between 2017 and 2020. PAO, periacetabular osteotomy.

follows: <0.5 = poor reliability; 0.5–0.75 = moderate reliability; 0.75–0.9 = good reliability; and >0.9 excellent reliability) (27). Cohen's Kappa was interpreted as follows: <0.00 = poor agreement; 0.00–0.20 = slight agreement; 0.21–0.40 = fair agreement; 0.41–0.60 = moderate agreement; 0.61–0.80 = substantial agreement; and >0.80 = perfect agreement (28). All statistical analyses were performed in Stata version 17.0 (StataCorp LLC, College Station, TX, USA).

Results

Within the study period, 314 **Danish** patients underwent PAO at the two study hospitals. Of these, 273 patients were eligible for inclusion. However, only 222 (81%) patients were included in the analysis due to missing or incomplete preoperative radiographs (Fig. 2). Included patients were primarily women (89%) with a mean age of 28 years (95% CI = 27–29 years) (Table 1).

Radiographic measurements indicative of hip instability improved as intended by PAO (Table 2). In addition, the number of patients classified as unstable decreased from 69 (33%) to 14 (7%) ($P < 0.001$). A total of 77 (53%) patients with a FEAR index ≤2° had borderline dysplastic hips preoperatively, defined by a CE angle in the range of 20°–25° and the mean FEAR index was −6° (−7° to –5°) for this group of patients. A total of 58 (40%) patients with a FEAR index ≤2° had a CE angle <20° and 11 (8%) had a CE angle >25°. For patients with a FEAR index >2°, 13 (17%) had borderline dysplastic hips preoperatively and the mean FEAR index was 6 (95% CI = 4–8) for this group of patients. A total of 63 (83%) patients with a FEAR index >2° had a CE angle <20° and there were no patients with a CE angle >25°. The proportion of patients with a CE angle in the range of 20°–25° was significantly higher among patients with a FEAR index ≤2° ($P < 0.001$).

Patients improved significantly in all five HOOS subscales from preoperative to six months postoperatively (<0.001) (Table 3). The difference was clinically relevant for all five subscales. When comparing patients with a FEAR index ≤2° and a FEAR index >2°, there were no significant differences in the change scores between the groups. This means that patient-reported hip pain, function, and quality of life were similar among patients with a stable and an unstable hip joint, identified by the FEAR index. In addition, the sub-analysis only including patients with borderline hip dysplasia and complete HOOS data did not show a significant difference in the change scores (Table 3).

The ICC between the two raters was in the range of 0.80–0.91 and was overall interpreted as a good reliability (Table 4). The Cohen Kappa for the Shenton's line was 0.32–0.42, indicating a fair to moderate agreement between the two raters.

Discussion

The present study found no differences in patient-reported outcomes between patients with an unstable hip, defined as having a preoperative FEAR index >2° and patients with a stable hip, defined as having a preoperative FEAR index ≤2°. In addition, the sub-analysis of patients with

Table 1. Baseline characteristics of the entire cohort of patients with a FEAR index ≤2° and patients with a FEAR index >2°.

	Total	FEAR ≤2°	FEAR >2°
No. of patients	222 (100)	146 (66)	76 (34)
Women	198 (89)	129 (88)	69 (91)
Age at the time of PAO (years)	28 (27–29)	28 (27–30)	28 (26–30)
Right side	126 (57)	80 (55)	46 (61)
Level of education			
General certificate of secondary education	42 (21)	31 (23)	11 (16)
Upper secondary school leaving	41 (20)	26 (19)	15 (22)
Vocational upper secondary education	28 (14)	21 (16)	7 (10)
Short-cycle higher education	19 (9)	13 (10)	6 (9)
Medium-cycle higher education	23 (11)	13 (10)	10 (15)
Bachelor education	26 (13)	17 (13)	9 (13)
Long-cycle higher education	23 (11)	14 (10)	9 (13)
PhD education	1 (0.5)	0 (0)	1 (1)
Tönnis score >0*	1 (0.5)	1 (0.7)	0 (0)
Positive Cam morphology	12 (5)	10 (7)	2 (3)

Values are given as n (%) or mean (95% CI).
*In one patient this information was missing, the results are thus based on 221 patients.
CI, confidence interval; FEAR, femoral-epiphyseal acetabular roof; PAO, periacetabular osteotomy.

Table 2. Radiographic measurements indicative of hip instability preoperatively and six months postoperatively for the entire cohort.

	n	Preoperative	Postoperative	*P*
Radiographic measurements indicative of hip instability				
Broken Shenton's line	214	20 (9)	6 (3)	<0.001
FEAR index	209	−1 (−3 to −0.3)	−12 (−13 to −10)	<0.001
Patients with a FEAR index >2°		69 (33)	14 (7)	<0.001
CE angle, mean (95% CI)	214	18 (17–19)	28 (27–29)	<0.001
Patients with a CE <20°		116 (54)	20 (9)	<0.001
AI angle	214	13 (12–14)	5 (4–6)	<0.001
Patients with an AI >10°		141 (66)	27 (13)	<0.001
NSA	222	135 (134–136)		
Patients with a NSA >135°		100 (45)		
Other radiographic measurements				
Extrusion index	214	0.27 (0.26–0.28)	0.18 (0.17–0.19)	<0.001
Positive PWS	214	113 (53)	38 (18)	<0.001
Positive cross-over sign	214	73 (34)	33 (15)	<0.001
Positive cliff sign	214	133 (62)	117 (55)	<0.001

Values are given as n (%) or mean (95% CI).
AI, acetabular index; CE, Wiberg's center-edge; CI, confidence interval; FEAR, femoral-epiphyseal acetabular roof; NSA, femoral neck-shaft angle; PAO, periacetabular osteotomy; PWS, posterior wall sign.

borderline hip dysplasia did not find differences in HOOS change scores between the two groups. In contrast to this, Zimmerer et al. found that patients with a FEAR index >2° reported significantly lower improvements in hip pain measured by the International Hip Outcome Tool-12 (iHOT-12) and a visual analogue scale (VAS), compared to patients with a FEAR index ≤2° (29). These patients had a CE angle in the range of 18°–25° and the change was calculated from preoperative to a mean of 43.8 months after hip arthroscopy. The contrasting results may be explained by differences in treatment as well as the small study sample of 36 patients divided into four clusters in the study by Zimmerer et al. (29). It is worth noticing that even though there were no differences between patients with a preoperative FEAR index >2° and patients with a preoperative FEAR index ≤2°, the cohort had a significant and clinically relevant improvement in all patient-reported outcomes measured by the HOOS.

The reliability of the radiographic measurements was generally good, except for the Shenton's line. The ICC was in the range of 0.80–0.91, indicating some disagreement. The differences in inter-rater agreement indicate that using only

Table 3. Analysis of the HOOS scores before and six months after PAO between patients with a FEAR index ≤2° and for patients with a FEAR index >2°.

	Total cohort (n = 195)		FEAR ≤2° (n = 129)		FEAR >2° (n = 66)		
HOOS	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative	*P**
Pain	49.1 (46.5–51.9)	76.4 (73.6–79.3)†	48.5 (45.1–52.0)	75.4 (71.5–79.3)†	50.5 (46.2–54.7)	78.4 (74.7–82.2)†	0.72
Symptoms	46.6 (43.9–49.4)	71.0 (68.1–73.9)†	46.6 (43.1–50.1)	70.2 (66.3–74.1)†	46.7 (42.3–51.1)	72.5 (68.4–76.6)†	0.49
ADL	60.1 (57.1–63.0)	83.1 (80.5–85.7)†	59.5 (55.8–63.3)	81.7 (78.2–85.2)†	61.2 (56.4–66.0)	85.9 (82.4–89.3)†	0.35
Sport	39.5 (36.1–42.8)	67.6 (64.1–71.2)†	39.1 (34.7–43.5)	65.7 (61.1–70.4)†	40.2 (35.0–45.3)	71.3 (66.2–76.4)†	0.25
QoL	29.8 (27.7–31.9)	57.7 (54.6–60.9)†	28.9 (26.4–31.5)	57.3 (53.2–61.3)†	31.4 (27.7–35.2)	58.6 (53.6–63.6)†	0.73
The sub-analysis of the patients with borderline hip dysplasia, defined as having a preoperative CE angle of 20°–25°							
	Total cohort (n = 79)		FEAR ≤2° (n = 66)		FEAR >2° (n = 13)		*P**
Pain	47.6 (43.4–51.8)	76.1 (71.3–81.0)†	47.1 (42.3–51.9)	75.5 (70.0–81.0)†	50.2 (40.5–59.9)	79.2 (68.1–90.3)†	0.92
Symptoms	46.6 (42.2–51.1)	70.4 (65.3–75.5)†	46.3 (41.2–51.4)	71.1 (65.4–76.7)†	48.5 (38.3–58.7)	66.9 (53.3–80.5)†	0.34
ADL	58.8 (54.3–63.4)	82.2 (77.6–86.9)†	57.9 (52.7–63.0)	81.1 (76.0–86.3)†	63.7 (53.9–73.5)	87.8 (77.3–98.3)†	0.88
Sport	37.3 (31.8–42.8)	66.9 (60.7–73.2)†	36.5 (30.2–42.7)	65.6 (58.7–72.6)†	41.3 (29.3–53.3)	73.6 (58.5–88.6)†	0.72
QoL	30.5 (27.3–33.9)	60.8 (55.4–66.2)†	29.1 (25.4–32.8)	60.3 (54.5–66.2)†	38.0 (30.0–45.9)	63.5 (47.3–79.6)†	0.40

Values are given as mean (95% CI).

**P* value for the difference in the change score between patients with a FEAR index ≤2° and patients with a FEAR index >2°.

†Statistically significant difference from preoperative to postoperative with a p-value <0.001.

ADL, activity limitations of daily living; CI, confidence interval; FEAR, femoral-epiphyseal acetabular roof; HOOS, Hip dysfunction and Osteoarthritis Outcome Score; PAO, periacetabular osteotomy; QoL, hip-related quality of life; Sport, activity limitations in sport and recreation.

Table 4. Inter-rater reliability of the five radiographic measurements indicative of hip instability.

	Preoperative (n = 165)		Postoperative (n = 165)	
	Inter-rater ICC (95% CI)	Agreement	Inter-rater ICC	Agreement
FEAR index	0.82 (0.76–0.86)	Good	0.80 (0.74–0.85)*	Good
CE angle	0.90 (0.87–0.93)	Good	0.86 (0.81–0.89)	Good
AI angle	0.90 (0.87–0.92)	Good	0.85 (0.80–0.89)	Good
NSA	0.88 (0.84–0.92)*	Good		
	Kappa (95% CI)	Agreement	Kappa (95% CI)	Agreement
Shenton's Line	0.42 (0.12–0.71)	Moderate	0.32 (−0.17 to 0.81)	Fair

*162 patients.

AI, acetabular index angle; CE, Wiberg's center-edge; FEAR, femoral-epiphyseal acetabular roof; ICC, intraclass coefficient; NSA, femoral neck-shaft angle; PAO, periacetabular osteotomy; PWS, posterior wall sign.

a single measurement to evaluate if a hip is stable or unstable is subject to some uncertainty. In the clinical setting, an evaluation should thus be backed up by measuring more than one of the radiographic measurements indicative of hip instability. Batailler et al. found the inter-rater reliability of the FEAR index, the CE angle, and the AI angle to be excellent (range = 0.91–0.96) (20). However, this may be due to differences in selection of patients, as the mean FEAR index was 8.3° ± 6.4 (20), compared to −1° (95% CI = −3 to –0.3) in our cohort.

Wyatt et al. developed the FEAR index to distinguish between stable and unstable hips among patients with borderline hip dysplasia (14). They suggest that patients with borderline hip dysplasia with a stable hip should be treated with hip arthroscopic surgery, while patients with borderline dysplasia with an unstable hip should undergo PAO (14). However, the PAO database in our study only contains information on patients who have undergone PAO. In 2018, a treatment algorithm by Danish orthopedic surgeons was published to guide clinicians when deciding the right treatment for young adults with hip pain in the interspace between PAO and hip arthroscopy (30). The treatment algorithm primarily relies on the CE angle as well as the posterior wall sign (PWS). In the future, the FEAR index should probably be incorporated in this algorithm. In this study, all patients who had undergone PAO between 1 January 2018 and 31 December 2020 at one of the two study hospitals were included. This meant that our cohort consisted of not only patients with borderline dysplasia as in the previously published literature on the FEAR index (14,20,29). This made it possible to investigate the FEAR index in a wide group of patients with hip dysplasia. Interestingly, only 17% of the patients with a FEAR index >2° had borderline dysplasia, while 53% of patients with a FEAR index ≤2° had borderline dysplasia.

As the FEAR index was the primary focus in this study, an association between the other radiographic measurements (Shenton's line, the CE angle, the AI angle, and the NSA) and the patient-reported outcomes were not investigated. However, Birch et al. found that the CE angle and the AI angle was not associated with the patients' health-related quality of life, measured with the Short Form-36 questionnaire among patients with hip dysplasia (18). Data were collected from the same database as the current study (18). We decided a priori to focus this paper on the FEAR index as this is a new measurement used in patients with hip dysplasia. In addition, the radiographic measurements used in this work were chosen a priori based on the article by Wyatt and Beck (16), as well as the data available. Other radiographic measurements related to hip dysplasia of interest could be the acetabular angles: the anterior-sector, the posterior-sector and the acetabular-anteversion angle (31); however, this would require that the patients had undergone computed tomography which was not the case.

A strength of this study was the use of a validated hip-specific questionnaire and the prospective data collection, eliminating the risk of recall bias. In addition, the HOOS has been found to be the most appropriate patient-reported outcome measure in patients undergoing PAO compared to the Western Ontario and Osteoarthritis Outcome Score (WOMAC) and the modified Harris Hip Score (25). The improvements found in all five subscales of HOOS in our study are similar to previously reported data on patients with hip dysplasia in other databases with prospective data collection (25,32,33), although previous studies compared patient-reported outcomes preoperatively to 12 months postoperatively. Another strength is the use of the same two blinded raters performing all radiographic measurements and investigating their inter-rater reliability. The measurements were performed by both a radiologist and an orthopedic surgeon, which increased the clinical relevance of the study as it is often the treating orthopedic surgeon who performs the radiographic measurements in clinical practice.

The present study also has some limitations. The first limitation is the amount of missing data in the database and the missing or incomplete radiographs. Only 81% of the included patients had useful radiographs and only

60% had both useful radiographs and preoperative and postoperative patient-reported outcomes. Second, the radiographic measurements were performed retrospectively, and the raters were thus not blinded to the treatment received. However, none of the two raters had been involved in the treatment decision or actual treatment of the included patients and the effect was thus considered minor.

In conclusion, the focus on hip instability in patients with hip dysplasia may be of interest to orthopedic surgeons. However, the FEAR index is not able to predict patient-reported outcomes after PAO. This suggests that hip instability might not be the driver of the symptoms in patients with hip dysplasia or that the FEAR index alone is not able to adequately define hip instability.

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Paper IV – The sports participation study

Sports participation among patients with hip dysplasia before and up to 20 years after periacetabular osteotomy

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Sports participation among patients with hip dysplasia before and up to 20 years after periacetabular osteotomy

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ABSTRACT

Background: Symptomatic hip dysplasia in skeletally mature young people is often treated with the periacetabular osteotomy (PAO). While studies have focused on radiographic and pain-related outcomes, evidence on sports participation is limited.

Hypothesis/Purpose: This study aimed to determine the proportion of patients who 1) participate in sports, 2) perform their preferred sports, and 3) report improved sports performance after PAO. A secondary aim was to investigate if preoperative patient characteristics could predict these outcomes during the first 5 years after PAO.

Study Design: This retrospective cohort study investigated self-reported sports function in patients who underwent PAO, using prospectively collected data from an institutional database.

Methods: Eligible patients had undergone PAO and completed at least one item related to sports participation. Patients reported on sports participation, ability to perform preferred sports and improvements in sports performance before PAO, as well as 6 months 2, 5, 10, 15 and 20 years after.

Results: Of 2398 patients surveyed, 1891 were eligible for inclusion. Out of the respondents at each time point, 45% reported participation in sports prior to PAO, and 56% and 60% reported sports participation 6 months and two years after PAO respectively. Being sports active, higher educational level or low pain levels before PAO, were associated with higher odds of participating in sports after PAO. Out of the respondents, improvement in sports function was reported by 56% at 6 months and 61% 2 years after PAO, and the ability to perform preferred sports was reported by 41% at 6 months to 63% at 15 years. Time, higher educational level or a good quality of life score were associated with higher odds performing preferred sports after PAO.

Conclusion: Up to 62% of patients undergoing PAO for hip dysplasia participate in sports after PAO. Over half report improved sports performance and eventually participate in their preferred sports. Being sports active or a better pain score before PAO was predictive of participating in sports, while a high quality of life score was predictive of performing preferred sports.

Key Terms: Hip Dysplasia, Periacetabular Osteotomy, Sports Participation, Sports Performance

What is known about the subject: Studies have shown that PAO surgery can improve hip pain, hip function and hip-related quality of life among patients with hip dysplasia [17]. In addition, physical activity and sports participation have also been found to improve following PAO [16].

What this study adds to existing knowledge: Our study confirms previous findings but does so based on a cohort that is almost 37 times larger than previous studies in a population ranging from those not participating in sports before PAO, to athletes competing at elite-level.

Clinical Relevance: Clinicians can use the results when informing patients about their prospects for return to sports, while making shared treatment decisions before undergoing PAO.

INTRODUCTION

Dysplasia of the hip is a developmental joint disease in which the hip socket does not cover the femoral head sufficiently [13]. The prevalence of hip dysplasia in Danish adults is estimated to be 3.4% [9], with the incidence of symptomatic hip dysplasia being up-to four times higher in women than in men [10], and with the risk of hip dysplasia being increased in those with a family history of the condition [4]. To assess whether a patient is suffering from hip dysplasia, a clinical evaluation and anteroposterior radiographs of the pelvis must be performed [6].

Reinhold Ganz first described the Bernese periacetabular osteotomy (PAO) in 1988 in order to preserve and normalise the anatomy of the hip joint, reduce pain, improve hip function and prevent degeneration of the hip joint [7]. This surgery allows for the acetabulum to be reoriented in three dimensions and increase the coverage of the femoral head. Over the years, multiple variations of the original surgical procedure have been developed [20].

Most studies investigating the effects of PAO have focused on radiographic measurements and pain-related outcomes, while evidence related to sports participation is limited [8,16]. A few studies report that patients undergoing PAO improve or maintain self-reported physical activity level after PAO, ranging from 42%-90% depending on population and assessment methodology [1,8,12,16]. However, these studies have a maximum follow up of five years and only included small patient samples (ranging from 36-111 patients).

To optimally treat patients following PAO and to inform patients about their likelihood of participate in sports after surgery, the identification of factors predicting the long-term outcome of PAO is crucial. Moreover, identifying preoperative characteristics that influence sports outcomes after PAO helps healthcare professionals inform patients about potential impact of surgery on sports participation, manage expectations, and guide treatment and rehabilitation decisions. Novais et al.

found that young age at surgery and a high preoperative physical activity level were significantly associated with a high self-reported physical activity score, measured with the University of California Los Angeles Activity Scale (UCLA-AS), one year after PAO in 51 patients [16]. However, demographic measures such as sex and Body Mass Index (BMI); preoperative self-reported pain (measured with the Western Ontario and McMaster universities osteoarthritis Index); and radiographic and surgical measures such as previous pelvic surgery, complications, and preoperative radiographic measurements (CE-angle, the anterior center-edge angle, and Tönnis grade) were not associated with self-reported physical activity one or two years after PAO.

Since 1998 Aarhus University Hospital and Mølholm Private Hospital have been systematically collecting clinical and demographic data on patients undergoing PAO both before and after surgery. This provides a unique opportunity for studying outcomes relating to sport in a large cohort of patients who has undergone PAO, followed for up to 20 years. The insights derived from such large-numbered longitudinal data may provide invaluable knowledge to both patients and clinicians when considering PAO.

Therefore, the primary aims of this study was to determine the proportion of patients that 1) participate in sports, 2) perform their preferred sports and 3) report improvements in sports performance, after PAO. The secondary aims were to investigate if the following preoperative patient characteristics (age, sex, education, BMI, CE-angle, AI-angle, pain, and quality of life) could predict the three sports related outcomes after PAO.

METHOD

This observational cohort study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[22], investigated the proportion of sports participation for

patients who had undergone PAO at either Aarhus University Hospital or Mølholm Private Hospital between 1st of January 1998 and 31st of December 2023. The study was approved by the Legal Office, Region Central Denmark (journal number 1-45-70-85-22) and reported to the Danish Data Protection Agency through registration at Region of Central Denmark's internal list of research projects (journal number 1-16-02-46-23).

Patients

Indications for PAO surgery at the two hospitals during the 26-year period were (i) persistent hip pain and reduced function, (ii) radiographically verified hip dysplasia, defined as having a CE-angle <25°, (iii) skeletal maturity and (iv) absence of hip subluxation. Contraindications for PAO were (i) reduced range of motion, defined as internal rotation ≤15° and hip flexion ≤110°, (ii) hip osteoarthritis defined as having a Tönnis grade >0, (iii) BMI >25 and (iv) age >45 years. The latter three contraindications were added in 2016. Since 2004 the minimally invasive transartorial approach has been used when performing PAO at both hospitals [19], prior to this the PAO outlined by Ganz was used [7].

All patients registered in the database who had provided at least one answer to the questions regarding sports participation were deemed eligible for this study. If a patient had undergone PAO in both hips, only the first hip to undergo surgery was included. The exclusion criteria were: (i) foreigner (defined as those without a Danish civil registration number), (ii) primary diagnosis registered as something other than hip dysplasia, (iii) surgical procedure registered as something else than PAO and (iv) age < 15 years.

Data Sources

The PAO-database was created in 2010 to systematically collect information on the effects of PAO and all patients operated since 2010 have thus been invited to participate in this institutional database located at Aarhus University Hospital [2,11,21]. The database contains patient demographic information, radiological findings, surgery related information, and patient-reported outcomes. Surgery-related data and patient characteristics on patients who underwent PAO between 1998 and 2010 was originally stored in paper format. In 2014 a secretary at the department retrospectively entered this data into the database, thereby allowing patients who had undergone PAO before the database was initiated to complete questionnaires from this timepoint forward. Radiological findings, surgical information and contact information are collected before and after surgery by the orthopaedic surgeons and entered prospectively into the database. Patient-reported outcomes are collected by e-mail preoperatively, 6 months after surgery and 2, 5, 10, 15 and 20 years after surgery. Data is stored using the software Procordo v3.0 (Procordo Aps, København, Denmark).

Predictors

Data was collected from the PAO-database. Age at surgery and sex was obtained from the patient's central person registration number, as registered in the database. If the date of surgery was missing, the date was calculated as the date of the first reply subtracted by the follow-up time. A link to a questionnaire on demographic information, including self-reported education and BMI, was emailed to patients before PAO. Self-reported education was defined as primary educational level (grade 0-10), secondary educational level (more than primary school, but no university degree) and higher educational level (obtained university degree). Information on pain and quality of life was collected using the Hip Osteoarthritis Outcome Score (HOOS) questionnaire. The pain subscale consists of 10 items and the quality of life (QoL) subscale consists of 4 items related to quality of life[15]. Each

158 item has five possible categories, ranging from 0-4 points. In accordance with the HOOS manual,
159 the points were converted to a score between 0-100, where 0 indicated severe problems and 100
160 indicated no problems[15]. In cases where one or two values were missing on a HOOS subscale,
161 values were substituted with the average value for the dimension. The minimal clinically relevant
162 difference is 10.3 points for pain and 11.2 for quality of life[23]. HOOS is a validated questionnaire
163 for collecting patient-reported outcomes regarding hip and groin pain among patients undergoing
164 PAO[23]. All radiographic measurements were assessed using the digital measurement tool IMPAX
165 client 6.5 (AGFA HealthCare, Mortsel, Belgium). The treating orthopedic surgeons (all consultant
166 surgeons) measured the CE- and AI-angle on anterior-posterior pelvic radiographs prior to surgery
167 and entered the results into the database. The CE-angle is defined as the angle formed between a
168 line extending through the center of the femoral head and perpendicular to a horizontal line
169 connecting the centers of both femoral heads, and another line drawn from the lateral edge of the
170 acetabular roof to the center of the femoral head[21]. The AI angle is defined as the angle between the
171 horizontal inter-teardrop line and a line extending from the lateral to the medial point of the weight-
172 bearing region of the acetabulum [21].

173

174 **Outcomes**

175 The orthopaedic surgeon who initiated the database established questions regarding sports. The first
176 question; “Are you participating in sports?” is answered “yes” or “no”. If the answer is “yes”, the
177 patient is further asked the following questions: (i) What type of sports are you participating in
178 (multiple choices from 17 different sports allowed); (ii) At what level do you participate in sports
179 (recreational/elite); (iii) Can you participate in the sports you prefer with your present hip function;
180 and (iv) Has PAO improved your sports performance. If the patient answered “no” to the first
181 question about sports participation, they are asked if their lack of sports activity is due to a hip

problem. The questions regarding the type of sports included 17 different sports often performed in Denmark. The type of sports were categorized into three categories, as previously done by Leopold et al. [12]. The categories were; (i) High-Impact Sports (athletics, badminton, dancing, gymnastics, handball, martial arts, running, soccer and tennis); (ii) Low-Impact Sports (cycling, fitness, golf, horseback riding, sailing, swimming and walking); (iii) Others (all type of sports not specified above).

Statistical Analysis

Data were analyzed using Stata, version 18 (StataCorp, College Station, TX, USA). Categorical data is presented as the number with percentages and continuous data is presented as mean with standard deviation (SD). Skewed data were presented using medians and 25^{th}-75^{th} percentile. Data was presented both for the entire cohort and for the subgroups of (self-)categorized athletes participating in sports. The athletes were further stratified based on their self-reported athletic level (elite or recreational) before PAO. The response rate was calculated as the proportion of responses at a given timepoint relative to the total number of patients that had reached that timepoint. To explore inclusion bias, baseline characteristics were compared at all timepoints after PAO, between patients who had answered the question about sports participation (responders) and patients who had reached the given timepoint but not answered the question about sports participation (non-responders).

Generalized estimating equations (GEE) modelling[3] was used to assess the association between independent and dependent variables. The results were presented as odds ratios (OR) with 95% confidence intervals (95% CI). For the adjusted models, the variables age, sex (i.e. male or female), education level (i.e. primary, secondary or higher), CE-angle, AI-angle, self-reported BMI, HOOS

Pain and HOOS QoL before surgery were considered as independent variables. The dependent variables were participation in sports, ability to perform preferred sports, and improvement in sports function six months, two, and five years after PAO, and these were all dichotomous (i.e. “yes” or “no”). Complete-case analysis was used for this analysis.

RESULTS

Data was collected over a 25-year period, between 1st of January 1998 and 31st of December 2023. From 2398 potentially eligible patients (3120 hips), a total of 1891 patients were included in this study. If a patient had undergone PAO in both hips, only the first operated hip was included. All patients that had provided information about sports were deemed eligible and 58 patients were further excluded for other reasons (Figure 1).

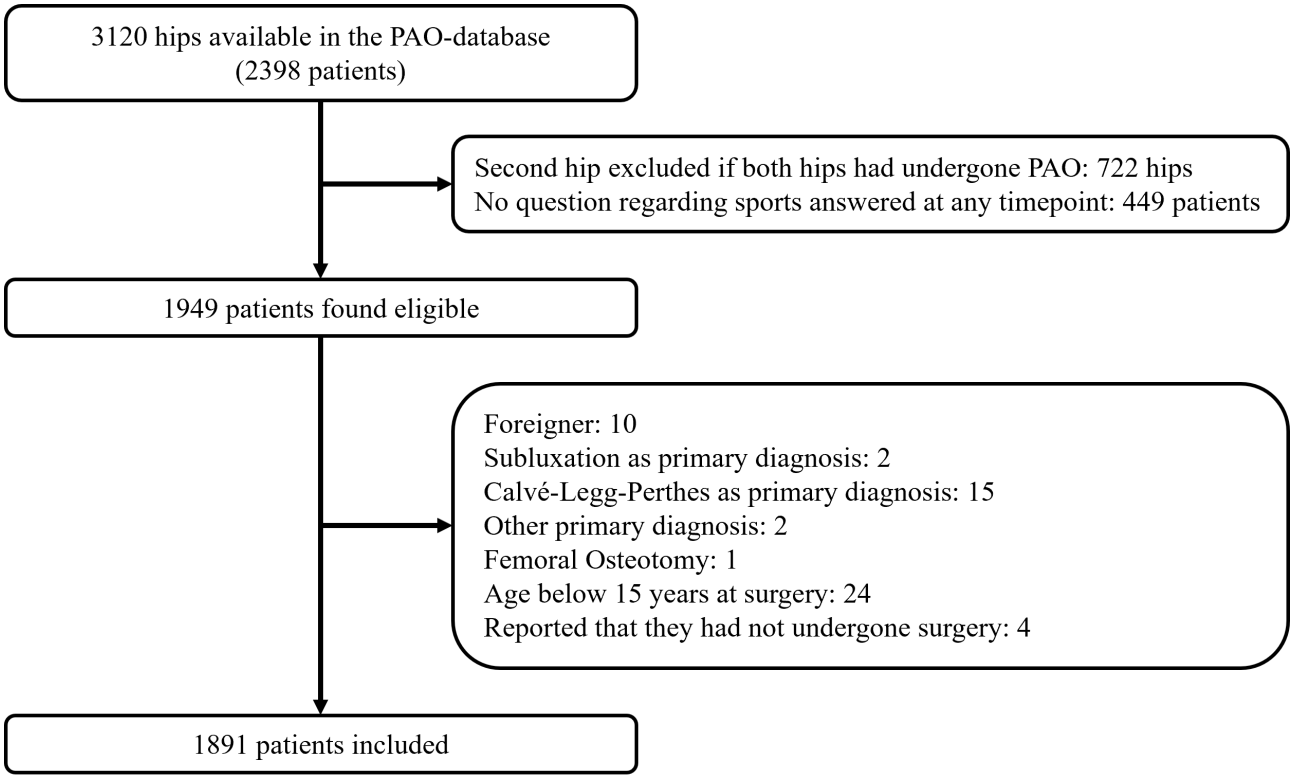

Figure 1. *Flowchart of the included cohort. PAO: Periacetabular Osteotomy.*

Patients

Patients in the cohort had a mean age of 30 years (SD 10.1) at the time of PAO and were predominantly women (84%) (Table 1). For the elite-level athletes the mean age was 23 years (SD 9.3) and 71% were women, whereas the mean age was 29 years (SD 9.4) in the recreational-level athletes where 86% were women. For those that were not sports active before PAO, the mean age was 28 (SD 9.3) and 86% were women. The type of sports and categories of sports that the patients reported to be participating in, remained the same throughout the study period, with most patients participating in low-impact sports (figure presented in the appendix, Figure A1). Fitness/resistance training was the most frequent exercise modality adopted by the patients at all the follow-up timepoints followed by running (appendix Table A1). Patients who had answered the question about sports participation (responders) did not differ substantially compared to patients who had not answered the question (non-responders), with regards to demographic and self-reported information (appendix Table A2).

Table 1. Demographic and preoperative data of all included patients (total cohort), and the subgroups of patients that were sports active before PAO (divided into elite-level or recreational-level athletes) and patients that were not sports active before PAO.

	Total cohort		Sports active before PAO				Not sports active before PAO	
			Elite-level		Recreational-level			
	Result	Responses	Result	Responses	Result	Responses	Result	Responses
Female, n (%)	1588 (84)	1891	25 (71)	35	428 (86)	500	552 (86)	642
Age at the time of surgery, mean (SD)	30.0 (10.1)	1891	22.8 (9.3)	35	28.9 (9.4)	500	28.3 (9.3)	642
Bilateral PAO, n (%)	581 (31)	1891	8 (23)	35	123 (25)	500	189 (29)	642
Positive impingement test, n (%)	1104 (97)	1139	33 (100)	33	428 (96)	446	559 (97)	576
Radiographic measurements								
CE-angle, mean (SD)	18.3 (7.7)	1530	19.8 (7.1)	34	19.0 (6.5)	470	19.7 (6.6)	607
AI-angle, mean (SD)	14.1 (7.1)	1531	12.3 (6.5)	34	13.6 (6.6)	470	13.0 (6.6)	608
Tönnis grade >0, n (%)	36 (3)	1158	0 (0)	33	16 (4)	448	15 (3)	577
Level of education, n (%)		1177		35		500		641
Primary[a]	205 (17)		15 (43)		57 (11)		133 (21)	
Secondary[b]	659 (56)		15 (43)		273 (55)		371 (58)	
Higher[c]	313 (27)		5 (14)		170 (34)		137 (21)	
Self-reported measurements, mean (SD)								
Height (cm)	170.9 (7.9)	1177	171.6 (9.0)	35	170.9 (7.9)	499	170.7 (7.8)	642
Weight (kg)	66.8 (10.7)	1171	65.6 (10.8)	35	66.7 (10.4)	495	66.9 (11.0)	640
BMI (kg/m^2)	22.8 (2.9)	1171	22.2 (2.5)	35	22.8 (2.7)	495	22.9 (3.0)	640
HOOS, mean (SD)								
Pain	50.5 (18.8)	1164	53.8 (20.2)	34	55.4 (17.0)	495	46.5 (19.3)	633
Symptoms	49.5 (19.7)	1163	52.4 (20.0)	34	53.5 (18.0)	495	46.2 (20.3)	633
ADL	61.7 (21.0)	1163	66.0 (18.9)	34	67.8 (18.4)	495	56.6 (21.7)	633
Sport	41.4 (23.7)	1163	48.5 (25.3)	34	48.2 (22.5)	495	35.7 (23.2)	633
Hip Related QoL	30.8 (15.9)	1163	37.3 (17.6)	34	35.5 (14.6)	495	26.8 (15.6)	633

[a]Primary: grade 0-10. [a]Secondary: more than primary school, but no university degree. [c]Higher: obtained university degree. ADL: Activities of Daily Living. AI: Acetabular Index. BMI: Body Mass Index. CE: Wiberg's Center-Edge. n: number. PAO: Periacetabular Osteotomy. QoL: Quality of Life. SD: Standard Deviation.

Sports participation

The percentage of patients reporting sports participation, alongside the response rate, is summarized in Figure 2. Before PAO, 45% [95% CI: 43;48] of the patients reported that they were participating in sports. As seen in Figure 2 (the blue solid line) the number of patients participating in sports increased to 56% at 6 months and then reached the highest proportion at 5, and 10 years after PAO (62%). From the 15 years follow-up point and onwards sports participation started to drop but remained higher than before PAO. All estimates can be found in the appendix (Table A3).

Being sports active before PAO was the strongest predictor of sports participation after PAO with an OR of 3.61 [95% CI: 2.84;4.59], indicating that the patients who participated in sports before

surgery were 261% more likely to participate in sports after PAO (Table 2). Education was also a predictor of sports participation, where higher educational level was associated with better odds of sports participation after PAO (OR 1.67, [95% CI: 1.21;2.30] for secondary educational level and OR 1.97 [95% CI: 1.35;2.88] for higher educational level). A better HOOS pain score before PAO was also associated with slightly better odds of participating in sports after PAO, with an OR of 1.01 [95% CI: 1.01;1.02], meaning that a one-point better HOOS pain score increased the odds by 1%. Time since surgery, age, sex, radiographic measures (CE- and AI-angle), BMI and HOOS QoL were not predictors of sports participation after PAO.

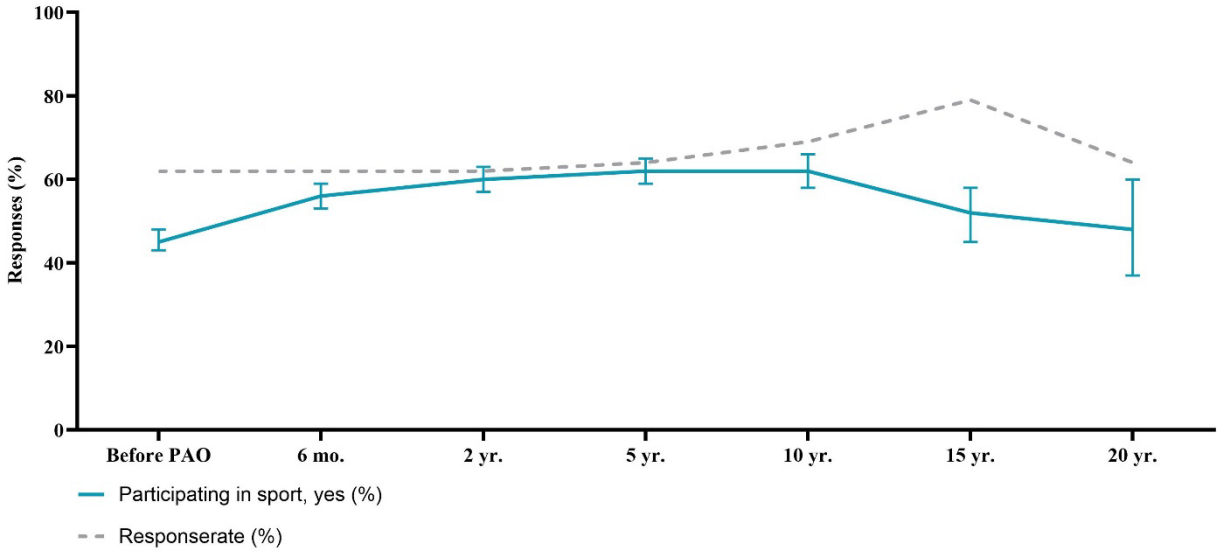

Figure 2. *The percentage of patients participating in sports alongside the response rates (calculated as the proportion of responses at a given timepoint relative to the total number of patients that had reached that timepoint) in percentage of included patients, at each timepoint. All data are presented as percentage (%). Mo: months. Yr.: years.*

Table 2. Odds ratios (OR) for predictors of sports participation, performing preferred sports and improvements in sports function, presented with 95% confidence intervals (95% CI) and marked as bold if the Bonferroni corrected p-values were below 0.005.

Variables	Sports participation		Performing preferred sports		Improvements in sports function	
	Crude	Adjusted	Crude	Adjusted	Crude	Adjusted
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Timepoint						
6 months	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
2 years	1.16 [1.00;1.33]	1.12 [0.94;1.33]	**1.92 [1.57;2.34]**	**2.08 [1.63;2.64]**	1.26 [1.04;1.53]	**1.41 [1.12;1.77]**
5 years	1.21 [1.04;1.42]	1.17 [0.94;1.45]	**1.95 [1.57;2.43]**	**2.25 [1.69;3.01]**	1.17 [0.96;1.44]	1.39 [1.01;1.81]
Sports active before PAO	**4.02 [3.23;5.01]**	**3.61 [2.84;4.59]**	1.02 [0.80;1.31]	0.92 [0.69;1.21]	0.70 [0.54;0.90]	0.83 [0.62;1.12]
Age	1.01 [1.00;1.02]	1.00 [0.99;1.02]	1.00 [0.99;1.01]	0.99 [0.98;1.01]	0.99 [0.98;1.00]	0.99 [0.98;1.01]
Sex						
Woman	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Man	1.11 [0.86;1.43]	1.11 [0.80;1.55]	0.95 [0.71;1.27]	0.71 [0.48;1.06]	0.75 [0.55;1.02]	0.64 [0.43;0.97]
Education						
Primary[a]	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Secondary[b]	**1.63 [1.23;2.16]**	**1.67 [1.21;2.30]**	0.85 [0.60;1.22]	0.79 [0.51;1.24]	0.96 [0.66;1.42]	0.98 [0.62;1.53]
Higher[c]	**2.35 [1.69;3.25]**	**1.97 [1.35;2.88]**	**0.48 [0.33;0.70]**	**0.45 [0.28;0.72]**	1.01 [0.66;1.53]	0.99 [0.61;1.61]
CE-angle	1.00 [0.99;1.01]	1.01 [0.99;1.04]	0.99 [0.98;1.01]	0.99 [0.96;1.02]	1.01 [0.99;1.02]	0.99 [0.96;1.03]
AI-angle	1.00 [0.99;1.02]	1.01 [0.98;1.04]	1.01 [0.99;1.03]	0.99 [0.96;1.02]	0.99 [0.97;1.01]	0.99 [0.95;1.02]
BMI	0.95 [0.91;0.99]	0.94 [0.90;0.99]	1.00 [0.96;1.05]	1.01 [0.96;1.07]	0.97 [0.92;1.02]	0.99 [0.93;1.05]
HOOS pain	**1.02 [1.01;1.03]**	**1.01 [1.01;1.02]**	1.00 [1.00;1.01]	0.99 [0.98;1.00]	0.99 [0.99;1.00]	1.01 [1.00;1.02]
HOOS QoL	**1.02 [1.01;1.02]**	0.99 [0.98;1.00]	**1.02 [1.01;1.03]**	**1.02 [10.1;1.04]**	**0.98 [0.97;0.99]**	**0.98 [0.97;0.99]**

[a]Primary education: grade 0-10. [a]Secondary education: more than primary school, but no university degree. [c]Higher education: obtained a university degree. AI: Actebular Index. BMI: Body Mass Index. CE: Wiberg's Center-Edge. CI: Confidence Interval. HOOS: The Hip disability and Osteoarthritis Outcome Score 2.0. N: number. OR: Odds Ratios. PAO: Periacetabular Osteotomy. Ref: Reference group. QoL: Quality of Life.

Performing preferred sports

For patients participating in sports, there was an increase in the number of patients who were able to perform their preferred sports activity throughout the follow up period (Figure 3). Before PAO, 13% (95% CI: 10;16) were able to perform their preferred sports activity, which increased to 41% [95% CI: 37;45] 6 months after PAO, 57% (95% CI: 53;61) 2 and 5 years after PAO and 55-63% 10-, 15- and 20 years after PAO (appendix Table A3).

Time was a significant predictor of being able to perform preferred sports, as the odds increased by 92% [95% CI: 57%;134%] from 6 months to 2 years after PAO, and 95% [95% CI: 57%;143%] from 6 months to 5 years after PAO (Table 2). Higher educational level at the time of surgery was associated with the ability to perform preferred sports. Moreover, an odds ratio of 0.45 [95% CI: 0.28;0.73] was found when higher educational level was compared to primary educational level, meaning that the odds of performing preferred sports were 55% [95% CI: 27%;72%] lower for patients with a higher educational level than patients with a primary educational level. A higher

score at the HOOS subscale QoL was associated with a 2% [95% CI: 1%;4%] better odds of being able to perform preferred sports after PAO for every one-point increase in the subscale. Being sports active before PAO, as well as age, sex, radiographic measures (CE- and AI-angle), BMI and HOOS pain were not predictors of the ability to perform the preferred sports after PAO.

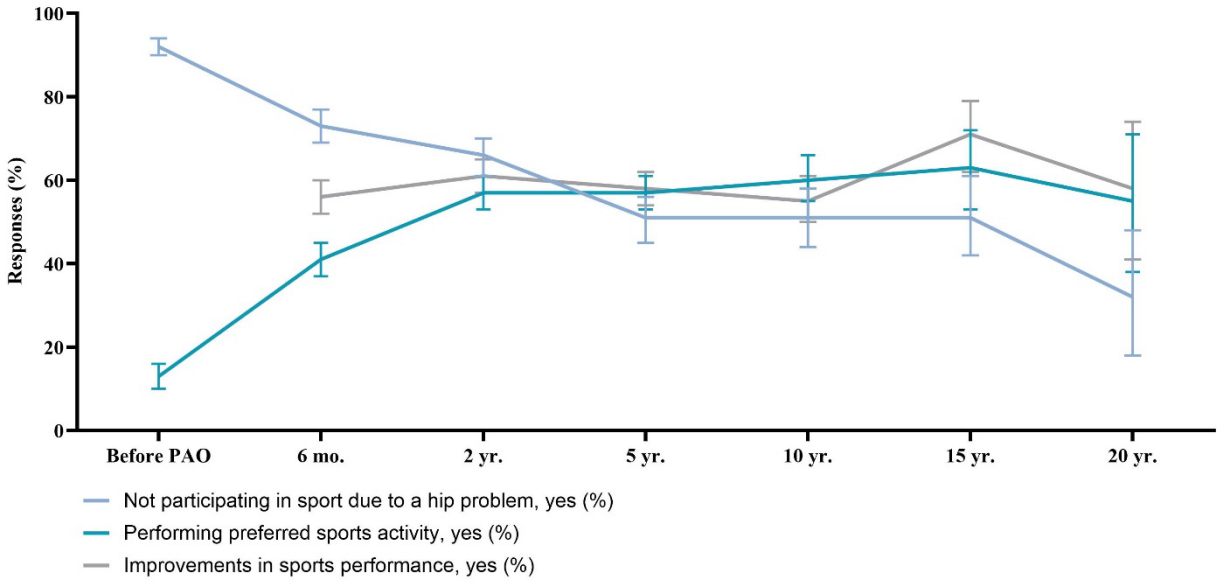

Figure 3. *The percentage of patients performing preferred sports activity, reported improvements in their sports performance and the percentage of patients not participating in sports due to a hip problem, at each timepoint. All data are presented as percentage (%). Mo: months. Yr.: years.*

Improvements in sports performance

The proportion of patients that reported that their sports performance had improved due to the PAO surgery, were consistent during the follow up timepoints, except for an increase at the 15-year timepoint were 71 [95% CI: 62;79] reported that their sports performance had improved after PAO (Figure 3). Time predicted improvements in sports performance after PAO, but only at the 2-year timepoint compared to the 6 months (OR 1.41, [95% CI: 1.12;1.77]) (Table 2). The QoL score at HOOS was also associated with improvements in sports performance after PAO, with an OR of 0.98 [95% CI: 0.97;0.99], meaning that a higher HOOS QoL score was associated with worse odds

of reporting that the surgery improved sports performance. Being sports active before PAO, age, sex, educational level, radiographic measures (CE- and AI-angle), BMI and HOOS pain were not predictors of improvements in sports performance after PAO.

Level of Sporting Competition

Of the 535 patients that were sports active before PAO, 35 reported that they participated in sports at elite level (i.e. self-reported elite-level athlete), while 500 participated in sports at a recreational level (Table 3). The number of patients that were able to perform their preferred sports activity increased after PAO for both the elite-level athletes and the recreational-level athletes. When the subgroup of elite-level athletes were asked if surgery had improved their sports performance, 44% [95% CI: 24;65] said yes at 6 months after PAO, and 62% [95% CI: 38;82] said yes at two years of follow up. Five years after PAO, only 29% [95% CI: 10;56] reported that surgery had improved their sports performance. Less than 3 of the elite-level athletes had a follow-up longer than 5 years after PAO.

Table 3. Patient-reported outcomes related to sports after PAO for patients who reported sports participation before PAO, stratified based on self-reported athletic level.

	Time after PAO				
	Pre	**6 mo.**	**2 yr.**	**5. yr.**	**10 yr.**
Sports participation					
Yes, % (95% CI)	NA	75 [71;79]	76 [71;80]	75 [69;80]	76 [63;87]
Responses, n (%)	535 (100)	433 (91)	369 (86)	231 (74)	55 (63)
Elite					
Yes, % (95% CI)	NA	86 [68;96]	88 [68;97]	89 [67;99]	100 [16;100]
Responses, n (%)	35 (100)	29 (91)	24 (86)	19 (86)	2 (50)
Recreational					
Yes, % (95% CI)	NA	74 [70;78]	75 [70;80]	74 [67;79]	75 [62;86]
Responses, n (%)	500 (100)	404 (91)	403 (86)	212 (73)	53 (64)
Performing preferred sports activity					
Yes, % (95% CI)	13 [10;16]	40 [35;46]	57 [51;63]	60 [52;67]	79 [63;90]
Responses, n	535	325	281	173	42
Elite					
Yes, % (95% CI)	29 [15;46]	60 [39;79]	52 [30;74]	59 [33;82]	NA
Responses, n (%)	35	25	21	17	
Recreational					
Yes, % (95% CI)	12 [9;15]	38 [33;44]	57 [51;63]	60 [52;68]	80 [64;91]
Responses, n (%)	500	300	260	156	40
Improvements in sports performance					
Yes, % (95% CI)	NA	51 [46;57]	60 [54;66]	60 [52;67]	64 [48;78]
Responses, n		325	281	173	42
Elite	NA				
Yes, % (95% CI)		44 [24;65]	62 [38;82]	29 [10;56]	100 [16;100]
Responses, n		25	21	17	2 (50)
Recreational	NA	52 [46;57]	60 [53;66]	63 [55;70]	63 [46;77]
Yes, % (95% CI)		300	260	156	40
Responses, n					

Mo: months. n: number. Yr.: years. PAO: periacetabular osteotomy.

DISCUSSION

More than half (56%) of patients in the study were participating in sports 6 months after PAO. This increased to 60% two years after PAO, and remained around that for the following years, before dropping at 15 years after PAO. For patients who participated in sports before undergoing PAO, 75% reported continuing to participate in sports 6 months and 5 years after PAO. Between 41% (6 months after PAO) and 63% (15 years after PAO) were able to participate in their preferred sports. We found that between 55% and 71% of patients felt their sporting performance improved following PAO surgery, with 71% at 15 years follow-up reporting improvement. Sports activity status, educational level and pain score before PAO predicted sports participation after PAO. Educational level and QoL predicted the ability to perform preferred sports, where patients with a higher educational level and better QoL before PAO had better odds of performing preferred sports after PAO. QoL also predicted improvements in sports performance, meaning that a patient with

low QoL had higher odds of improved sports performance, than a patient with high QoL before PAO

Two years after PAO, 60% of patients in our study were participating in sports, consistent with Novais et al. who found that physical activity level among 51 patients, measured with the University of California-Los Angeles Activity Scale (UCLA-AS), was significantly improved 1 and 2 years after PAO, with 61% reporting a score of 8 or higher [16]. Conversely, Leopold et al. found that the number of patients who resumed sports participation more than 6 months after PAO was 42% [12], and thus lower than the 48%-62% found in our study. In our study, 63% of the patients participating in sports, reported being able to perform their preferred sports activity with present hip function 15 years after PAO. Leopold et al. found an increase in patients participating in low-impact sports and a decrease in high-impact sports after PAO [12]. We found that 56% of patients believe that PAO surgery improved their sports performance 6 months after PAO surgery, increasing to 71% 15 years after PAO. Leopold et al. found a similar result, with 58% of their 111 patients reporting surgery had improved their sports ability [12].

Being sports active, having a secondary or higher educational level, or less pain before PAO was associated with higher odds of sports participation after PAO. This result is consistent with Novais et al., who also found that high preoperative physical activity was significantly associated with a high self-reported physical activity score, measured with the UCLA-AS, one year after PAO (n=51) [16]. However, unlike our findings, Novais et al. found that older patients had worse physical activity one year after PAO and that self-reported pain was not associated with activity one year after PAO. These differences may be due to varying sample sizes and outcomes, with Novais et al. using the UCLA-AS to measure physical activity. The mean age in our study was 30 years (SD 10.1), where it was 27 (SD 10.7) in the study by Novais et al. [16] A review from 2023 of 62 studies on patient-reported outcomes among patients with hip dysplasia undergoing PAO, found that the mean age

ranged from 17 to 45 years [17]. Patients in our study might be older than patients in most studies due to the database dating back to 1988 when the surgical criteria for PAO were not as strict as nowadays.

Like sports participation, a higher educational level before PAO was also associated with higher odds of performing preferred sports after PAO. Conversely, we found that low QoL before PAO was associated with higher odds of improvements in sports function. This finding could be explained by differences in expectations, meaning a patient with low QoL could have lower expectations to the surgery and therefore more likely to experience an improvement in sports performance. However, this is speculative as there was no information on expectations available in the PAO-database. Like our study, Novais et al. found no association between sex, BMI, and the CE-angle [16]. Novais et al. also examined if preoperative Tönnis grade predicted return to sports after PAO, among 51 patients, with 21 (41%) having a grade above 0, but found no association [16]. Our study did not investigate Tönnis grade due to a change in PAO criteria in 2016, limiting surgery to patients with a Tönnis grade of 0.

Six months after PAO, the number of patients in our study who reported that a hip problem was the reason for not participating in sports decreased from 92% to 73%. Twenty years after PAO only 32% of patients reported not participating in sports due to a hip problem. Leopold et al. found that most patients who had stopped participating in sports reported this was due to lower exercise tolerance/pain, and 31% reported not participating in sports due to reasons unrelated to surgery. Other reasons for a decrease of sports activity after surgery could be changes in life circumstances [1].

In the subgroup of elite-level athletes, 86% participated in sports 6 months after PAO and 88% two years after PAO, consistent with Heyworth et al. who reported a return to sports rate of 80% at 9 months after PAO measured with the UCLA-AS in a retrospective study of 46 hips among 41 elite-

level athletes [8]. After 5 years, 89% of the elite-level athletes in the present study were participating in sports. Another study by Bogunovic et al. found that 71% of 36 elite-level athletes maintained or increased their activity level 5 years after PAO [1]. Based on our findings, athletes undergoing PAO have a 76% chance of returning to sport two years after PAO. For athletes participating in sports at an elite-level, 88% will return to sports 2 years after PAO. Novais et al. found that the preoperative score for the activity level alongside age were strong independent predictors for the activity level after PAO [16]. Prehabilitation (i.e. exercise prior to surgery) could increase activity level and therefore the likelihood of participating in sports after PAO. Another recent study has also speculated potential benefits of sports participation in athletes with hip dysplasia[18]. Information about the exact reasons for not participating in sports, if not due to a hip problem, are still unknown. Future research should therefore focus on identifying additional reasons for not participating.

Besides supporting a shared decision-making process between patients and clinicians regarding treatment, our findings can be used in clinical practice to (I) inform patients that being sports active before PAO increases the likelihood of sports participation as well as performing preferred sports after PAO, helping to manage expectations, (II) emphasize that better pain scores before surgery may correlate with higher sports participation, guiding discussions on pain management and setting realistic goals, (III) develop tailored rehabilitation plans that consider individual preoperative characteristics, optimizing recovery and sports participation, and (IV) focus less on age, sex, BMI and radiographic measurements in predicting sports outcomes, thus streamlining assessments and discussions.

Limitations of our study includes the use of individual sports-related questions instead of a validated questionnaire, leading to uncertainty about the construct being investigated, especially as sports was not defined and relied on the patient's perception of sports. The UCLA-AS, used to report return to sports among patients undergoing PAO, was not validated into a Danish version

406 until 2021 [14] and was unavailable when the PAO-database was established. Missing data is another
407 limitation, with 19% of patients excluded due to missing sports participation data, potentially
408 introducing selection bias. Recall bias is a third limitation, as asking patients about surgery
409 performed years ago might introduce some bias, though only one question relies on memory.
410 Despite these limitations, our findings are based on a large sample of patients, extended follow-up
411 period and relatively high retention rates, making this the most extensive study on sports outcomes
412 in patients with hip dysplasia undergoing PAO.

413

414 **CONCLUSION**

415 Patients undergoing PAO for hip dysplasia have a 56% chance of participating in sports 6 months
416 after PAO, and a 48% chance of maintaining sports 20 years later. Most patients believe the surgery
417 improves their sports performance (56% to 71%), and 20 years after the surgery 55% of patients
418 participate in their preferred sports. Elite-level athletes are more likely to participate (86%) and
419 maintain (89%) sports performance after PAO than recreational-level athletes. Being sports active
420 before PAO and having a better pain score predicts sports participation, while a high QoL score
421 predicts performing preferred sports, and not improving sports performance after PAO. Higher
422 educational level also predicts sports participation and performing preferred sports. Age, sex, self-
423 reported BMI and radiographic measures did not predict sports outcomes after PAO.

424

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APPENDIX

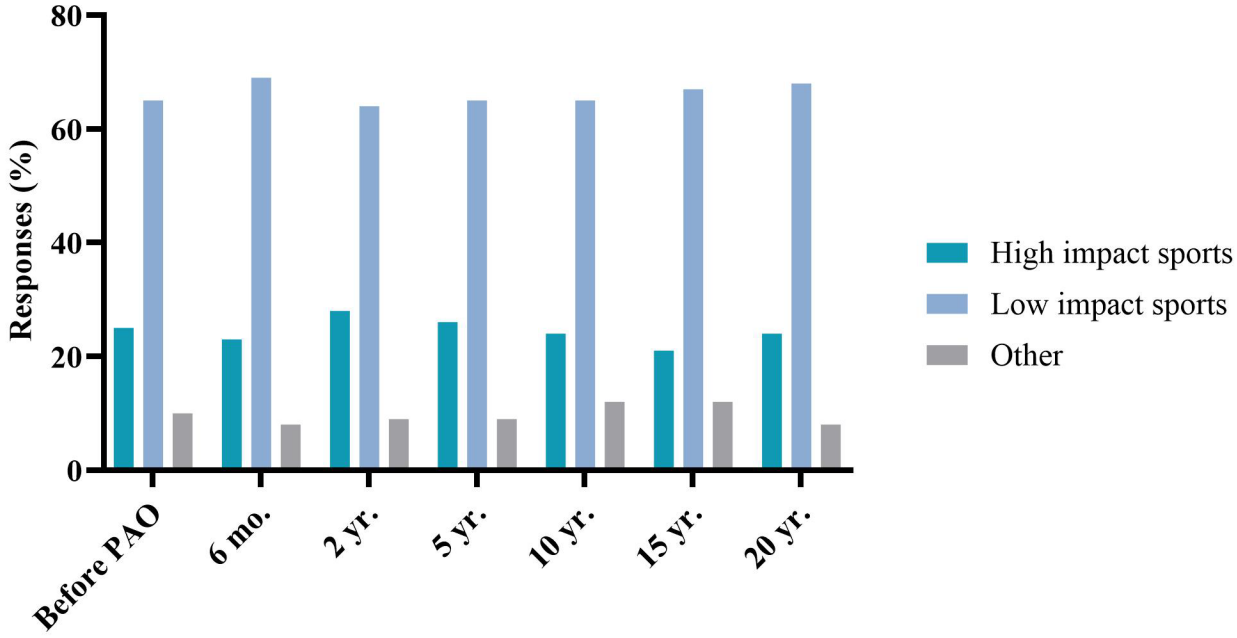

Figure A1. *Sports categories reported by patients at each timepoint (reported as a percentage of all sports)* [10]*. All data are presented as percentage (%). Mo: months. Yr.: years. PAO: periacetabular osteotomy.*

Table A1. Sports categories[10] and type of sports that patient reported to be currently participating in at follow-up timepoints.

	Time after PAO						
	Before PAO	**6 mo.**	**2 yr.**	**5 yr.**	**10 yr.**	**15 yr.**	**20 yr.**
Number of responses	**927**	**1217**	**1221**	**1083**	**666**	**223**	**71**
High-Impact Sports	**232 (25)**	**276 (23)**	**336 (28)**	**278 (26)**	**158 (24)**	**47 (21)**	**17 (24)**
Athletics	2	0	1	0	0	0	0
Badminton	13	12	12	16	8	1	0
Dancing	28	23	24	21	16	8	1
Gymnastics	21	30	30	26	21	12	5
Handball	17	6	13	11	4	1	0
Martial arts	8	10	11	6	3	1	1
Running	109	169	205	172	90	20	9
Soccer	29	23	30	22	11	3	1
Tennis	5	3	10	4	5	1	0
Low-Impact Sports	**602 (65)**	**839 (69)**	**780 (64)**	**709 (66)**	**430 (65)**	**150 (67)**	**48 (68)**
Cycling[a]	86	123	113	119	63	29	8
Fitness[b]	336	448	402	343	186	50	17
Golf	4	3	10	15	14	6	0
Horseback riding	36	41	38	29	15	10	2
Sailing	6	4	7	11	2	0	0
Swimming	50	79	78	62	40	17	7
Walking[c]	84	141	132	130	110	38	14
Other	**93 (10)**	**102 (8)**	**105 (9)**	**96 (9)**	**78 (12)**	**26 (12)**	**6 (8)**

All data are presented as number (%). [a]Cycling involves both road and mountainbike.
[b]Fitness also includes resistance training. [c]Walking also includes nordic walking. Mo: months.
Yr.: years. PAO: periacetabular osteotomy.

Table A2. Patient characteristics of responders and non-responders at all timepoints.

	Responders						Non-responders					
	6 mo.	**2 yr.**	**5 yr.**	**10 yr.**	**15 yr.**	**20 yr.**	**6 mo.**	**2 yr.**	**5 yr.**	**10 yr.**	**15 yr.**	**20 yr.**
Patients, n (%)	1093 (62)	1025 (62)	880 (64)	535 (69)	225 (79)	79 (65)	676 (38)	636 (38)	491 (36)	242 (31)	59 (21)	42 (34)
Female, n (%)	943 (86)	885 (86)	737 (84)	434 (81)	178 (79)	58 (73)	546 (81)	508 (80)	397 (81)	195 (81)	41 (69)	31 (74)
Age at the time of surgery, mean (SD)	29 (10)	29 (10)	31 (10)	33 (11)	33 (11)	32 (11)	32 (11)	32 (11)	30 (11)	31 (10)	33 (11)	32 (11)
Positive impingement test, n (%)	890 (97)	748 (96)	435 (94)	31 (72)	NA		105 (100)	143 (98)	185 (98)	29 (81)	NA	
Radiographic measurements												
CE-angle, mean (SD)	20 (11)	19 (12)	18 (14)	16 (8)	13 (10)	10 (12)	15 (9)	15 (9)	16 (9)	14 (10)	12 (10)	10 (9)
AI-angle, mean (SD)	13 (6)	14 (6)	15 (7)	16 (7)	18 (8)	21 (9)	16 (8)	16 (8)	16 (8)	18 (9)	18 (8)	20 (8)
Tönnis grade >0, n (%)	26 (3)	22 (3)	23 (5)	8 (16)	NA		7 (6)	10 (6)	5 (3)	7 (16)	NA	
Level of education, n (%)												
Primary[a]	168 (18)	143 (18)	89 (17)	13 (13)			24 (21)	35 (22)	41 (22)	17 (21)		
Secondary[b]	519 (55)	439 (55)	295 (58)	60 (60)	NA		66 (58)	89 (57)	96 (52)	51 (62)	NA	
Higher[c]	255 (27)	217 (27)	128 (25)	27 (27)			23 (20)	33 (21)	49 (26)	14 (17)		
Self-reported measurements, mean (SD)												
Height (cm)	171 (8)	171 (8)	171 (8)	170 (8)	NA		171 (8)	171 (8)	170 (8)	171 (7)	NA	
Weight (kg)	66 (10)	66 (10)	67 (11)	66 (11)	NA		66 (11)	66 (12)	66 (11)	67 (11)	NA	
BMI (kg/m^2)	23 (3)	23 (3)	23 (3)	23 (3)	NA		22 (3)	22 (3)	23 (3)	23 (3)	NA	
HOOS, mean (SD)												
Pain	50 (19)	51 (19)	52 (18)	58 (18)	NA		49 (19)	49 (19)	50 (19)	53 (17)	NA	
Symptoms	49 (20)	50 (20)	50 (20)	56 (21)	NA		50 (18)	48 (20)	49 (20)	53 (20)	NA	
ADL	61 (21)	62 (21)	62 (21)	69 (18)	NA		60 (21)	59 (20)	61 (21)	64 (21)	NA	
Sport	41 (24)	41 (24)	42 (24)	48 (23)	NA		42 (24)	41 (24)	40 (22)	45 (24)	NA	
Hip Related QoL	30 (16)	31 (16)	32 (16)	36 (14)	NA		30 (16)	31 (16)	30 (16)	35 (16)	NA	

[a]Primary: grade 0-10. [a]Secondary: more than primary school, but no university degree. [c]Higher: obtained university degree. ADL: Activities of Daily Living. AI: Acetabular Index. BMI: Body Mass Index. CE: Wiberg's Center-Edge. n: number. NA: not applicable. PAO: Periacetabular Osteotomy. QoL: Quality of Life. SD: Standard Deviation. Yr. = years.

Table A3. Patient-reported outcomes related to sport and physical activity.

	Time after PAO						
	Before PAO	**6 mo.**	**2 yr.**	**5 yr.**	**10 yr.**	**15 yr.**	**20 yr.**
Sports participation							
Yes, % (95% CI)	45 [43;48]	56 [53;59]	60 [57;63]	62 [59;65]	62 [58;66]	52 [45;58]	48 [37;60]
Responses, n	1177 (62)	1093 (62)	1025 (62)	880 (64)	535 (69)	225 (79)	79 (64)
Performing preferred sports activity							
Yes, % (95% CI)	13 [10;16]	41 [37;45]	57 [53;61]	57 [53;61]	60 [55;66]	63 [53;72]	55 [38;71]
Responses, n	535	617	617	546	332	116	38
Improved sports performance							
Yes, % (95% CI)	NA	56 [52;60]	61 [57;65]	58 [54;62]	55 [50;61]	71 [62;79]	58 [41;74]
Responses, n		617	617	545	332	116	38
Not participating in sports due to a hip problem							
Yes, % (95% CI)	92 [90;94]	73 [69;77]	66 [61;70]	51 [45;56]	51 [44;58]	51 [42;61]	32 [18;48]
Responses, n	643	476	408	334	202	109	41

Mo: months. n: number. NA: not applicable. PAO: periacetabular osteotomy. Yr.: years.

Paper V – The validation study

Validation of the Aarhus periacetabular osteotomy database

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LT, PK, IM and SJ designed the study and performed the approval applications. LT and PK were responsible for retrieving data from the Danish National Patient Registry, while LT were responsible for retrieving data from the Aarhus PAO-database. LT performed the reviewing of the electronic records and LT, FF and JB conducted the data analysis. LT drafted the manuscript, while PK and IM revised it. All authors approved the final version.

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ABSTRACT

Background: Periacetabular osteotomy (PAO) is the preferred surgical treatment for hip dysplasia. In Denmark, patients undergoing PAO at two orthopaedic departments are registered in a disease registry, the Aarhus PAO-database. This study aimed to validate the Aarhus PAO-database by assessing the registration completeness compared to the Danish National Patient Registry (DNPR).

Materials and Methods: Patients registered in the Aarhus PAO-database were compared to patients identified in DNPR as having undergone PAO for hip dysplasia. Further, a random selection of 20 entries (hips that had undergone PAO due to hip dysplasia) from each registry per year (2014-2021) was validated by comparing the information from the registries to the hospital's electronic medical records.

Results: Between 2014-2021, 1144 hips were registered in the Aarhus PAO-database and 1150 in DNPR. The overall registration completeness was 94.7% (95% CI: 93.3;95.9) with 1116 hips included in both datasets. The diagnosis and surgery were verified as hip dysplasia and PAO for all randomly selected patients, and almost all discrepancies were resolved, using the medical records.

Conclusion: The Aarhus PAO-database has effectively captured all patients who underwent PAO for hip dysplasia from 2014 to 2021. It appears to be a valid resource for future research as well as for ensuring and improving the quality of hip dysplasia treatment.

Keywords: Hip dysplasia, Periacetabular osteotomy, Validation, Danish National Patient Registry

INTRODUCTION

Hip dysplasia is a developmental joint disease, affecting 3.4% of Danish adults (1). Hip dysplasia is characterised by a shallow oblique acetabulum, ligament laxity, and proximal femur abnormalities leading to insufficient femoral head coverage (2) This insufficient coverage often includes deficient lateral acetabulum coverage, sometimes with anterior or posterior deficiency (3). Typical symptoms include hip and/or groin pain, altered gait and reduced range of motion, though not all adults with hip dysplasia are symptomatic (4, 5). Those experiencing pain may undergo periacetabular osteotomy (PAO), a surgery that reorients the acetabulum to increase femoral head coverage (6).

Since 1998, patients undergoing PAO at either Aarhus University Hospital or Mølholm Private Hospital have been registered in, the Aarhus PAO-database. This disease registry has been used for research on hip pain, function, quality of life, the familial prevalence of hip dysplasia, complication rates and radiographic measurement's reliability (7-12). However, the data has never been validated and the number of missing registrations compared to the Danish National Patient Registry (DNPR) has not been investigated. DNPR is an administrative registry ensuring hospitals are paid for healthcare services and is considered the gold standard for hospital healthcare services (13). All PAO procedures should be registered in DNPR and validation can be done by comparing DNPR information to the individual patient's medical records (13, 14).

The first aim of this study was to investigate the registration completeness in the Aarhus PAO-database compared to DNPR. The second aim was to investigate the positive predictive value (PPV) of the diagnosis and surgical procedure from a random sample of 160 patients each from the Aarhus PAO-database and DNPR, compared to their electronic medical records. The third aim was to investigate the PPV of the diagnosis and surgical procedure for patients with discrepancies between the two registries, using electronic medical records.

METHOD

This validation study on the Aarhus PAO-database and was approved by the Legal Office of the Regional Midtjylland Secretariat (journal number 1-45-70-85-22) and registered at the Region of Central Denmark's internal list of research projects (journal number 1-16-02-46-23).

Indications for PAO surgery

Indications for PAO surgery during the study period were (i) persistent hip pain and reduced function, (ii) radiographically verified hip dysplasia, defined as having a lateral center edge angle of Wiberg < 25°, (iii) skeletal maturity and (iv) absence of hip subluxation. Contraindications were (i) reduced range of motion, defined as internal rotation ≤ 15° and hip flexion ≤ 110°, (ii) hip osteoarthritis, defined as having a Tönnis grade > 0, (iii) body mass index > 25 and (iv) age > 45 years. The last three contraindications were added in 2016. Since 2004 the minimally invasive transartorial approach has been used when performing PAO at both hospitals (6).

Data Sources

The Aarhus PAO-database

The disease registry was created in 2010 and includes prospectively gathered data from patients undergoing PAO at Aarhus University Hospital and Mølholm Private Hospital. Data from patients operated from 1998-2010 were stored in paper format and retrospectively entered into the registry in 2014 by a secretary at the department of Orthopedic Surgery at Aarhus University Hospital. The registry contains information on patient demographic, radiological findings, surgery related information and patient-reported outcomes. Radiological findings and surgical information are collected before and after surgery and entered prospectively into the registry by the orthopaedic

surgeon. Patient-reported outcomes are collected by e-mail preoperatively, 6 months after surgery as well as 2, 5, 10, 15 and 20 years after surgery. The patient-reported questionnaires are emailed to the patients and all data is stored using the software Procordo v3.0 (Procordo Aps, København, Denmark).

The Danish National Patient Registry

The DNPR is a national registry, which has collected data from all Danish hospitals, both public and private, since 1978 (13). The registry contains information on all hospital contacts, including surgical procedures and diagnoses and each hospital is required by Danish law to submit standardised data to the DNPR monthly (13). (13). In DNPR diagnosis are registered using the Internal Classification of Diseases 10th revision (ICD-10) codes, while surgical procedures are registered with NOMESCO Classification of Surgical Procedures (NCSP) codes and hospitals with SHAK codes (Health Care Classification System) (13).

Medical Record

The electronic medical records in the Central Denmark Region include individual healthcare-related registrations for each hospital visits linked with date, time, department and the healthcare professional. While the DNPR is based on these records, the medical records contain more comprehensive information and notes from the health professionals, making them the gold standard for information regarding diagnosis and treatment (14).

Study population

The Aarhus PAO-database

From the Aarhus PAO-database all patients registered were considered eligible. Exclusion criteria included (i) PAO performed before 2014 or after 2021, (ii) double entry (second PAO on the same hip), (iii) diagnosis of Legg-Calvé-Perthes, (iv) femur osteotomy as the surgical procedure, and (v) skeletal immaturity (age < 15 years at surgery).

The Danish National Patient Registry

The 1st of January 2014 was defined as the starting time point, as Aarhus University Hospital used to be three hospitals that were merged in 2011, but the SHAK codes for the three hospitals remained active until late 2013.

Patients were identified as having undergone PAO using the NCSP codes “NEK59” (pelvic osteotomy) and “NET49” (correction of pelvis deformity). Patients with ICD-10 code “Q658” (congenital malformation of the hip) as the diagnosis code, were eligible for inclusion. Aarhus University Hospital is in DNPR defined by the SHAK code “6620” and Mølholm Private Hospital has the SHAK code “6010”. In addition, information regarding social security number, department and age at the time of surgery was extracted to exclude patients treated before skeletal immaturity. To avoid extracting unnecessary data, it was decided to only include patients from DNPR were both the diagnosis (hip dysplasia) and the treatment (PAO) had been registered as well as the treating hospital being either Aarhus University Hospital or Mølholm Private Hospital. As not all patients with hip dysplasia undergo PAO, a data extraction based solely on the diagnosis would include many irrelevant patients. The exclusion criteria were thus limited to skeletal immaturity (age < 15 years at surgery).

Medical Record

From the medical records hip dysplasia was defined as any mention of hip dysplasia as the primary reason for symptoms recorded by an orthopaedic surgeon based on a clinical and radiographic assessment. PAO was defined as a surgical description by the treating orthopaedic surgeon identifying PAO as the surgery performed. All information from the medical records was extracted by a single independent researcher (LT), who was not involved in the treatment of these patients, using a standardised form in Research Electronic Data Capture (REDCap) (15, 16).

Statistical Analysis

The results are presented as the number of included and missing patients from the Aarhus PAO-database and the DNPR. The completeness of registration was assessed by calculating the number of entries (hips that had undergone PAO due to hip dysplasia) registered in both the Aarhus PAO-database and DNPR divided by the number of entries registered in the Aarhus PAO-database or DNPR, with 95% confidence intervals (95% CI). This was done for the entire period as well as for each year from 2014-2021. A sensitivity analysis was done by adding the date of the PAO surgery. In the sensitivity analysis date registration could only differ by one day between the PAO-database and the DNPR to calculate the registration completeness. In addition, a computer-generated random selection of 20 entries from the Aarhus PAO-database for each year (2014-2021) was validated by comparing the information in the Aarhus PAO-database and DNPR to the information in the electronic medical records. The PPV was calculated as the proportion of diagnoses and procedures in the Aarhus PAO-database and DNPR confirmed by the hospital's medical records from the patients from the random sample. Additionally, information on diagnosis, surgery, the date of surgery, hip side and hospital, was extracted from the medical records. In cases with discrepancies between the Aarhus PAO-database and DNPR, the PPV was calculated among the entries with

discrepancies, as the proportion of diagnoses and procedures confirmed by the medical records. All data from the medical records was managed using the secure and web-based software platform, Research Electronic Data Capture (REDCap) hosted at Aarhus University (15, 16). All statistical analysis was performed in Stata version 18.0 (StataCorp LLC, College Station, TX, USA).

RESULTS

From the Aarhus PAO-database 2976 entries from 2290 patients were found eligible (Figure 1). After excluding 1832 entries based on the exclusion criteria 1144 entries from 947 patients were included. From the DNPR 1194 entries from 999 patients were found eligible. After excluding 44 entries due to patients being younger than 15 at the time of surgery, 1150 hips from 959 patients were included. Most entries were from women and had undergone PAO at Aarhus University Hospital (Table 1). There were no differences between age, sex and hip side between the two datasets. For 18 entries the hospital information was missing in the Aarhus PAO-database.

Completeness of registration

The first aim of this study was to investigate the registration completeness in the Aarhus PAO-database compared to DNPR. There were 1178 entries in total and 1116 were included in both datasets (Table 2). 34 entries (2.9%) were included in DNPR but not in the Aarhus PAO-database, while 28 (2.4%) were included in the Aarhus PAO-database but not in DNPR. When stratified by hospital, 97.3% entries from Aarhus University Hospital and 92.1% from Mølholm Private Hospital were included in both datasets (Table 2). The overall registration completeness between the Aarhus PAO-database and DNPR was 94.7% (95% CI: 93.3;95.9) and remained consistent over time (Table 3). The sensitivity analysis, allowing a maximum of 1 day difference in the data of surgery between

the two registries, showed a registration completeness of 87.1% (95% CI: 85.0;90.0). The median difference between the two registries, in registered date of surgery among patients with more than one days difference was 3 days (interquartile range: 2;99 and range 2;878).

The randomly selected sample

320 entries were randomly selected (160 from each registry) and their registered diagnosis and surgical procedure in the Aarhus PAO-database and DNPR were validated using the electronic medical records. All 320 entries were confirmed to have hip dysplasia and had undergone PAO. The hospital registered in DNPR matched the Aarhus PAO-database for 318 entries, with a PPV were 0.99 (95% CI: 0.98;1.00). For 67 entries the PAO date differed between the two datasets and the medical records, with a median difference of 1 day (interquartile range: 1;2) ranging from 1 to 930 days. For 61 entries the difference was less than a week. The PPV for the date of PAO among the randomly selected entries was 0.79 (95% CI: 0.74;0.83).

The discrepancies

There were 62 entries with a discrepancy between DNPR and the Aarhus PAO-database, ranging from < 5 to 16 per year (Table 3). Most of these patients were verified as having hip dysplasia and PAO using the medical records. Fewer than 5 of the 62 entries with a discrepancy could not be verified, these entries were either diagnosed with a different condition or had undergone a different surgery than PAO. These entries were all from DNPR, the PPV was 0.97 (95% CI: 0.89;1.00) overall, and 0.95 (95% CI: 0.82;0.99) for DNPR.

DISCUSSION

The overall registration completeness was 94.7% (95% CI: 93.3;95.9) between the Aarhus PAO-database and DNPR, meaning that 95% of hips undergoing PAO due to hip dysplasia are registered in both the Aarhus PAO-database and DNPR. The registration completeness for the Aarhus PAO-database is therefore a lot higher than the 80% that is considered acceptable for a national registry (17). Both registries had registered a small number of patients (2-3%) that were not found in the other registry. The high completeness suggests that these two registries are highly accurate and thus a valuable resource when investigating patients with hip dysplasia that undergo PAO. In addition, almost all patients with a discrepancy could be verified as having undergone PAO due to hip dysplasia, using the medical records. Less than 5 entries from DNPR had not undergone PAO due to hip dysplasia, and none in the Aarhus PAO-database, indicating that the Aarhus PAO-database was marginally more accurate than the DNPR. The registration completeness was 8% lower when the date of PAO was added to the analysis. Even though the median difference in date of surgery was only 3 days, among patients with more than 1 days difference, this information is important for future research investigating outcomes shortly after the operation, such as complications or days of hospitalisation.

To the best of our knowledge this is the first validation study investigating the registration completeness in a disease registry for patients with hip dysplasia undergoing PAO, despite the existence of similar registries (18, 19). However, registries regarding other diagnoses have been validated in a similar way (20-23). The overall completeness of registration for primary total hip arthroplasty in the Danish Hip Arthroplasty Register compared to DNPR, was 94.1 % (95% CI: 93.9%;94.4%) from 1995-2000 among all hospitals in Denmark (20). The registration completeness is thus similar to the registration completeness in the present study, despite a large difference in the number of sites, as The Danish Hip Arthroplasty Register includes 48 orthopaedic departments in

Denmark, whereas the Aarhus PAO-database includes two, due to PAO being a highly specialised surgical procedure. In addition, the present study included both a public and a private hospital, whereas the study by Pedersen et al., excluded all patients that underwent surgery at a private hospital (20).

The Danish Knee Ligament Reconstruction Register was compared to DNPR in 2013, investigating the registration completeness of knees that had undergone reconstruction of the anterior cruciate ligaments (ACL) (21). The overall completeness of registration was 79% (95% CI: 78;79) from 2005-2021, and increasing over time (21). The authors suggest that the increase over time might be due to surgeons becoming more familiar with the registration task. This might be the reason that there were no substantial differences in the registration completeness over time in the present study, as the surgeons are likely already familiar with the registration task as the Aarhus PAO-database was created in 2010. In addition, the registration completeness in the study by Rahr-Wagner et al. was calculated as the number of knees registered in both the Danish Knee Ligament Reconstruction Register and DNPR, divided by the number of knees registered in DNPR (21). If the same approach was used in the present study the registration completeness would be 97.0% (95% CI: 95.9%;97.9%) and thus better than the 94.7% found, however as we suspected there were discrepancies in both registries and the conservative estimate reflects this.

To investigate the Aarhus PAO-database's value as a research resource, the number of included patients were compared to the DNPR, and further validated against the medical records, considered the gold standard for treatment information. Despite the comprehensive validation, this study has some limitations. Firstly, only patients that had undergone PAO at either Aarhus University Hospital or Mølholm Private Hospital were included. Although these are a public and a private hospital, the same surgeons operated at both sites making registration differences unlikely. Thus, the hospitals can be considered a combined or single site for registration purposes. Secondly, only

patients that had undergone PAO between 2014-2021 were included so the validation only applies to this period. Future research should have this in mind and preferably use data from 2014 and onwards. Thirdly, the registration completeness estimates sensitivity (24), but the specificity could not be investigated due to the study setup.

In conclusion, the registration completeness was 95% between the Aarhus PAO-database and DNPR. The Aarhus PAO-database has thus managed to include almost all patients that had undergone PAO due to hip dysplasia from 2014 to 2021. The PAO-database therefore seems to be a valid resource for future research projects, as well as for the quality assurance and development of the treatment offered for patients with hip dysplasia.

AUTHOR CONTRIBUTIONS

LT, PK, IM and SJ designed the study and performed the approval applications. LT and PK were responsible for retrieving data from the Danish National Patient Registry, while LT were responsible for retrieving data from the Aarhus PAO-database. LT performed the reviewing of the electronic records and LT, FF and JB conducted the data analysis. LT drafted the manuscript, while PK and IM revised it. All authors approved the final version.

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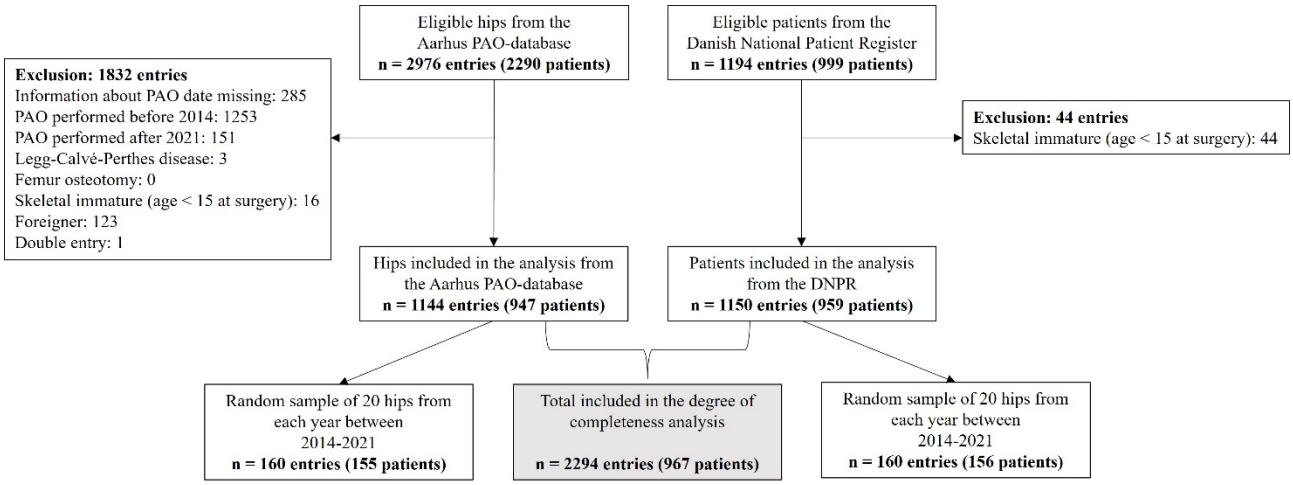
FIGURES AND TABLES

Figure 1. Flow chart of the included hips from the Aarhus periacetabular osteotomy database (Aarhus PAO-database) and the Danish National Patient Register (DNPR).



375 **Table 1.** The patient characteristics of all included entries (hips that had undergone PAO due to hip
376 dysplasia) based on the information collected form the Danish National Patient Registry (DNPR)
377 and Aarhus PAO-database.

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Patient characteristic	Both DNPR[a] and Blinded1 PAO-database[b]	DNPR[a] only	Blinded1 PAO-database[b] only
Number of patients, n (%)	967	959	947
Number of hips, n (%)	1178	1150	1144
Blinded1 University Hospital, n (%)	884 (75.0%)	880 (76.5%)	863 (75.4%)
Blinded2 Private Hospital, n (%)	278 (23.6%)	270 (23.5%)	263 (23.0%)
Women, n (%)	1010 (85.7%)	990 (86.1%)	982 (85.8%)
Age at the time of surgery, mean (SD)	28.8 (9.6)	28.9 (9.6)	28.3 (9.6)
Age < 18 years, n (%)	97 (8.2%)	94 (8.2%)	97 (8.5%)
Age 18-40, n (%)	871 (73.9%)	849 (73.8%)	845 (73.9%)
Age > 45, n (%)	210 (17.8%)	207 (18.0%)	202 (17.7%)
Operation side			
Right side, n (%)	587 (49.8%)	578 (50.3%)	635 (55.5%)
Left side, n (%)	482 (40.9%)	463 (40.3%)	509 (44.5%)

379 [a]Less than 5 entries from DNPR had missing information on sex and age and 109 missing operations side in DNPR. [b]18
380 entries from the Blinded1 PAO-database had missing information on hospital. DNPR: Danish National Patient Registry,
381 PAO: Periacetabular Osteotomy.

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Table 2. The number of included and missing entries (hips that had undergone PAO due to hip dysplasia) in the Aarhus PAO-database and the Danish National Patient Registry (DNPR).

		Blinded1 PAO-database					
		Total		AUH		Blinded2	
		Included	Missing	Included	Missing	Included	Missing
Danish National	Included	1116 (94.7%)	34 (2.9%)	860 (97.3%)	20 (2.3%)	256 (92.1%)	14 (5.0%)
Patient Registry	Missing	28 (2.4%)	NA	< 5 (0.5%)	NA	8 (2.9%)	NA

18 entries from the Blinded1 PAO-database had missing hospital information. AUH: Blinded1 University Hospital. DNPR: Danish National Patient Registry, PAO: Periacetabular Osteotomy.

Table 3. Completeness of registration of periacetabular osteotomy (PAO) among patients with hip dysplasia in the Aarhus PAO-database compared with the Danish National Patient Registry (DNPR).

Year	Total, n	DNPR, n (%)	Blinded1 PAO-database, n (%)	Both DNPR and Blinded1 PAO-database, n (%)	Degree of completeness, % (95% CI)
2014-2021	1178	1150	1144	1116 (94.7%)	94.7 (93.3;95.9)
2014	145	144	140	139 (95.9%)	95.9 (91.2;98.5)
2015	171	170	161	160 (93.6%)	93.6 (88.8;96.7)
2016	190	177	187	174 (91.6%)	91.6 (86.7;95.1)
2017	159	155	155	151 (95.0%)	95.0 (90.3;97.8)
2018	129	127	125	123 (95.4%)	95.3 (90.2;98.3)
2019	150	148	146	144 (96.0%)	96.0 (91.5;98.5)
2020	146	143	143	140 (95.9%)	95.9 (91.3;98.5)
2021	88	86	87	85 (96.6%)	96.6 (90.4;99.3)

CI: Confidence Interval. DNPR: Danish National Patient Registry, PAO: Periacetabular Osteotomy.

Declarations of co-authorship

AARHUS UNIVERSITY

Declaration of co-authorship concerning article for PhD dissertations

Full name of the PhD student: Lisa Urup Tønning

This declaration concerns the following article/manuscript:

Title:	Periacetabular osteotomy to treat hip dysplasia: a systematic review of harms and benefits
Authors:	Tønning LU, O'Brien M, Semciw A, Stewart C, Kemp JL, Mechlenburg I

The article/manuscript is: Published ☒ Accepted ☐ Submitted ☐ In preperation ☐

If published, state full reference: Archives of Orthopaedic and Trauma Surgery

If accepted or submitted, state journal:

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

No ☒ Yes ☐ If yes, give details:

Your contribution

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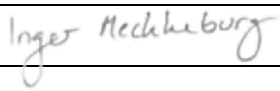
A. Has essentially done all the work (>90%)
B. Has done most of the work (67-90 %)
C. Has contributed considerably (34-66 %)
D. Has contributed (10-33 %)
E. No or little contribution (<10%)
F. N/A

Category of contribution	Extent (A-F)
The conception or design of the work:	B
Free text description of PhD student's contribution ***(mandatory)*** The PhD candidate designed the study and wrote the PROSPERO protocol under guidance from the main supervisor and co-authors.	
The acquisition, analysis, or interpretation of data:	C
Free text description of PhD student's contribution ***(mandatory)*** The PhD candidate was one of the reviewers that screened the studies through the title/abstract and full text screening process, extracted data and performed the quality and certainty assessments. The PhD candidate further performed the data analysis and interpretation of data.	
Drafting the manuscript:	A
Free text description of PhD student's contribution ***(mandatory)*** The PhD candidate wrote the manuscript and revised it after comments from the author group.	
Submission process including revisions:	A

Free text description of PhD student's contribution ***(mandatory)***
The PhD candidate (LT) performed the submission and lead the work on the revisions.

Signatures of first- and last author, and main supervisor

Date	Name	Signature
30.01.2025	Lisa U. Tønning	
03.02.2025	Inger Mechlenburg	

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This declaration concerns the following article/manuscript:

Title:	Functional performance and muscle strength in patients with hip dysplasia compared to healthy volunteers - a cross-sectional study
Authors:	Tønning LU, Jakobsen SS, Dalgas U, Kjeldsen T, Mortensen L, Mechlenburg I

The article/manuscript is: Published ☐ Accepted ☐ Submitted ☒ In preperation ☐

If published, state full reference:

If accepted or submitted, state journal: Journal of Orthopaedic & Sports Physical Therapy Open

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The acquisition, analysis, or interpretation of data:	B
Free text description of PhD student's contribution ***(mandatory)*** The PhD candidate was a part of the inclusion of patients and healthy subjects and was one of the assessors. The PhD candidate performed the data analysis and interpretation of data.	
Drafting the manuscript:	A
Free text description of PhD student's contribution ***(mandatory)*** The PhD candidate wrote the manuscript and revised it after comments from the author group.	
Submission process including revisions:	A

Free text description of PhD student's contribution ***(mandatory)***   The PhD candidate (LT) performed the submission of the manuscript.

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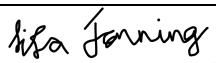
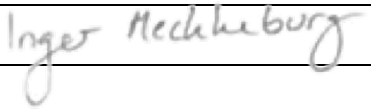
13.03.25	Lisa U. Tønning	
13/03/25	Inger Mechlenburg	

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Title:	Is the Femoral-Epihyseal Acetabular Roof (FEAR) Index associated with hip pain in patients with hip dysplasia?
Authors:	Tønning LU, Schmid M, Barroso J, Hovind B, Hessain D, Balling M, Jakobsen SS, Mechlenburg I

The article/manuscript is: Published ☒ Accepted ☐ Submitted ☐ In preperation ☐

If published, state full reference: Acta Radiologica

If accepted or submitted, state journal:

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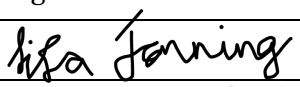
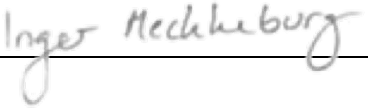
30.01.2025	Lisa U. Tønning	
03.02.2025	Inger Mechlenburg	

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Full name of the PhD student: Lisa Urup Tønning

This declaration concerns the following article/manuscript:

Title:	Sports participation among patients with hip dysplasia before and up to 20 years after periacetabular osteotomy
Authors:	Tønning LU, Jakobsen SS, Kemp JL, Livera AD, O'Brien MJM, Dalgas U, Mechlenburg I

The article/manuscript is: Published ☐ Accepted ☐ Submitted ☒ In preperation ☐

If published, state full reference:

If accepted or submitted, state journal: American Journal of Sports Medicine

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

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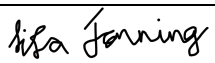
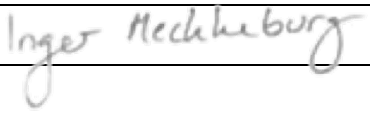
13.03.25	Lisa U. Tønning	
13/03/25	Inger Mechlenburg	

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This declaration concerns the following article/manuscript:

Title:	Validation of the Aarhus periacetabular osteotomy database
Authors:	Lisa U. Tønning, Frederik N. Foldager, Josefine B. Larsen, Pia K. Kristensen, Inger Mechlenburg, Kjeld Søballe and Stig S. Jakobsen

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Free text description of PhD student's contribution ***(mandatory)*** The PhD candidate accuired the data alongside the 2nd and 3rd author, and performed the data analysis and interpretation of data.	
Drafting the manuscript:	A
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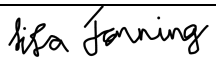
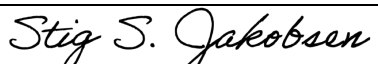
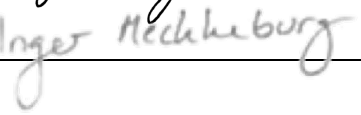
13.03.25	Lisa U. Tønning	
14.3.2025	Stig S. Jakobsen	
14.03.25	Inger Mechlenburg	

Date: 13.03.2025

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