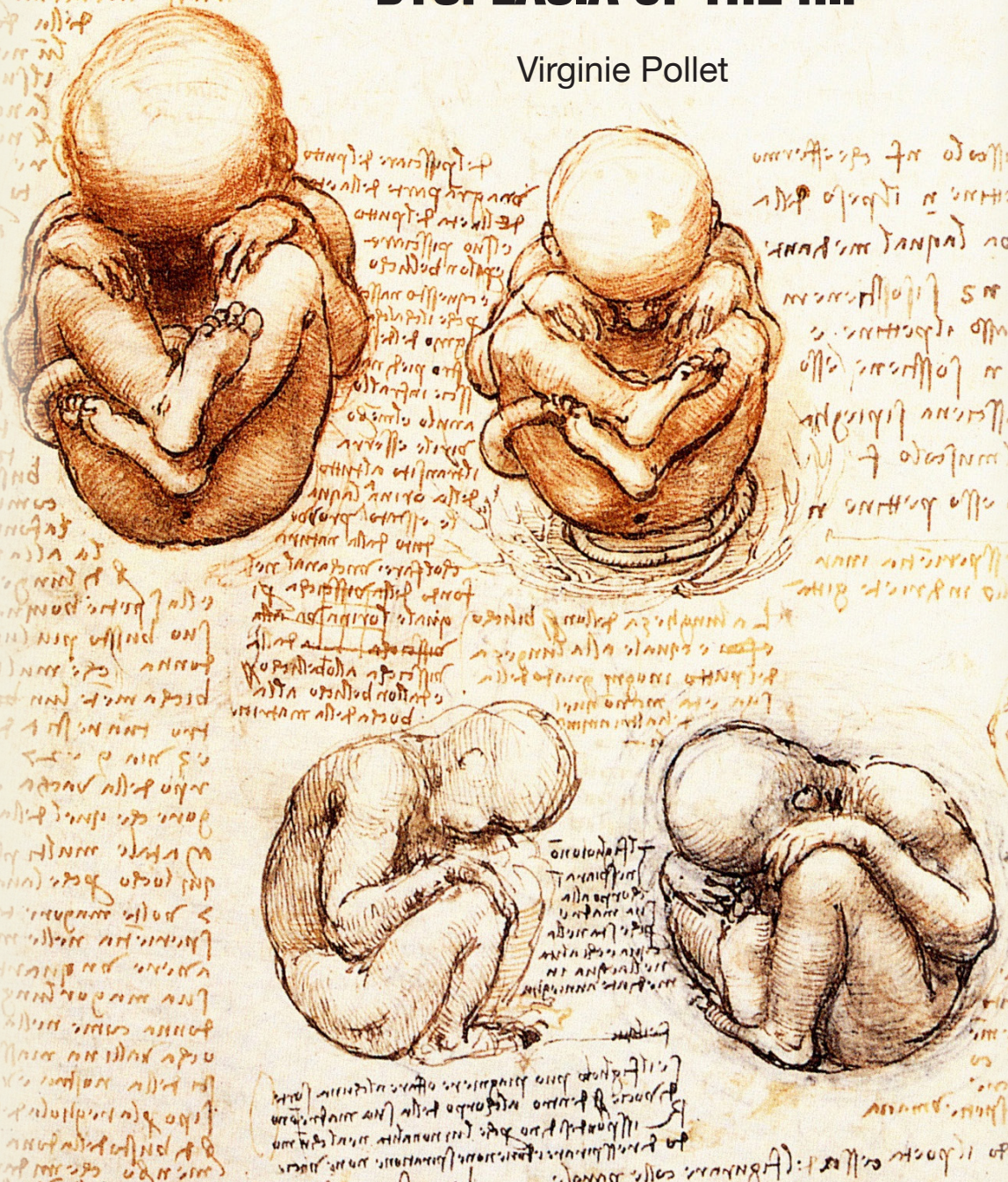
FROM DIAGNOSIS TO OUTCOME IN DEVELOPMENTAL DYSPLASIA OF THE HIP

Virginie Pollet



From Diagnosis to Outcome in Developmental Dysplasia of the Hip

VIRGINIE POLLET

From Diagnosis to Outcome in Developmental Dysplasia of the Hip

Diagnostiek en effect van behandeling bij heup dysplasie

(met een samenvatting in het Nederlands)

Proefschrift

ter verkrijging van de graad van doctor aan de
Universiteit Utrecht
op gezag van de
rector magnificus, prof.dr. H.R.B.M. Kummeling,
ingevolge het besluit van het college voor promoties
in het openbaar te verdedigen op

donderdag 10 december 2020 des ochtends te 11.00 uur

door

Virginie Marianne Luc POLLET

geboren op 9 februari 1972
te Waregem, België

This thesis is financial supported by the Anna Fonds and the Nederlandse Orthopaedische Vereniging (NOV).

ISBN: 978-94-6419-087-8
Cover: Ilse Modder | www.ilsemodder.nl
Lay-out: Ilse Modder | www.ilsemodder.nl
Printed by: Gildeprint Enschede | www.gildeprint.nl

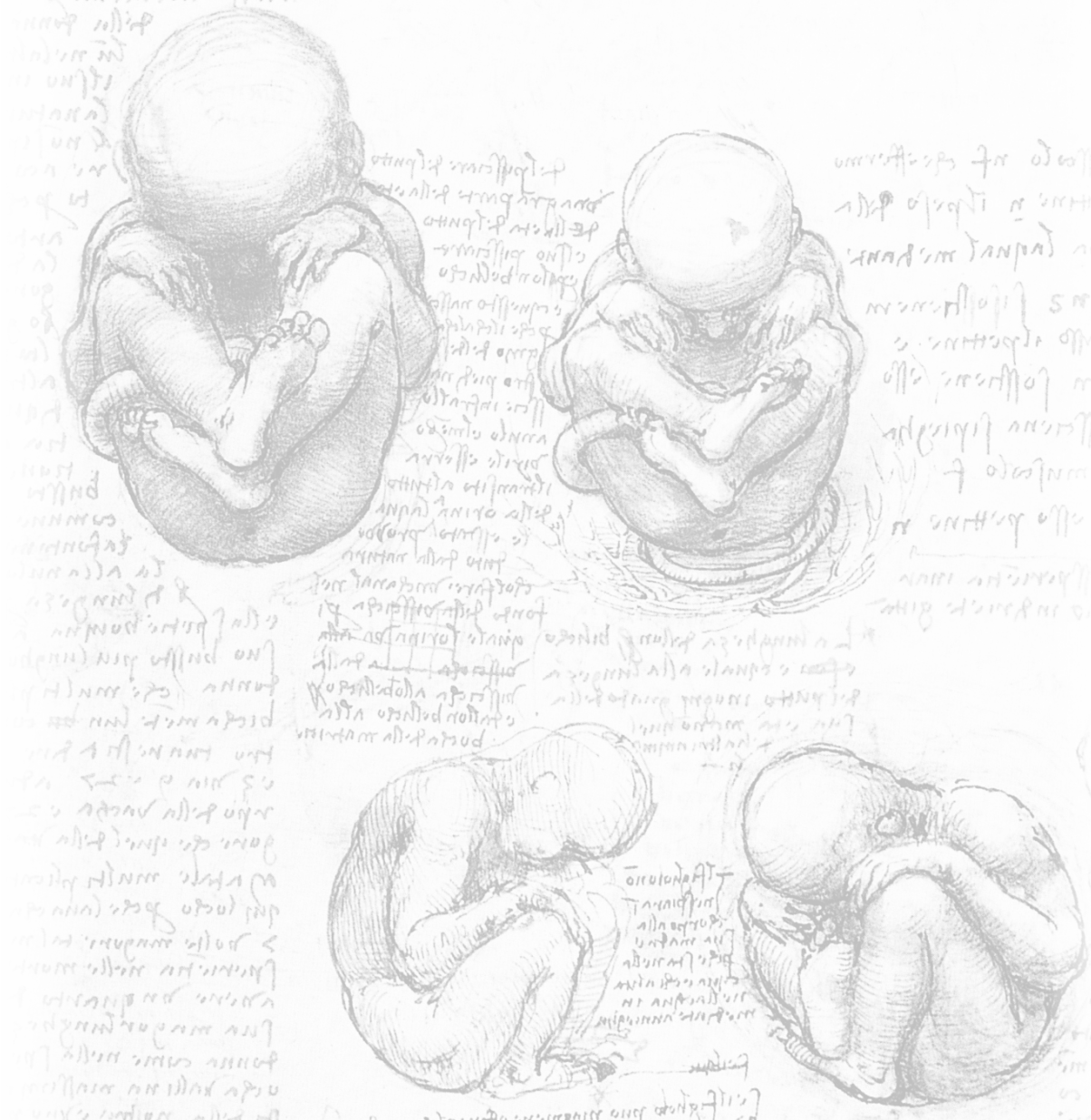
Promotor:
Prof. dr. R.M. Castelein

Copromotor:
Dr. R.J.B. Sakkers

TABLE OF CONTENTS

CHAPTER 1

Introduction, aims and outline of this thesis



INTRODUCTION

Developmental dysplasia of of the hip (DDH) is the most common hip disease in children where the altered hip morphology is a risk factor for the development of early-onset osteoarthritis (OA).[1] Despite the early mentioning of the hip abnormality by Hippocrates (400-300BC) followed by several anatomy studies and early publications in the 19th and 20th century, there is still no consensus on the correct terminology of the disease with congenital and developmental both being used throughout the current literature. Congenital Dislocation of the Hip (CDH) and Developmental Dysplasia of the hip (DDH) are both used to describe a wide range of hip abnormalities from mildly dysplastic to full dislocation, regardless of age. The "Developmental" aspect of hip dysplasia was first proposed in 1989 by Klisic to replace the word "congenital" as hip dysplasia also appears later in life and not just before birth. [2]

Anatomic development/Etiopathogenesis

Embryology

The hip starts to develop around the seventh week of gestation with a fully developed joint at 11 weeks, the earliest a dysplastic hip could start to develop. [3] The pressure of the spherical femoral head in the acetabular socket determines the concave shape of the acetabulum. Furthermore, interstitial growth within acetabular cartilage, appositional growth under the perichondrium and growth of the adjacent bones will shape the acetabulum. Most of this shape is obtained around 8 years of age. Ultimately, there is an adolescent growth spurt with final acetabular growth from 3 secondary ossification centers: acetabular epiphysis (ilium), os acetabulum (pubis) and 2nd ossification center from the ischium. In DDH, most of the abnormality is due to acetabular changes either primary (genetically pre-determined?) or secondary due to abnormal pressure of the femoral head in relation to muscle pull and forces transmitted across the hip joint. [3,4]

Dysplasia means there is an inadequate development of the joint, which will lead to mechanical changes in loading and increased contact stress. The latter will contribute to accelerated wear and tear of the cartilage and labrum acetabulare which is a risk factor for later development of degenerative hip disease, osteoarthritis (OA). Walker et al compared the anatomy of 24 dysplastic hip joints (12 normal and 12 teratologic) with 280 normal joints from stillbirths or perinatal deaths. [5] His findings were in line with previous studies that the abnormal features where not a mere result of cell destruction but growth retardation based on measurement of the femoral head and acetabular depth. Typical dysplastic abnormalities were rarely seen before the 20e week of gestation.

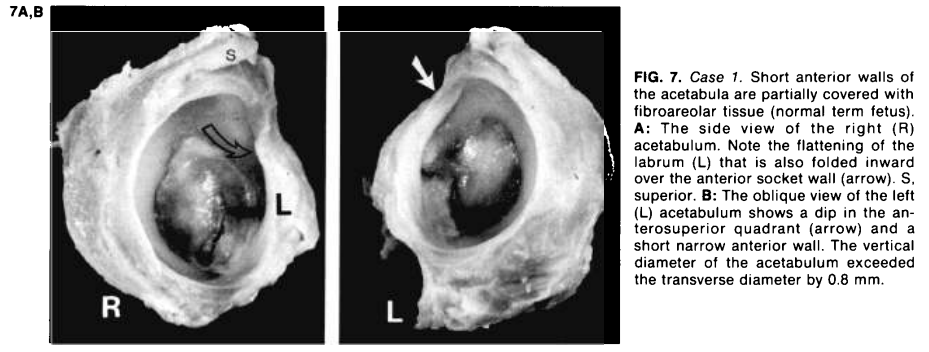


FIG. 7. *Case 1.* Short anterior walls of the acetabula are partially covered with fibroareolar tissue (normal term fetus). **A:** The side view of the right (R) acetabulum. Note the flattening of the labrum (L) that is also folded inward over the anterior socket wall (arrow). S, superior. **B:** The oblique view of the left (L) acetabulum shows a dip in the anterosuperior quadrant (arrow) and a short narrow anterior wall. The vertical diameter of the acetabulum exceeded the transverse diameter by 0.8 mm.

Fig 1. Fetal anatomic specimen of the hip.
(ref: Walker J.M. (1983)Comparison of normal and abnormal human fetal hip joints: a quantitative study with significance to congenital disease. J Ped Orthop 3: 173-183)

In another pre- and neonatal hip study in 22 hips, Avisse et al observed that the fetal acetabulum remains cartilaginous until birth.[6] The acetabular cartilage consist of a thick layer of homogeneous hyaline cartilage with thinly dispersed round chondrocytes adjacent to the endochondral bone formation of the ilium, ischium and pubis. (Fig 2).

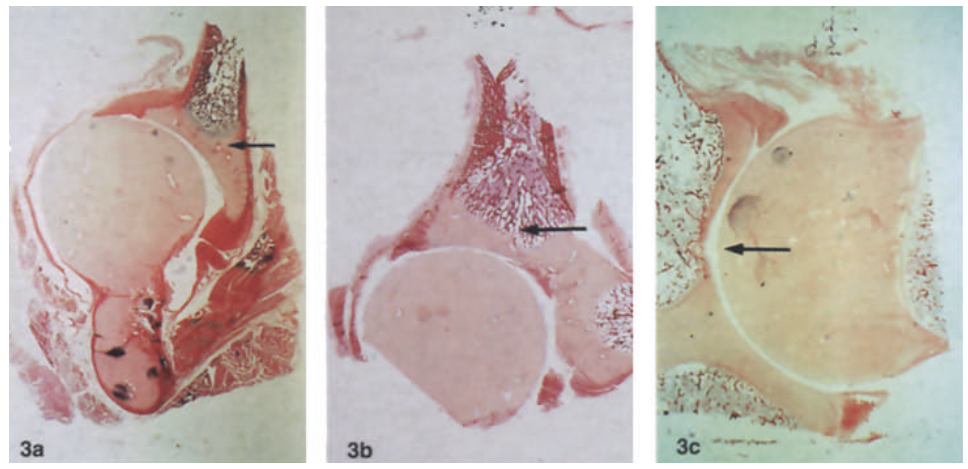


Fig 2. Histologic sections (frontal plane through the center of the hip. **a**. In the fetus, the acetabular cartilage consists of a homogeneous layer of hyaline cartilage (arrow). Note the convexity of the growth plate. **b.** In the newborn, the growth plate is flattened (arrow) oppostie the femoral head. **c.** At 3 months, degenerative changes affect the cartilage and growth-plate opposite the femoral head pressure zone (arrow), leading to the formation of a cup-shaped bony cavity.
(ref Avisse C, Gomes C, Delvinquier V et al. (1997) Anatomic study of the pre- and neonatal hip. Physiopathogenic considerations on dysplasia and congential dislocation of the hip. Surg Radiol Anat 19: 155 -159.)

The acetabulum of the fetal hip is very easily deformed with minor pressure. In the neonatal period, the shape of the acetabulum is determined by a progressive cavitation of the iliac metaphysis, extending around the femoral head during the first 3 months of age. Both metaphyseal extension and cavitation forms the acetabular rim, protruding over the postero-superior half of the femur. They suggested an insufficient postero-superior iliac metaphyseal expansion allows deformation of the acetabular cartilage and subsequent femoral subluxation inhibits metaphyseal growth. Based on these findings, together with the histopathology studies published by Ponseti where he described a cartilaginous degeneration process caused by femoral head pressure, they concluded that these histological studies help understand the various etiopathogenesis of DDH namely, genetic dysplasia, mechanical fetal and postnatal postural dislocation.

Epidemiology & Demographics

Loder et al published an extensive systemic review in 2011 on epidemiology and demographics of hip dysplasia.[7] The incidence ranges from 0.06/1000 live births in Africans to 76.1 in Native Americans. The left hip is mainly affected (64%) and most often unilateral involvement (63.4%). The incidence of neonatal hip instability (NHI) is somewhat higher with 0.4/1000 live births for Africans to 61.7/1000 for Polish Caucasians. Risk factors are breech position, positive family history and female gender with associated conditions such as congenital muscular torticollis and talipes equinovarus deformity. Often, the contralateral hip will be abnormal too (abduction contraction). Interestingly, there is a tendency of seasonal variation with higher number of DDH births in winter probably due to swaddling and somewhat more restricted movements due to tighter clothing. The incidence of late-diagnosed DDH (with a variable definition of “late”) varies from 2.4 in Norway to 0.84 in Scotland. There is some evidence the right hip is more often affected than the left in late DDH. In case of bilateral involvement, the diagnosis will more often be delayed than in unilateral DDH.

Diagnostics

We can only estimate the true incidence of DDH due to the wide variety in terminology and diagnostics. Clinical examination will depend on physicians’ experience and relaxed status of the infant to detect limited abduction, instability (tested with Ortolani (reducibility) and Barlow (dislocatability) maneuvers) and shorter affected leg in case of full dislocation (Positive Galleazi sign). The golden standard for diagnosis during the first 6 months of life remains ultrasound as most of the joint is still cartilaginous which limits the use of X-rays. Both Harcke and Graf described their method in the early nineteen eighties and in 1993, they merged their method including a dynamic assessment (Femoral head coverage %) (Harcke) with a static view of the hip morphology, measuring the bony roof angle α (Graf) as a degree of dysplasia.[8] The cartilage roof angle β is less often used as the inter- and intra-reliability has been proven to be poor. [9] Table 1 shows the classification of hip dysplasia

according to Graf. (10) There are 4 types of dysplasia based on the degree of acetabular dysplasia and/or (sub)luxation of the femoral head. Figure 3 shows a normal hip ultrasound on the left and a dislocated hip on the right.

Table 1. Graf Classification.

Type	Alpha angle (°)	Beta angle (°)	comment
I a/ Ib	> 60	< 55 / >55	normal
IIa	50 - 59	Covers femoral head	< 3mos, physiological immaturity
IIb	50 -59	Covers femoral head	Delayed ossification
IIc stable unstable	43 - 49	< 77	Critical age, still covers femoral head
D	43 - 49	<77	Decentered hip
III	< 43	Pressed upwards	Eccentric hip
IV	< 43	Pressed downwards	Dislocated with labrum interposed between femoral head and acetabulum

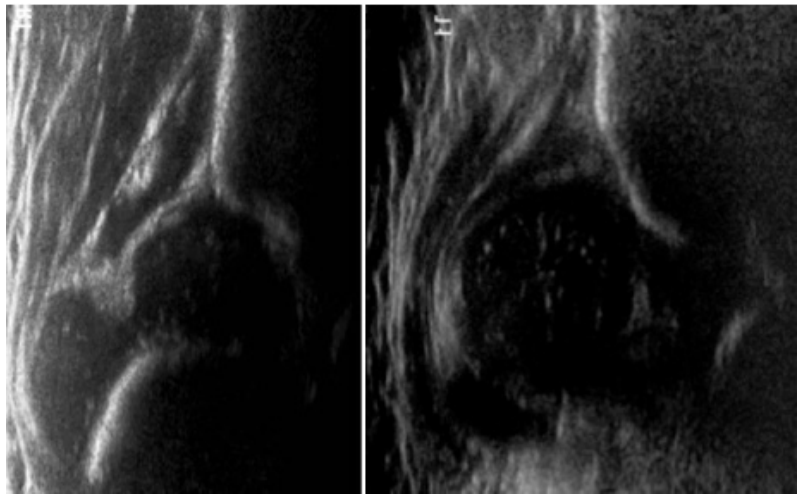


Fig 3. Graf Type I normal hip *(left)* and Graf type III dislocated hip *(right)*.

There is still controversy around universal or selective screening for DDH by ultrasound and this will vary from country to country. [3,11] The opponents of universal screening question the efficiency, logistic and financial burden and the rate of overtreatment. Selective screening of infants with risk factors appears to be the most common practice in many countries. Roposch et al studied the variation in diagnostic criteria, based on 4 domains: history/ patient characteristics, physical examination, ultrasound and X-rays in 35 countries. [12]

They found a poor consistency with an overall ICC of 0.33(98%CI 0.24 - 0.45). The clinical examination scored the best (ICC 0.50(0.33-0.73). Figure 4 shows the geographic variation of consistency based on ICC. Interestingly the ultrasonographic criteria were the least consistent. They highlighted the importance of aligning diagnostic practices, as this would also improve the standards of management of DDH.

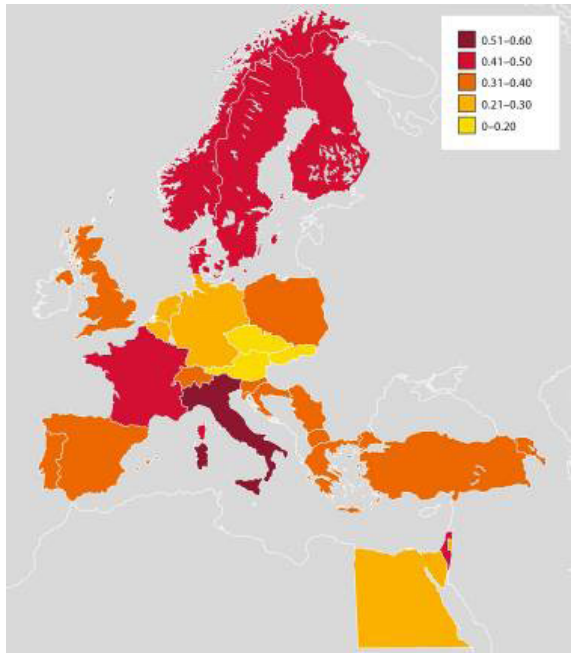


Fig 4. Geographic variation of consistency based on ICC.
(ref Roposch, A., Liu, L. Q., & Protopapa, E. (2013). Variations in the use of diagnostic criteria for developmental dysplasia of the hip. Clinical Orthopaedics and Related Research, 471(6), 1946–1954. https://doi.org/10.1007/s11999-013-2846-5)

Treatment

The main goal of the treatment in DDH is to obtain a concentric stable hip joint. Residual dysplasia will lead to secondary degenerative changes in the joint with early development of OA. The treatment differs depending on the child's age and severity of hip dysplasia. During the first 6 months of life, the golden standard of treatment is the Pavlik Harness, developed by Arnold Pavlik in early 1950. [13] The harness was designed to reduce the rate of avascular necrosis by allowing a dynamic reduction of a reducible dislocated hip, avoiding rigid forced abduction and fixation in a spica cast. This dynamic bracing of the hips in abduction and flexion is successful, depending on the severity of DDH, allowing the femoral head to reduce in the acetabulum, it promotes healthy acetabular development with correction of dysplasia.[14]

There is a wide geographic variation in treatment and other methods are being used with a similar aim, such as a Freijka pillow and Van Rosen Splint. More so, it is an on-going debate if all dysplastic hips should be treated and what the duration of treatment should be. There is no universally accepted algorithm. Some studies have shown persistent dysplasia after Pavlik harness in up to 20% at pre-adolescence, reason why all children should be observed till skeletal maturity. [15]

When the Pavlik harness fails or the child is older than 6 months, the next step will be closed reduction under general anaesthesia with spica cast application. The use of preliminary traction is still questioned and is regionally dependent. Traction, however, facilitates closed reduction and was shown to decrease the incidence of Avascular Necrosis (AVN), especially in children under 3 years of age. [16]

If all of the above fails to achieve adequate reduction, open hip reduction will be the final step to obtain concentric reduction, with or without pelvic/femoral osteotomy, followed with spica cast application. Both medial and anterior approaches have been described with similar rates of concentric reduction and risk of AVN. [17,18] A further area of debate is the duration of spica cast, change of cast and the use of an abduction orthosis after removal of the cast.

Complications

As mentioned above, two main complications of (the treatment of) DDH are residual dysplasia (RD) and AVN. Firstly, RD is linked to early degeneration of the hip joint causing pain and discomfort with decreased Quality of Life (QoL) in (young) adulthood. Especially a persistent degree of subluxation at skeletal maturity will continue to develop and further damage the cartilage of the hip joint. Changes in contact forces and loading will not only deteriorate the acetabular dysplasia but also lead to proximal femoral deformity with decreased femoral-neck offset and subsequently cam-type impingement as the femoral head radius enlarges.[19] This can be treated potentially with Peri-Acetabular Osteotomy (PAO) in conjunction with correction of the cam impingement, if the latter is present. However, Wyles et al showed that the progression to Total Hip Arthroplasty is high in patients with RD/AD, especially if early degeneration (Tönnis grade 1) is present. [1]

Secondly, AVN is probably the most feared complication by the paediatric orthopaedic surgeon as this iatrogenic interruption of the bloodstream to the epiphysis leads to alteration of the proximal femoral growth with subsequently changes to the joint congruency and RD with unpredictable outcome. A lot will depend on the remaining remodelling potential of the child during growth. Several classifications describe the changes to the proximal femur, as well as different severity of growth disturbance. Bucholz-Ogden and Kalamchi-McEwen

are the most frequently used classifications and are based on morphologic descriptions on pelvis X-rays.[20,21] Both classifications divide AVN in 4 types describing growth disturbances at the epiphyis and/or proximal growth plate. Not all AVN hips will have a poor outcome as long as the hip maintains roundness of the femoral head and is adequately covered by the acetabulum at skeletal maturity. Treatment will consist of restoring the shape and biomechanics of the hip joint as best as possible.

AIMS AND OUTLINE OF THIS THESIS

DDH is a complex disease with many aspects and multi-variable outcome. The aim of this thesis is to obtain answers related to natural history, treatment and outcome and to establish direction for future research.

CHAPTER 2: Relative Risk and Incidence for Developmental Dysplasia of the Hip
The etiopathogensis of DDH is multifactorial with higher incidence in certain populations. [22] Modern life and traveling made migration much easier. Canada reflects such a culturally diverse population. The province of Manitoba has large Indigenous, French-Canadian and Hutterite communities. We aimed at establishing the incidence and risk factors for DDH in this modern society without universal screening.

CHAPTER 3: The natural history of abnormal ultrasound findings in hips of infants under six months of age.
Screening programmes for DDH aim to identify children who are at risk of developing long-term morbidity due to residual dysplasia (RD). There is still controversy about the best screening tool and if all children should be tested. Despite ultrasound (US) being the golden standard, high quality reviews have shown the highly sensitive but poorly specific aspect of US, resulting in unnecessary treatment. [23] The purpose of this study is to look at the natural history of US abnormal findings in children younger than 6 months of age.

CHAPTER 4: Abduction treatment in stable hip dysplasia does not alter the acetabular growth: results of a randomized clinical trial
Abduction treatment such as Pavlik harness for DDH is preferably started in the first months of life and is considered the standard of care for all types of hip dysplasia until the age of around 6 months. However, there is a considerable geographic variation in consistency of diagnostic criteria and therefore management.[12] Furthermore, 85% of mild infantile DDH will resolve spontaneously by the age of 3 months. (24, **chapter 3**). We hypothesized that abduction treatment in stable dysplastic hips, diagnosed by ultrasound, will have no added effect on acetabular development. Hence, we designed a multi-center randomized control trial comparing treatment versus active surveillance for stable DDH in 3-4 month old children.

CHAPTER 5: Results of Pavlik harness treatment in children with dislocated hips between the age of six and twenty-four months.
In **chapter 3 and 4** we included only children younger than 6 months of age. In late DDH, children are generally older than 6 months and with ongoing motor development, they start to sit and roll. The Pavlik harness is too dynamic to withstand the forces of the core and hip flexor muscles and a more rigid form of bracing or as casting is necessary. The iliopsoas and adductor muscles will also start to develop contractures, especially if the hip is dislocated. The standard of care is closed or open reduction under general anaesthesia for late DDH. In Children's hospital of the University Medical Center of Utrecht (UMCU), the Pavlik harness was on occasion tried prior to closed reduction with the idea to loosen contractures in this age group. We wondered how effective this conservative treatment was in late-diagnosed DDH (after 6 months of age). We also studied if adding a rigid abduction splint improved the success rate.

CHAPTER 6: Long-term outcomes following the medial approach for open reduction of the hip in children with developmental dysplasia.
If closed reduction fails, open hip reduction is the next step in treatment of DDH. Both anterior (Smith-Peterson) and medial (Ludloff, Ferguson or Weinstein) approaches are commonly used to remove any obstacle to concentric reduction. The main advantage of the anterior approach is the possibility to perform a capsulorraphy securing the femoral head in the acetabulum, and the possibility to perform pelvis osteotomies. Both techniques are linked to a high rate of AVN (± 25%) [17,18] The medial approach has a higher potential to damage the medial femoral circumflex artery with subsequent AVN. At the Sophia Children's hospital of the Erasmus Medical Center (EMC) in Rotterdam, the medial approach was routinely done for many years. We studied the long-term radiographic and clinical outcomes of this approach.

CHAPTER 7: Morphological variants to predict outcome of avascular necrosis in Developmental Dysplasia of the Hip.
In **chapter 6**, we studied the rate of AVN and outcome after open hip reduction. The poor outcome is linked to loss of normal hip joint congruency and residual dysplasia due to growth disturbance induced by AVN. The classification systems, such as Bucholz-Ogden, describe the abnormal hip morphology but have limited prognostic value and have poor to moderate inter-/intra-reliability.[20,21,25,26,27] The Severin classification is used to grade the outcome of DDH based on a pelvis X-ray measuring the Center-Edge (CE) angle of Wiberg and morphological descriptions of the femoral head and acetabulum. There is no direct outcome classification for AVN complicated dysplastic hips. In absence of predictive value

of current classification systems, we hypothesized that certain hip morphologies can predict outcome of AVN. We used Statistical Shape Modeling (SSM) to indentify shape variants in AVN hips and studied the correlation to poor Severin outcome and Bucholz-Ogden classification.

REFERENCES

1. Wyles C, Heidenreich M, Jeng J, Larson D, Trousdale R., Sierra R. The John Charnley Award: Redefining the Natural History of Osteoarthritis in Patients With Hip Dysplasia and Impingement 2017 Clin Orthop Relat Res 2017 475: 336-350.
2. Klisic PJ. Congential dislocation of the hip: a misleading term. J Bone Joint surg Br. 1989:71:136.
3. Weinstein S, Mubarak S, Wenger D. Developmental hip dysplasia and dislocation: part 1. Instr Course Lect AAOS 2004; 53: 523-530.
4. Hogervorst T, Eilander W, Fikkers J, Meulenbelt I. Clin Orthop Relat Res 2012; 470:3284-3296.
5. Walker JM. Histological study of the fetal development of the human acetabulum and labrum: significance in congenital hip disease. Yale J Biol Med. 1981; 54: 255-263.
6. Avisse C, Gomes C, Delvinquiere V, Ouedraogo T, Lallemand A, Delattre J, Flament J. Anatomic study of the pre-and neonatal hip. Physiopathogenic considerations on dysplasia and congenital dislocation of the hip. Surg Radiol Anat 1997; 19: 155-159.
7. Loder R, Skopelja E. The epidemiology and demographics of hip dysplasia. ISRN Orthopedics 2011;21; 486512.
8. Harcke HT. Personal email communication to author, 12 October 2018.
9. Hell A, Becker J, Rühman O, von Lewinski G, Lazovic D. Inter- and intra-observer reliability in Graf's sonographic hip examination. Z Orthop unfall. 2008; 146: 624 -629.
10. Graf R. The use of ultrasonography in develomental dysplasia of the hip. Acta orthop traumatol Turc 2007; 41 (1): 6-13
11. Shorter D, Hong T, Osborn D. Cochrane review: screening programes for developmental dysplasia of the hip in newborn infants. Evid Based Child Health 2013; 8(1): 11-54.
12. Roposch A, Liu L, Protopapa E. Variations in the use of diagnostic criteria for developmental dysplasia of the hip. Clin Orthop Relat Res 2013; 471:1946-1954.
13. Pavlik A. The functional method of treatment using a harness with stirrups as the primary method of conservative therapy for infants with congenital dislocation of the hip. 1957. CORR. 1992; 281:4-10.
14. Morcuende J, Weinstein S. Developmental dysplasia of the hip: natural history, results of treatment and controversies. 2002
15. TucciJ, Kumar S, Guille J, Rubbo E. Late acetabular dysplasia follwig early successful Pavlik harness treatment in congentical dislocation of the hip. J ped Orthop.1991. 11:502-505.
16. Rampal V, Sabourin M, Erdeneshoo E, Koureas G, Seringe R, Wicart P, Closed reduction with traction in developmental dysplasia of the hip in children aged between 1 and 5 years. J Bone Joint Surg - Br. 2008 90(7);858-863.
1.
17. Hoellwarth JS, Kim YJ, Millis MB, et al. Medial versus anterior open reduction for developmental hip dislocation in age-matched patients. *J Pediatr Orthop* 2015;35:50-56
18. Konigsberg DE, Karol LA, Colby S, O'Brien S. Results of medial open reduction of the hip in infants with developmental dislocation of the hip. *J Pediatr Orthop* 2003;23:1-9.
19. Wells J, Nepple J, Crook K, Ross J, Bedi A, Schoenecker P, Clohisy J. Remoral morphology in the dysplastic hip: three-dimensional characterizations with CT. Clin Orthop Relat Res

2017; 475(4): 1045-1054.

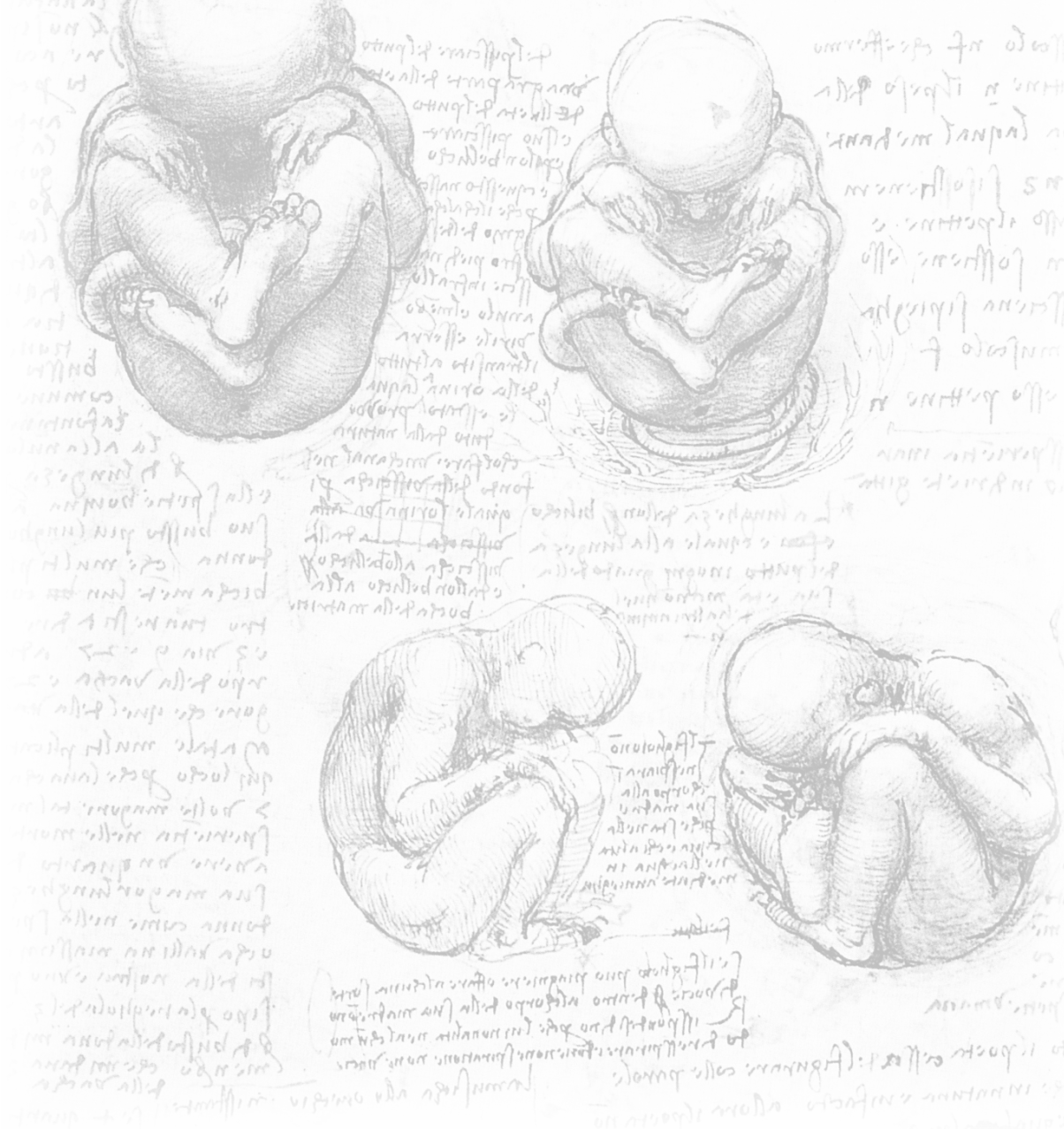
20. Bucholz RW. Patterns of ischemic necrosis of the proximal femur in non-operatively treated congenital hip disease in the hip. Proc 6th Open Scientific meeting of the hip society. 1978; vol 2:43-63
21. Kalamchi A, MacEwen GD. Avascular necrosis following treatment of congenital dislocation of the hip. J Bone Joint Surg Am. 1980; 62(6):876-88
22. Ortiz-Neira C, Paolucci E, Donnon T. A meta-analysis of common risk factors associated with the diagnosis of developmental dysplasia of the hip in newborns. Eur J Radiol.2011;1-8
23. Patel H, Canadian Task Force on Preventive Health Care. Preventive health care, 2001 update: screening and management of developmental dysplasia of the hip in newborns. *CMAJ* 2001;164:1669-1677
24. Ward WT, Vogt M, Grudziak JS, Tümer Y, Cook PC, Fitch RD. Severin classification system for evaluation of the results of operative treatment of congenital dislocation of the hip. A study of intraobserver and interobserver reliability. *J Bone Joint Surg* Am. 1997;79:656-663
25. Gardner RO, Bradley CS, Howard A, Narayanan UG, Wedge JH, Kelley SP. The incidence of avascular necrosis and the radiographic outcome following medial open reduction in children with developmental dysplasia of the hip: a systematic review. Bone Joint J. 2014;96-B(2):279-86.
26. Roposch A, Liu LQ, Offiah AC, Wedge JH. Functional outcomes in children with osteonecrosis secondary to treatment of developmental dysplasia of the hip. J Bone Joint Surg Am. 2011;93(24):e145.
27. Roposch A, Wedge JH, Riedl G. Reliability of Bucholz and Ogden classificaton for osteonecrosis secondary to developmental dysplasia of the hip. Clin Orthop Relat Res. 2012;470(12): 3499 - 505.

CHAPTER 2

Relative risk and incidence for developmental dysplasia of the hip

Virginie Pollet, Vanessa Percy, MD, Heather J. Prior

J Pediatr. 2017 Feb;181:202-207



ABSTRACT

Objective

Manitoba reflects the culturally diverse population in Canada with children from all backgrounds, including large Indigenous, French Canadian and Hutterite communities. There are anecdotal citations of clinical observations dating back to 1950 describing a high rate of DDH.

The aim of the present study is to determine the incidence and associated risk factors of DDH in a modern population without universal screening.

Methods

Children with DDH were identified from the Manitoba Centre for Health Policy's (MCHP) Data Repository, using ICD diagnosis codes as well as physician billing tariffs for surgical procedures for DDH for all children born between 1995 and 2012. To identify the outpatient treated patients, ultrasound and radiographic imaging for DDH were reviewed for 2004-2012. Overall incidence was calculated based on birth rate for the province per year. Relative risks of gender, first born, breech position, clubfoot deformity, multiple gestations as well as regional health areas were analysed using Chi-square tests.

Results

We identified 1716 cases of DDH out of 258 499 newborns. The incidence of DDH is calculated at 6.6/1000 newborns. The late-presenting DDH was 2.2/1000 newborns. Female first-born children, clubfoot deformity and breech position were significantly associated with an increased risk. Children with DDH born in rural areas of the Northern and Central part of Manitoba presented at a later age than those who are born in the urban areas ($p<0.0001$)

Conclusion

This study shows the need for improved early detection and awareness at well-baby clinics of risk factors and regional differences for DDH.

INTRODUCTION

Developmental Dysplasia of the Hip (DDH) is a spectrum of hip pathology in children including mild dysplasia of the acetabulum, subluxation and complete dislocation of the hip joint. If left untreated, the dysplastic hip can further deteriorate with subluxation, muscle contractures, gait disturbances and osteoarthritis eventually.

Ideally, the child is treated with a Pavlik harness before the age of 6 months. This is a minimal invasive outpatient treatment with excellent outcomes and very low complication rate. [1] However, if the diagnosis is made at an older age and the child approaches walking age, interventions such as open hip reposition, femoral osteotomies and pelvis osteotomies will be necessary. Therefore, late-diagnosed DDH will increase the risk for residual dysplasia or avascular necrosis of the femoral head as complication of the treatment. It is estimated that 1 in 6 children treated for DDH will develop osteoarthritis by 45-50 years of age. [2] As there is no true cause for DDH - the anatomy of the hip joint has a normal development in utero and is therefore not a congenital deformity but rather a developmental disease - multiple risk factors have been identified such as breech position, female gender, first born child, family positive history, foot deformity, multiple gestation and oligohydramnios. [3,4] The incidence rate for DDH ranges from 1/1000 to 20/1000 depending on the literature and regional differences. [5,6,7] The incidence of late diagnosed DDH is less and is estimated to be around 1/5000. [1,5,8] In Canada, there is no universal screening program for DDH compared to other countries in Europe and Australia. [1,5,9,10] Children are seen at well-baby clinics. The detection of clinical abnormalities such as limited abduction, hip instability testing (Ortolani and Barlow) will depend on the experience of the nurse or doctor. It is known that there is a wide variety of knowledge leading often to late-diagnosed DDH, even after walking age when the child starts limping due to leg length discrepancy. Manitoba reflects the culturally diverse population of Canada with children from all backgrounds, including large Indigenous, French Canadian and Hutterite communities. There is a total population of almost 1,2 million people: 16,7% is of Aboriginal identity, 15.7% are Immigrants and 13.1% is a visible minority (non-Caucasian, non-Aboriginal) population. (Source: Statistics Canada, 2011 National Household survey (NHS)). These are anecdotal citations of clinical observations dating back to 1950 describing a high rate of DDH. The purpose of this study is to establish the incidence of early and late diagnosed DDH in Manitoba and to identify the risk factors associated with DDH within this population.

METHODS

After Ethics board approval, we conducted a retrospective cohort review. All children age 0

to 17 diagnosed with DDH between 1995 and 2012 were identified using the ICD diagnosis codes for DDH (ICD-9-CM codes 754.3, 755.63 and ICD-10-CA code Q65) as well as physician billing tariffs for surgical procedures for DDH, i.e., dislocation reduction and spica casting from Manitoba Centre for Health Policy's (MCHP) – Population Health Research Data Repository.

To identify the conservatively treated patients, we used the records from the radiology department - both ultrasound and pelvis x-rays - as all children were seen and treated at the single Children's hospital for the province between 2004 and 2012. As there can be an important inter-rater variability in ultrasound and to avoid over-diagnosing, we used a 55 degrees or less of bony roof angle (alpha angle) as described by Graf to diagnose DDH. The Pelvis X-rays were examined for interrupted Shenton line, dysplastic acetabular index, (sub) luxation of the hip.

In order to examine risk factors of DDH and regional differences, a birth cohort of children born 1995 to 2012 were followed from birth to death, migration out of province or December 31, 2012, whichever came first. Demographic information for patients such as place of birth, gender, age at diagnosis/treatment, first born, multiple gestation and breech birth position (at birth registered presentation code) were identified using the MCHP's Data Repository. ICD-9-CM and ICD-10-CA diagnosis codes for clubfoot were also identified from the Repository and linked to the DDH population.

Children diagnosed with cerebral palsy, spina bifida or arthrogryposis multiplex congenita were excluded from the birth cohort.

Canada has a public Health Care System that is governed by each province. Manitoba consists of 5 Regional Health Authorities (RHA) (previously 11 (2013)). For crude rates, DDH cases were assigned the RHA they resided in as of diagnosis date. For the relative risk calculations, children in the birth cohort were assigned their RHA using their postal code at date of birth.

Statistical analysis

Crude rates of DDH and 95% confidence intervals (95% CIs) were calculated per 1,000 newborns, overall, per year and per RHA. For the birth cohort, the relative risk (RR) of DDH and 95% CIs were calculated to assess for differences in risk factors such gender, multiple gestation and clubfoot. Statistical significance of relative risks was tested with the Chi-Square test. An ANOVA regression model was run to measure regional differences in the average age at presentation. Differences in least squared means and 95% CIs were calculated, comparing the mean age at diagnosis for each region to the provincial average.

RESULTS

We identified 1716 cases of DDH for a total of 258 499 newborns between 1995 and 2012. For the birth cohort, we identified a subset of 1469 cases; the remaining cases would be for children diagnosed in 1995-2012, but born prior to 1995, or born out of province. Sixty-five per cent of DDH cases were female compared to 35% male for the birth cohort. Of the female DDH patients, 46.8% were first born. Breech position was present in 19.3% of the DDH patients. Only 1.9% consisted of twins or triplets. Breech position in multiple gestations was only present in less than 1 %. Out of the 1469 cases of DDH, 42 patients were also diagnosed with clubfoot deformity.

The incidence of DDH was 6.6/1000 newborns. In 66% of the cohort, the diagnosis was made within the first 6 months of age. Of the 1716 patients, only 42 patients were diagnosed between the age of 3 and 6 months. Therefore we defined 6 months as late-diagnosed DDH as Pavlik harness treatment can still be effective in this younger age group. The remainder received treatment after 6 months with still 16% after walking age. The radiology dataset added another 8,6% DDH cases for 2004-2012 but did not change the incidence significantly.

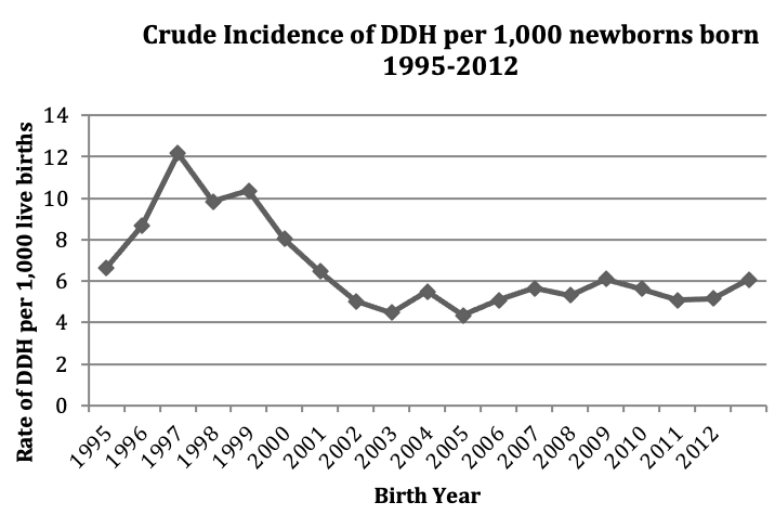


Fig 1. Incidence of DDH per 1000 newborns in 1995-2012

The patient related relative risks of DDH were significant for female gender and first born female child. Breech presentation was also a significant risk factor both in Singletons and Multiple gestations. At the other hand, breech position compared to other birth presentations

in multiple gestations showed a significant reduces risk for DDH. The presence of a clubfoot was also associated with a higher risk of DDH. Macrosomia was associated with a reduced risk of DDH. Multiple gestations (none breech) were not found to be a higher risk of DDH.

Table 1. Relative risk (95% CI and p-value) of DDH Female first born, Breech position and presence of a clubfoot showed all significant higher risk for DDH.

Risk factor	Relative Risk (95%CI)	p-value
Females vs. Males	1.33 (1.28, 1.38)	<.0001
First born	1.15 (1.09, 1.22)	<.0001
First born F vs. M	1.37 (1.30, 1.45)	<.0001
First born F vs. other F	1.18 (1.11, 1.27)	<.0001
Multiple Birth	0.73 (0.50, 1.06)	0.0925
Breech Birth	5.03 (4.51, 5.60)	<.0001
Clubfoot	10.34 (7.60, 14.05)	<.0001
Macrosomia	0.88 (0.77, 1.00)	0.0441

Although there are elevated rates of DDH in Interlake-Eastern and the north of the province, regional related relative risks of DDH showed no significant difference for each region of the province compared to Manitoba overall, with exception of Prairie Mountain Health, RR = 0.61, (95% CI 0.50, 0.74).

As these rural areas are less accessible and parents have to travel long distances to get medical care, we studied the age at presentation in relation to rural areas compared to more urbanized parts of the province. Early-diagnosed/treated was defined as diagnosis/ treatment of DDH before 6 months of age versus late-diagnosed/treated DDH when presented after 6 months of age. The mean age at diagnosis/treatment was 12.3 months CI95% (10.7,14 months) for the rural areas compared to 6.4 months CI95%(4.9,7.8 months) for the urban areas. Also when looked at diagnosis/treatment after walking age (18 months), 29% compared to 13% presented at this age for rural versus urban areas respectively. (p<0.0001)

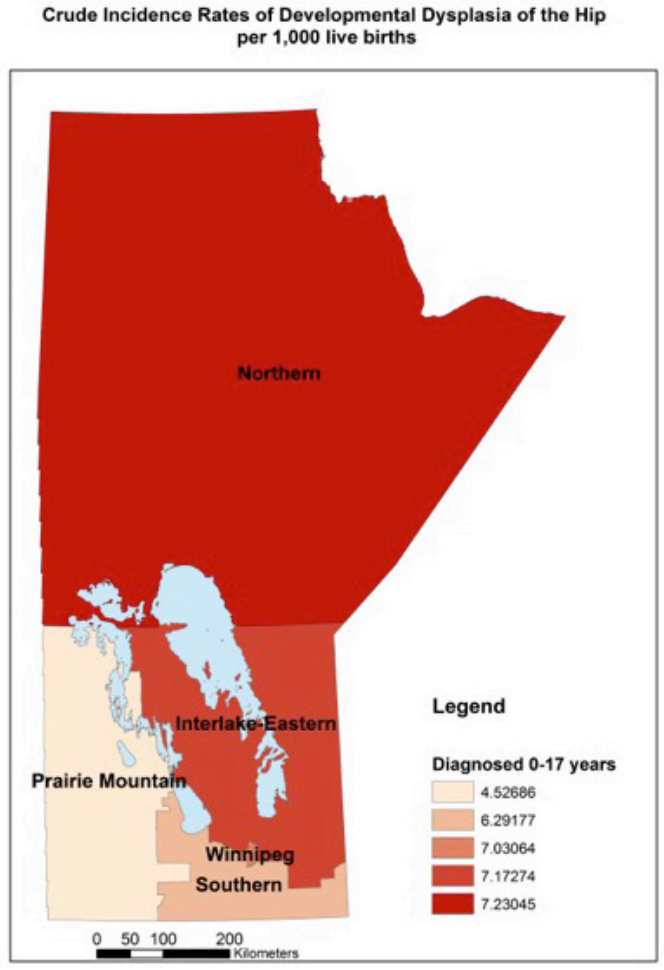


Fig 2. Incidence of DDH per 1000 newborns for the 5 Regional Health Authorities of Manitoba. Higher rates are found in Interlake-Eastern and Northern regions of the province.

Table 2. Difference in Age(months) at Diagnosis by RHA compared to Manitoba average. Older age at presentation combined with regional differences showed an increased risk for late-resenting DDH for children born in the Northern region and Prairie mountain region. Being born in Winnipeg, the capital of the province, has a protective effect on late-diagnosed DDH

RHA versus Manitoba average	Difference between means	CI95%	p-value
Interlake-Eastern vs. Manitoba Average	0.13	-4.20; 4.45	non-significant
Northern vs. Manitoba Average	5.87	1.97; 9.78	<0.05
Southern vs. Manitoba Average	2.56	-0.95; 6.06	non-significant
Prairie Mountain vs. Manitoba Average	5.19	0.16; 10.21	<0.05
Winnipeg vs. Manitoba Average	-2.62	-3.88; -1.35	<0.05

DISCUSSION

This retrospective cohort study shows an incidence of DDH of 6.6/1000 newborns.

We cannot assume that all patients were diagnosed that year, however the vast majority is diagnosed before 3 months of age. In terms of source, about 22,5% are identified through reduction/surgery and 69% through diagnosis. The radiology dataset available as of 2004, provided added an additional 8,5% of cases but did not significantly change the results.

Other studies described an average incidence of 1 - 2/1000 based on clinical screening only. Lehman et al found an incidence of 1.1/1000 in British Columbia, Canada, after introducing clinical screening based on risk factors. [11] The overall incidence did not change but the age at presentation did (from 10 months to 7 months of age). This was a study done in 1961 before any ultrasound screening took place.

Our very high rate of late-diagnosed/treated DDH after the age of 6 months (2.2/1000) is difficult to compare with previous studies as definition of late-diagnosed DDH varies from one-month to six-months depending in the literature. A similar study from Ireland (2015), although only a small number of patients are included, found an overall incidence of 6.7/1000 based on clinical screening with a late presentation of 2.7/1000 at the age of 3 months. [12] It is not clear how many of these children were seen after 6 months of age. A South Australian population-based study of 118,379 live births showed an incidence of 7.74/1000 based on a state wide clinical screening program introduced in 1964. Surgical incidence after the age of 3 months was only 0.19/1000. [13] In the UK (2012), 0.34/1000 children presented with late DDH (after 3 months) based on a sonographic screening program of 107440 children.[14] In Norway (2013), Laborie and colleagues found late presentation (after 1 month) in 0.32/1000 newborns based on a neonatal ultrasound screening of a large group of newborns with risk factors and/or clinical findings.[15]

The more worrisome 1 in 6 children being treated after walking age reflects clinical findings in daily practice. Often children present when waddling gait and leg length discrepancy become apparent. This makes treatment more difficult and more invasive with higher changes for avascular necrosis of the femoral head and residual dysplasia.

Paterson noted a significant decrease of presentation at walking age after introducing of a clinical screening program in 1964 in Australia. [16] The incidence of 1.2/1000 live births that was present in 1960-1964 decreased to 0.2/1000 in 1970-1973.

Although the Canadian Task force stated there is “fair evidence in favour of serial clinical examination of the hips to detect DDH in periodic health examination of all infants (2001)”, no routine clinical screening is performed in Manitoba.[7] A more recent update in 2009 on well-baby and -child care, Rourke concluded “ there is insufficient evidence to recommend routine screening for DDH, but examination should be included in periodic health examination until one year of age or until the child walks”.[17] This is a vague statement for family doctors and nurses at well-baby/child clinics who have often difficulties recognizing a Barlow/Ortolani positive hip. The Rourke Bay record has been endorsed by the College of family physicians of Canada (CFCP) and Canadian Pediatric society (CPS) since 2000. It is known that universal screening by ultrasound will increase the incidence and possibility of overtreatment. [18,19,20] This is mainly due to stable but dysplastic hips that will only be detected on ultrasound as well as a large number of neonatal hip instability cases that might otherwise go undetected as they stabilize and normalize within the first 3 months of age.[21] Nonetheless, studies have shown that introducing standard clinical and/or sonographic screening of high risk population decrease the incidence of late presentation and surgical incidence at later age.[11,22,23,24]

Our study shows that being first born female, breech position and presence of clubfoot deformity are significant higher risks for developing a dysplastic hip.

The correlation of clubfoot and DDH has been questioned in the literature. Although several observational studies of clubfeet show findings of 3-8% of the children associated with a dysplastic hip. [25,26,27] This means that the incidence of DDH in this subgroup is higher than in the overall population without clubfoot deformity and warrants the need for screening for DDH.

Others have studied the influence of age at diagnosis in relation to risk factors and have found that at an older age (i.e. older than 3 months) not only female gender and rural birth but vertex presentation and normal delivery are more common in this age group in contrast to breech position. [35] Seventy per cent of our cohort was diagnosed before the age of 3 months. This could explain why breech position was significant in our study. Looking at Manitoba, the province reflects a modern population with ethnic diversity. A large percentage of the population is represented by the First Nations Cree-Ojibwa community. While the total Aboriginal population is 15% for the province, this becomes 25% for the Interlake-Eastern RHA and even up to 70% for the Northern RHA. Both regions have the highest incidence of DDH in our study. These findings are consisting with anecdotal citations in the literature. In 1950, Corrigan described a high incidence of dislocated hips at Island Lake, a central region with significant higher incidence in our study. [28] At the time of this observation, access was only possible by water or ice roads in winter. Up to today, the First Nations population still, although less frequently, has cultural customs of keeping the young child laced in a cradle

board often till 1 year of age or longer. The lack of sidewalks for baby carriages, use of snowmobiles and boats encourages the use of cradleboards. It has been suggested that the limited ROM of the hips in extended and adducted position might develop DDH. [33,34]

Walker continued Corrigan's observations in 1971 with a review of medical records between 1949 en 1971. [29] The annual rates ranged from 35 to 600 per 1000 live births. Although the Tihkināk an or cradleboard was used in almost all children, he observed spontaneous improvements. A similar observation in a Navajo population did not correlate the use of the cradleboard to a higher rate of incidence especially since the introduction of diapers in the 1960 where the hips radiographs of babies in cradleboard showed the slightly abducted position. [30] The same rate of cradleboard use was noticed in the children with or without hip dislocation. Rabin suggested it was not the extended-adducted position but rather vertical position with unusually early weight bearing in combination of neonatal laxity in a semi-extended and minimally abducted hip that might delay normal development of the hip joint especially when used in the first month of life. We can question the methodology of these older studies but they point out the high incidence of dislocated hips regardless. All three observational studies showed a rather high hereditary etiological factor as primary cause of a dislocated hip. This is likely not different today in our population where there is a higher incidence in the First Nations and Hutterite communities where emigration and interracial marriage are less common. Other similar findings were found in Lapps, Bretons and central European areas, all small rather isolated populations where people tend to stay and marry locally. [32,31]

It is clear that cultural and ethnic diversity around the world will require different screening programs that should be adjusted for the region, even within one country. As Rabin stated in his observation of the Navajo population, "acceptance of a limping person, without pain and "getting along", meaning marriage, having children, performing household tasks and living as long as anyone else leads to acceptance and a dislocated hip is not seen as a disability". Where a failed surgery with pain and discomfort is. [30]

The purpose of early detection with minimal invasive treatment such as abduction bracing is of upmost importance avoiding complicated surgeries or early onset osteoarthritis. Based on our results, a clinical and/or sonographic screening program in Manitoba of all first born, girls, breech born babies and babies with clubfoot deformity - especially for those living in rural areas - could improve early detection and long term outcome. In a recent study by Studer et al. in South Australia, the role of screening was questioned as they detected an increase in late-diagnosed DDH cases despite implementation of a clinical screening program.[36] They call for a greater awareness, not only for first born and breech babies, amongst practitioners involved in hip screening and early child care, as well as better availability of educational material and family support. A screening program alone will not be able to avoid late presentation all together, which is almost impossible due to the broad spectrum of a "developmental" disease, variation in definitions, inter-rater reliability in ultrasound and cultural/regional differences. But screening programs help promote awareness and therefor help improve treatment outcome.

Our study has limitations, as this was a cohort study collected from a database and not a hospital chart review. Exact date of diagnosis of DDH was known in almost 70% of the cases. Our incidence is an incidence of diagnosis and treatment for DDH. A prospective study of the efficacy of a selective screening program and training of the physicians and nurses at the well-baby clinics - based on the regional at risk groups - could help decrease late presentation of DDH, surgery rate and improve overall long-term outcome.

CONCLUSION

This retrospective cohort study of a modern population with ethnic diversity in Manitoba, Canada, shows a significant high rate of late presenting DDH, even more so in the rural areas. First-born, female, breech position and clubfoot deformity were associated with an increased risk. A selective screening program as well as promoting awareness at well-baby clinics could improve early detection, treatment and outcome.

REFERENCES

1. Azzopardi T, van Essen P, Cundy P, Tucker G, Chan A. Late diagnosis of developmental dysplasia of the hip: an analysis of risk factors. J Ped Orthop B. 2011;20(1):1-7.
2. TerjesenT. Residual hip dysplasia as risk factor for osteoarthritis in 45 years follow-up of late-detected hip dislocation. J Child Ortho. 2011;5(6):425-431.
3. Klisic. Congenital dislocation of the hips - a misleading term: brief report.JBJS Br.1989;71(1):136.
4. Kotlarsky P, Haber R, Bialik V, Eidelman M. Developmental dysplasia of the hip: what has changed in the last 20 years? World J Orthop. 2015;6(11):886-901.
5. Lehmann H, Hinton R, Morello P, Santoli J. Developmental dysplasia of hip practice guideline: technical report. Committee on Quality improvement and subcommittee on developmental dysplasia of the hip. Pediatrics. 2000; 105(4):E57.
6. Ortiz-Neira C, Paolucci E, Donnon T. A meta-analysis of common risk factors associated with the diagnosis of developmental dysplasia of the hip in newborns. Eur J Radiol.2011;1-8.
7. Patel H. Preventive health care, 2001 update: screening and management of developmental dysplasia of the hip in newborns. CAMJ.2001;164(12):1669-1677.
8. Roposch A, Liu L, Hefti F, Clarke N, Wedge J. Standardized diagnostic criteria for developmental dysplasia of the hip in early infancy. CORR.2011;469 (12):3451-61.
9. Delaney L, Karmazyn B. Developmental dysplasia of the hip: background and the utility of ultrasound. Semin Ultrasound CT MR.2011;32(2):151-156.
10. Kosar P, Ergun E, Yigit H, Gökharman F, Kosar U. Developmental dysplasia in male infants: risk factors, instability and ultrasound screening. Hip int.2011;21(4):409-414.
11. Lehman E, Street D. Neonatal screening in Vancouver for congenital dislocation of the hip. CMAJ.1981; 124:1003-1008.
12. Phelan N, Thoren J, Fox C, O'Daley B, O'Beirne J. Developmental dysplasia of the hip: incidence and treatment outcomes in the Southeast of Ireland. Ir J Med Sci. 2015; 184:411-415.
13. Chan A, Cundy P, Foster B, Keane R, Buronn-Scott R. Late diagnosis of congenital dislocation of the hip and presence of a screening programme: South Australian population-based study. The Lancet. 1999;354:1514 -1517.
14. Clarke N, Reading I, Corbin C, Taylor C, Bochmann T. Twenty years of experience of selective secondary ultrasound screening of congenital dislocation of the hip. Arch Dis Child 2012;97:423-429.
15. Laborie L, Markestad T, Davidsen H, Bruras K, Aukland S, Bjorlykke J et al. Selective ultrasound screening for developmental hip dysplasia: effect on management and late detected cases. A prospective survey during 1991-2006. Pediatr Radiol;2014(44):410-424.
16. Paterson D. Early diagnosis and treatment of congenital dislocation of the hip. Austr NZ J surg. 1976;46(4):359-366.
17. Rourke L, Leduc D, Constantin E, Carsley S, Rourke J. Update on well-baby and well-child care from 0 to 5 years. What's new in the Rourke Baby Record? Can Fam Physician. 2010;56:1285-1290.
18. Kolb A, Schweiger N, Mailath-Pokorny M,Kaider A, Hobusch G, Chiari C et al. Low incidence of early developmental dysplasia of the hip in universal ultrasonographic screening of newborns: analysis and evaluation of risk factors. International Orthopaedics. 2016; 40:123-127.
19. Shorter D, Hong T, Osborn D. Screening programmes for developmental dysplasia of the hip in newborn infants. Cochrane Database of Systematic Reviews. 2011(9) Art. No.: CD004595.
20. Roovers E, Boere-Boonekamp M, Castelein R, Zielhuis G, Kerkhoff T. Effectiveness of ultrasound screening for developmental dysplasia of the hip. Arch dis child fetal Neonatal ed. 2005;90:F25-F30.
21. Roovers E, Boere-Boonekamp M, Mostert A, Castelein R, Zielhuis G, Kerkhoff T. The natural history of developmental dysplasia of the hip: sonographic findings in infants of 1-3 months of age. J Ped Orthop B. 2005;14:325-330.
22. Wirth T, Stratmann L, Hinrichs F. Evolution of late presenting developmental dysplasia of the hip and associated surgical procedures after 14 years of neonatal ultrasound screening. J Bone Joint Surg 2004;86-B:585 -589.
23. Thaler M, Biedermann R, Lair J, Krismer M, Landauer F. Cost-effectiveness of universal ultrasound screening compared with clinical examination alone in the diagnosis and treatment of neonatal hip dysplasia in Austria. J Bone Joint Surg 2011;93-B:1126-1130.
24. Tréguier C, Chapuis M, Branger B, Bruneau B, Grellier A, Chouklati K et al.. Pubo-femoral distance: an easy sonographic screening test to void late diagnosis of developmental dysplasia of the hip. Eur Radiol. 2013;23:836-844.
25. Paton R, Choudry Q, Jugdey R, Hughes S. Is congenital talipes equinovarus a risk factor for pathological dysplasia of the hip?: a 21 year prospective longitudinal observational study. Bone Joint J. 2014; 96-B(11):1553-1555.
26. Perry D, Tawfiq S, Roche A, Shariff R, Garg N, James L et al. The association between clubfoot and developmental dysplasia of the hip. J bone Joint Surg Br. 2010; 92(11): 1586-1588.
27. Zhao D, Rao W, Zhao L, Liu J, Chen Y, Shen P et al. Is it worthwhile to screen the hip in infants born with clubfeet? Int Orthop. 2013;37(12):2415-2420.
28. Corrigan C, Segal S. The incidence of congenital dislocation of the hip at Island Lake, Manitoba. CMAJ. 1950;62:535-540.
29. Walker J. Congenital hip disease in a Cree-Ojibwa population: a retrospective study. CMAJ.. 1977;116:501-504.
30. Rabin D, Barnett C, Arnold W, Freiberger R, Brooks G. Untreated congenital hip disease. A study of the epidemiology, natural history and social aspects of the disease in a Navajo population. Am J public Health. 1965; 55 (suppl).
31. Larchet M, Bourgeois J, Billon P, Chilard C, Simon J, Aldebert B et al. Comparative evaluation of clinical and ultrasonographic screening of hip dislocation in Breton and Languedoc populations. Arch Pediatr. 1994;1(12):1093-1099.
32. Getz B. The hip joint in Lapps and its bearing on the problem of congenital dislocation. Acta Orthop Scand suppl. 1955;18:1-81.
33. Mulpuri K, Schaeffer E, Andrade J, Sankar W,Williams N, Matheney T et al. What risk factors and characteristics are associated with late-presenting dislocations of the hips in infants? Clin Orthop Relat Res. 2016: symposium: the hip from childhood to adolescence.
34. Wang E, Liu T, Edmons E, Zhao Q, Zhang L, Zhao X et al. does swaddling influence developmental dysplasia of the hip? an experimental study of the traditional straight-leg swaddling model in neonatal rats. J Bone Joint Surg am. 2012;94(12):1071-1077.
35. Sharpe P, Mulpuri K, Chan A, Cundy P. Differences in risk factors between early and late diagnosed developmental dysplasia of the hip. Arch Dis Child

Fetal Neonatal Ed. 2006;91:158-162.

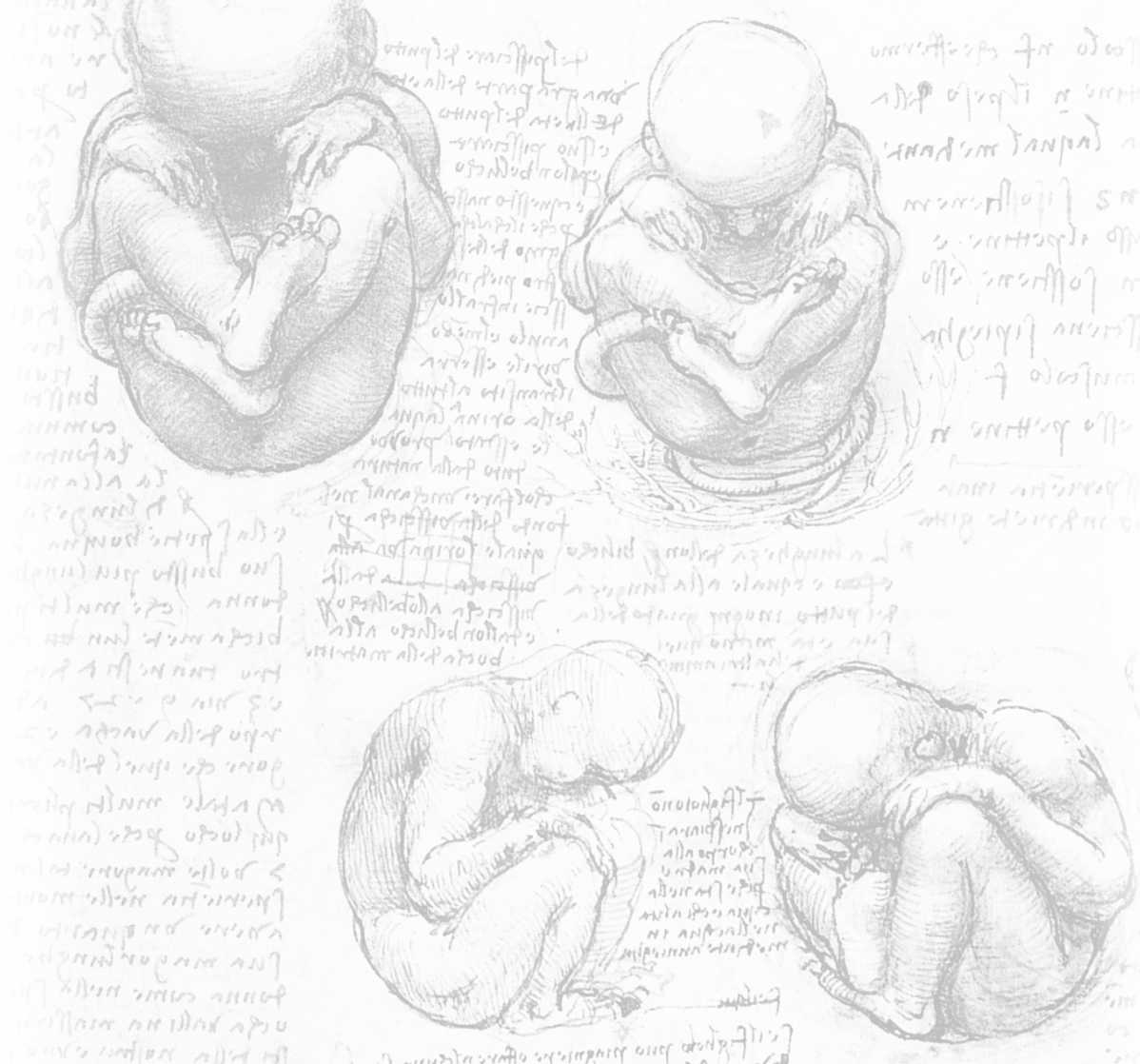
36. Studer K, Williams N, Antoniou G, Gibson C, Scott H, Schell W. et al. Increase in late diagnosed developmental dysplasia of the hip in South Australia:risk factors, proposed solutions. MJA.2016;204(6):e1-e6.

CHAPTER 3

The natural history of abnormal ultrasound findings in hips of infants under six months of age.

R. Sakkers, V. Pollet

J Child Orthop 2018;12:302-307



ABSTRACT

Purpose

To collect and describe data on the natural history of abnormal ultrasound (US) findings in hips of infants under six months of age to serve as a reference to the design of screening programmes and treatment algorithms in the care for children with hip dysplasia.

Methods

A search in PubMed of the terms “DDH” and “ultrasound” was done to find hips with abnormal US findings that were not treated. In cases of multiple periods of follow-up, the classification of every period was evaluated separately (individual hip follow-up periods).

Results

Data of 13 561 hips with 16 991 follow-up periods were collected and analyzed. Most quantifiable classifications and follow-up periods were according to Graf (14 876) and a minor number of the hips had follow-up periods with femoral head coverage (FHC) (2115). Normal development without treatment in the first six months was for Graf 2a between 89% and 98%, for Graf 2c between 80% and 100% and for clustered data Graf 2a to 2c between 80% and 97%. For Graf 3 hips more than 50% were reported to develop into normal hips without treatment. As for Graf 4 hips this percentage was reported below 50%. For children with an FHC less than 50%, normalization was reported between 78% and 100%.

Conclusion

The natural history of developmental dysplasia of the hip (DDH) shows a benign course, especially in the well-centered hips. This outcome probably contributes to the fact that all studies on US screening of hips for detection of relevant DDH in order to improve outcomes of treatment are rated as substantially underpowered.

INTRODUCTION

Osteoarthritis of the hip is one of the major burdens of disease, with a wide spectrum ranging from the quality of life of the individual patient to global economic costs. The incidence rate is around 16% at around the age of 45 years, rising to 25% to 40% in people over the age of 75 years.[1-3] Early osteoarthritis of the hip is associated with hip dysplasia in early childhood. The consequences of hip dysplasia depend on its severity. Hip dysplasia with persistent subluxation of the femoral head has the highest risk for developing early painful hip osteoarthritis between the ages of 20 to 50 years and can already be present shortly after skeletal maturation in cases of severe subluxation.[4]

The relationship between hip dysplasia in childhood and its related short-term and long-term morbidity is one of the motives for the development of screening programmes for hip dysplasia in the first weeks after birth. Well-known tests for diagnosing hip dysplasia after birth by physical examination, like Ortolani and Barlow, were developed in the first and second half of the last century and are still practiced today.[5,6] The limitations of radiographic depiction of the hip, due to the absence of the ossific nucleus in the first months after birth, have been combatted by ultrasound (US), and this method has become popular since the first paper describing it by Graf in 1980.[7] The cartilaginous anatomy of the hip can clearly be outlined sonographically. Since then many other authors have published results in more than ten different classification systems.[8] The most frequently used classifications are the static method of Graf, the stability test by Harcke and the femoral head coverage (FHC) by Morin et al and Terjesen et al and combinations of these methods as published by Rosendahl and Toma.[9,10,11,12] The alpha and beta angle by Graf and the FHC by Morin and Terjesen produced quantifiable parameters. The classifications from these methods are aiming at defining the different grades of hip dysplasia and providing a prognosis for its sequelae. Although a hip dislocation can clearly be diagnosed, classifications for hip dysplasia and subluxation vary. The borders of the categories in these classifications are made by the authors on the basis of their experience or on consensus in expert panels. Differences in image acquisition and interobserver variation can significantly influence the diagnosis in the border zones between the different categories of the classifications. Diagnosing relevant hip dysplasia in the first months of life does not meet the World Health Organization standards since seven of the 11 criteria cannot be not met.[13] Cochrane and other high-quality reviews conclude that diagnosis by US is ‘highly sensitive but poorly specific’, and that it is not clear how much unnecessary treatment is instituted today due to the lack of a benchmark for diagnosis.[14] For stable hip dysplasia it is even questionable if the current treatment alters the natural history of the development of the hip. Randomized trials of abduction treatment of dysplastic hips according to the existing classification systems have failed to show a difference between the treatment and non-treatment groups between six weeks and three

months and between three months and six months.[15,16] The natural history of the dysplastic hip in the first six months therefore remains one of the most intriguing subjects to study in hip dysplasia.

MATERIAL AND METHODS

In order to find data on the natural history of US abnormalities of the hip in children under six months of age, a search in PubMed of the terms “DDH” and “ultrasound” was done to find reports on hips with abnormal US findings that were not treated during a part of or the total course of their development. All untreated hips with abnormal US findings were counted. Groups were made according to the time of first US exam, classification of abnormal US findings, the change in classification during follow-up without treatment and time of follow-up without treatment. Data were corrected for the numbers lost to follow-up. In cases of multiple moments of follow-up, the classification of every moment in follow-up was evaluated separately (individual hip follow-up periods). Totals of every group were counted in numbers and changes in classification were calculated in percentages.

RESULTS

The search in PubMed resulted in 568 hits. Reports on stability were combinations of clinical and US instability and very heterogeneous. Most reports that investigated instability at birth reported no correlation between instability at birth and subsequent development of the hips. Therefore, instability at birth was left out of the analysis trend in this report. From the 568 articles, 23 articles included descriptions of the history of hips with abnormal US outcomes of hips that were not treated. The natural history of a total of 13 561 hips ranging from immature hips to complete dislocation was analyzed. The reports showed a relatively large variety in age of first US, follow-up time periods, protocols, decision trees and classification systems. The classification according to Graf and the FHC according to Morin and Terjesen were used to classify the dysplasia. In this analysis, Graf IIa+ and Graf IIa- hips were merged into the group Graf IIa. In the context of the slight differences in the definition of abnormal between different authors and the different age groups in the FHC classification, the coverage of 50% was defined as the border between normal and abnormal in the articles that reported on the follow-up of FHC.[17] The time period of non-treatment in these reports varied between two weeks and eight years. The times of follow-up of different groups varied depending on the start of treatment of hips that did not develop to Graf I or a FHC of more than 50% at the different times of follow-up.

Reports on hips classified according to Graf

In 18 of the 23 articles that included descriptions of the history of hips with abnormal US outcomes of hips that were not treated, hips were classified according to Graf. (Table 1)[18-35] One of the first reports was by Gardiner and Dunn.[18] A group of 59 hips was not treated initially (21 Graf IIa, 12 Graf IIc, 20 Graf III and six Graf IV). After two weeks, 37 hips (71%) ranging from Graf IIa to IV remained untreated (19 Graf IIa = 90%, eight Graf IIc = 66%, seven Graf III = 35% and three Graf IV = 50%). All of these hips were normal at age one year.

Table 1. Natural history of hips GRAF IIa-IV

Classification	Follow-up period	Hips at start of period (n)	Percentage normalization
Graf IIa	0 to 2 wks[18]	21	90
	0 to 1 mth[19-23]	2140	89
	0 to 3 mths[22,24,25]	1578	93
	0 to 6 mths[26]	272	98
	0 to 1 yr[27]	7	85
	1 to 2 mths[23,28]	1528	79
	2 to 3 mths[22,23,28]	400	85
	2 wks to 1 yr[18]	19	100
Graf IIc	0 to 2 wks[18]	12	67
	0 to 1 mth[19]	3	100
	0 to 6 wks[29]	54	80
	0 to 6 mths[25,26]	135	88
	0 to 1 yr[27]	17	76
	6 wks to 3 mths[29]	42	71
	2 wks to 1 yr[18]	8	100
Graf D	0 to 6 mths[26]	53	77
	0 to 1 yr[27]	43	70
Graf III	0 to 2 wks[18]	20	35
	0 to 1 mth[21]	4	75
	0 to 6 wks[26]	18	78
	0 to 3 mths[21]	1	100
	0 to 1 yr[27]	21	95
	2 wks to 1 yr[18]	7	100
Graf IV	0 to 2 wks[18]	6	50
	0 to 6 wks[26]	17	29
	0 to 1 yr[27]	15	47
	2 wks to 1 yr[18]	3	100
Graf III to IV	1 to 4 mths[28]	2	100
Graf D tp III	6 wks to 6 mths[30]	4	25
Graf IIa to D	0 to 6 wks[33]	3251	80
	0 to 3 mths[32]	548	97
	0 to 6 mths[31]	101	96
	2 wks to 15 mths[34]	88	92
	6 wks to 6 mths[30]	35	94
Graf IIa to IV	0 to 1 yr[35]	301	93

In studies with follow-up periods between 0 and one month, 89% of 2140 Graf IIa hips developed to Graf I hips without treatment.[19-23] Between 0 and three months 93% of 1578 Graf IIa hips developed to Graf I hips without treatment.[22,24,25] In the study by Bialik et al 98% of Graf IIa hips that were not treated developed to normal by age six months.[26] Rosenberg and Bialik reported normalization of six out of seven Graf IIa hips after follow-up of one year.[27] In several studies the first US investigation was not within the first week of birth but at a later age dependent on the structure of the screening programme in that particular study. Of 1528 Graf IIa hips at age one month, 79% developed to Graf I at age two months.[23,28] Of 1528 Graf IIa hips at age one month, 79% developed to Graf I at age two months.[23,28] Of 400 hips that had Graf IIa hips at two months, 85% developed into Graf I by age three months.[22,23,28] Reports on Graf IIc hips also showed a wide variety in natural history prior to treatment. Three hips Graf IIc had become Graf I by age four weeks.[19] In all, 80% of 54 Graf IIc hips followed up from birth to age six weeks developed into normal hips as well as 88% of 135 Graf IIc hips at age six months.[25,26,29] One study reported follow-up of Graf IIc hips to the age of one year: 76% of 17 hips became normal without treatment.[27] Of 42 Graf IIc hips diagnosed at six weeks, 71% became Graf I by age three months.[29] Two studies were found with separate reports on Graf D hips. One study reported 77% spontaneous normalization of Graf D hips at age six months, and another study showed 70% normalization of 43 hips at age one year. [26,27] Sampath et al defined major dysplasia as an alpha angle below 43° or subluxation.[30] The number of hips with developmental dysplasia of the hip (DDH) in the children was not described. Of four children diagnosed with major dysplasia at age three months, one developed normal hips at the age of one year without treatment. Of the children with minor dysplasia detected at the age of six weeks, 94% had no DDH at age six months. Reports on the natural history of hips with Graf III and Graf IV were rare. Chen et al had four Graf III hips untreated of which three (75%) developed to Graf I in one month.[21] The fourth hip was left untreated and was normal at follow-up at three months. Bialik et al followed 18 Graf III hips and 17 Graf IV hips until the age of six weeks.[26] Around 78% of the Graf III hips developed spontaneously to normal *versus* only 29% of the Graf IV hips. Roovers et al had two hips with dislocation at age one month that were not treated and were normal at age four months.[28]

In many studies the classifications were clustered in the outcomes in groups Graf IIa to D, Graf IIa to IV. For the groups Graf IIa to D (4023 individual hip follow-up periods), the outcomes of normalization without treatment were, respectively, 80%, 97% and 96% at ages six weeks, three months and six months.[31-33] Two smaller reports with follow-up times between two weeks and 15 months and six weeks and six months had similar results of 92% and 94%. [30,34] In one report Graf IIa to IV was not reported separately in 301 abnormal hips in week one and 93% of the hips had normalized at age one month. All these hips were still normal at follow-up at age one year.[35]

In eight studies data were found of Graf IIa hips that deteriorated in time (Table 2).

Table 2. Graf IIa hips with deterioration in time

Graf IIa deterioration	Follow-up period	Hips at start of period (n)	Percentage deterioration
First investigation	0 wks >[18,19,22,23,24,26,27]	2823	5.5
First investigation	4 wks >[28]	1279	5

Table 3. Natural history of hips with femoral head coverage (FHC) < 50%

Classification FHC < 50%	Follow-up period	Hips at start of period (n)	Percentage normalization
	0 to 1 mth[36]	514	78
	0 to 2 mths[36]	514	90
	0 to 3 mths[37]	306	83
	0 to 5 mths[37]	306	91
	0 to 6 mths[38]	260	90
	2 wks to 15 mths[34]	93	86
	4 mths to 5 to 8 yrs[39]	122	100

The amount of Graf IIa hips that received treatment at some time during follow-up was 155 out of 2823 (5.5%).[18,19,22,23,24,26,27] In the study by Roovers et al the first US measurement for Graf IIa hips was at age one month: 64 (5%) out of 1279 Graf IIa hips developed to abnormal by the age of three months.[28]

Reports on hips classified with FHC

In five of the 23 articles that included descriptions of the history of hips with abnormal US outcomes of hips that were not treated, hips were classified with the FHC. (Table 3)[34,36-39] For reports on FHC less than 50%, 2115 individual hip follow-up periods were counted. Marks et al described a group of 514 hips with a FHC less than 50% at zero weeks.[36] At the next follow-up, a few weeks later with a mean around the age of one month and two months, respectively, 78% and 90% of the hips were spontaneously normalized. Terjesen et al followed 306 abnormal hips and reported spontaneous normalization of 83% and 91% at, respectively, three and five months.[37] The same results were found by Holen et al who reported spontaneous normalization at follow-up at six months in 90% of 260 hips. [38] In the study of Lorente Molto et al 86% of hips that had a FHC less than 50% had spontaneously normalized at age 15 months.[34] Tegnander et al had 170 children with normal clinical examination and FHC's less than 50% at birth. [39] At five months ten children were treated (94%/160 not treated). From this group (90% of 170 patients), 87 children with 122 abnormal hips that were not treated could be retrieved at a follow-up of six to eight years. All untreated hips were normal.

DISCUSSION

To describe the natural history of abnormal US findings of hips in infants under six months, the literature was searched for hips that were not treated for a shorter or longer time since the first US examination. The vast amount of 13 561 hips was found through PubMed. Although there will be some reports that have been missed or that are out the regular field of language, the studies that were found can be considered to be representative in outlining general trends. Most studies had the first US examination within the first few days after birth; however, in some studies, the first US examination was a few weeks later or at different times within the same study population. For the follow-up, the outcome of every single follow-up period was quantified. Many studies had more follow-up times resulting in more follow-up periods than hips (16 991 versus 13 561). The majority of follow-up periods before starting treatment of hips with US abnormalities did not go beyond the age of three months. However, especially in reports from the 1990s, some authors did not treat for a longer time, even for periods to up to the age of one year or older. There seems to be a tendency in the last decade to treat earlier, despite the good outcomes of the wait-and-see policy in hips with US abnormalities. This trend should have a negative effect on the rise in the amount of data on the outcome of wait-and-see policies, especially with regard to the more serious US abnormalities found in the first weeks after birth. Most quantifiable classifications were according to Graf (14 876), and a lesser proportion of the studies classified according to the FHC (2115). Furthermore, there was a rather large variation in follow-up moments. In several reports the data switched from the number of hips found with US abnormalities to the number of patients treated in the follow-up or to percentages without reporting the actual numbers. This made reconstruction of the raw data difficult. Therefore, only data that could be traced back to the number of hips or that could be calculated from percentages from the original number of hips were used. Various percentages of hips dropped out of the follow-up at the different follow-up moments in time. Only the hips per follow-up period that remained in the follow-up were calculated. In the studies that clustered the different types of US abnormalities, the outcome of the clustered groups was calculated separately. Given all the recalculations, one can discuss the accuracy of the absolute numbers. However, the discussion on this accuracy should not affect the general trends that can be deduced from the outcomes of these calculations. The majority of the quantified follow-up periods of hips were Graf IIa hips. As expected, a high percentage of Graf IIa hips showed a natural course to development of a normal hip in the 5965 follow-up periods calculated, with mean percentages of 89% to 98% at different follow-up times between two weeks and six months. These data suggest that Graf IIa can safely be followed for a longer time without treatment in order to detect the relatively few hips that will show a deterioration in time. Deterioration of Graf IIa hips appeared rarely in the data but treatment at some moment in time was still around 5%. Although there were only between 200 and 300 Graf IIc reported hips, a vast majority also showed a benign course when untreated with percentages between 80% and 100% at the different follow-up periods up to six months. The very small number of hips that were followed until the age of one year all developed into normal hips. These data, combined with favourable outcomes of the clustered data of Graf IIa to IIc between follow-up times of six weeks to six months of between 80% and 97%, also brings up the question of whether Graf IIc hips should be treated early or just followed for a few months. The data also raise questions with regard to power calculations on the effect of treatment when the treatment should be investigated in randomized trials, and which effect of treatment of stable well-centered hips at which age in the first six months of life is clinically relevant. One of the problems is that clinical information such as limited abduction of the hip or instability is often absent in the data reported and in those reports that report instability, the correlation between initial instability, US classification and outcome after longer follow-up cannot be made. The number of follow-up data of the natural history of Graf III and Graf IV hips was relatively small (n = 87) because these hips were immediately treated in most studies. The outcomes, especially of Graf III hips at birth that were not treated was still surprisingly good, which still leaves room for discussion as to when to start treatment. The clinical information in the reports was insufficient to understand which of these dislocated hips at birth were not treated and on which grounds. The outcome of the clinical investigation still seems the most important factor in the process of decision-making for treatment.[40] This suggests a bias in the outcomes of the dislocated hips that were not treated. It is even more difficult to assess treatment based on US given the reported poor consistency in diagnostic criteria using US in DDH and the fact that there is no consensus on which degree of acetabular dysplasia, as defined by US, to treat or not.[41,42]

CONCLUSION

The natural history of DDH seems to show a benign course, especially in stable, well-centered hips. The fact that even the unstable and dislocated hips do relatively well without treatment in a substantial percentage probably contributes to the fact that all studies on US screening of hips for detection of relevant DDH in order to improve outcomes of treatment are rated as substantially underpowered.[43]

REFERENCES

1. Wyles CC, Heidenreich MJ, Jeng J, et al. The John Charnley Award: Redefining the natural history of osteoarthritis in patients with hip dysplasia and impingement. *Clin Orthop Relat Res* 2017;475:336-350.
2. Murphy LB, Helmick CG, Schwartz TA, et al. One in four people may develop symptomatic hip osteoarthritis in his or her lifetime. *Osteoarthritis Cartilage* 2010;18:1372-1379.
3. Jordan JM, Helmick CG, Renner JB, et al. Prevalence of hip symptoms and radiographic and symptomatic hip osteoarthritis in African Americans and Caucasians: the Johnston County Osteoarthritis Project. *J Rheumatol* 2009;36:809-815.
4. Ziegler J, Thielemann F, Mayer-Athenstaedt C, Günther KP. The natural history of developmental dysplasia of the hip. A meta-analysis of the published literature. *Orthopade* 2008;37:515-516, 518-524.
5. Ortolani M. Un segno poco noto e sua importanza per la diagnosi precoce di prelussazione congenita dell'anca. *Pediatria (Napoli)* 1937;45:129-136.
6. Barlow TG. Early diagnosis and treatment of congenital dislocation of the hip *J Bone Joint Surg [Br]* 1962;44-B:292-301.
7. Graf R. The diagnosis of congenital hip-joint dislocation by the ultrasonic Combound treatment. *Arch Orthop Trauma Surg* 1980;97:117-133.
8. Bracken J, Ditchfield M. Ultrasonography in developmental dysplasia of the hip: what have we learned? *Pediatr Radiol* 2012;42:1418-1431.
9. Harcke HT, Grissom LE. Performing dynamic sonography of the infant hip. AJR Am J Roentgenol 1990;155:837-844.
10. Morin C, Harcke HT, MacEwen GD. The infant hip: real-time US assessment of acetabular development. *Radiology* 1985;157:673-677.
11. Terjesen T, Bredland T, Berg V. Ultrasound for hip assessment in the newborn. *J Bone Joint Surg [Br]* 1989;71-B:767-773.
12. Rosendahl K, Toma P. Ultrasound in the diagnosis of developmental dysplasia of the hip in newborns. The European approach. A review of methods, accuracy and clinical validity. *Eur Radiol* 2007;17:1960-1967.
13. Paton RW. Screening in Developmental Dysplasia of the Hip (DDH). *Surgeon* 2017;15:290-296.
14. Patel H, Canadian Task Force on Preventive Health Care. Preventive health care, 2001 update: screening and management of developmental dysplasia of the hip in newborns. *CMAJ* 2001;164:1669-1677.
15. Wood MK, Conboy V, Benson MK. Does early treatment by abduction splintage improve the development of dysplastic but stable neonatal hips? *J Pediatr Orthop* 2000;20:302-305.
16. Pollet V, Sakkers R, Beek E, et al. Abduction bracing versus natural history in hip dysplasia: multicenter randomized trial. *J Child Orthop* 2016;10:S30-S31.
17. Harcke HT, Pruszczynski B. Hip ultrasound for developmental dysplasia: the 50% rule. *Pediatr Radiol* 2017;47:817-821.
18. Gardiner HM, Dunn PM. Controlled trial of immediate splinting versus ultrasonographic surveillance in congenitally dislocatable hips. *Lancet* 1990;336:1553-1556.
19. Riboni G, Bellini A, Serantoni S, Rognoni E, Bisanti L. Ultrasound screening for developmental dysplasia of the hip. *Pediatr Radiol* 2003;33:475-481.
20. Dessì A, Crisafulli M, Vannelli E, Fanos V. Ultrasound in developmental dysplasia of the hip: A screening study in Sardinian newborns. *J Ultrasound* 2009;12:80-84.
21. Chen HW, Chang CH, Tsai ST, et al. Natural progression of hip dysplasia in newborns: a reflection of hip ultrasonographic screenings in newborn nurseries. *J Pediatr Orthop B* 2010;19:418-423.
22. Koşar P, Ergun E, Yiğit H, Gökharman FD, Kosar U. Developmental dysplasia in male infants: risk factors, instability and ultrasound screening. *Hip Int* 2011;21:409-414.
23. Munkhuu B, Essig S, Renchinnyam E, et al. Incidence and treatment of developmental hip dysplasia in Mongolia: a prospective cohort study. *PLoS One* 2013;24:e79427.
24. Falliner A, Hahne HJ, Hassenpflug J. Sonographic hip screening and early management of developmental dysplasia of the hip. *J Pediatr Orthop B* 1999;8:112-117.
25. Rosendahl K, Markestad T, Lie RT. Developmental dysplasia of the hip: prevalence based on ultrasound diagnosis. *Pediatr Radiol* 1996;26:635-639.
26. Bialik V, Bialik GM, Wiener F. Prevention of overtreatment of neonatal hip dysplasia by the use of ultrasonography. *J Pediatr Orthop B* 1998;7:39-42.
27. Rosenberg N, Bialik V. The effectiveness of combined clinical-sonographic screening in the treatment of neonatal hip instability. *Eur J Ultrasound* 2002;15:55-60.
28. Roovers EA, Boere-Boonekamp MM, Mostert AK, et al. The natural history of developmental dysplasia of the hip: sonographic findings in infants of 1-3 months of age. *J Pediatr Orthop B* 2005;14:325-330.
29. Rosendahl K, Dezateux C, Fosse KR, et al. Immediate treatment versus sonographic surveillance for mild hip dysplasia in newborns. *Pediatrics* 2010;125:e9-e16.
30. Sampath JS, Deakin S, Paton RW. Splintage in developmental dysplasia of the hip: how low can we go? *J Pediatr Orthop* 2003;23:352-355.
31. Castelein RM, Sauter AJ, de Vlieger M, van Linge B. Natural history of ultrasound hip abnormalities in clinically normal newborns. *J Pediatr Orthop* 1992;12:423-427.
32. Rosendahl K, Markestad T, Lie RT. Ultrasound screening for developmental dysplasia of the hip in the neonate: the effect on treatment rate and prevalence of late cases. *Pediatrics* 1994;94:47-52.
33. Laborie LB, Markestad TJ, Davidsen H, et al. Selective ultrasound screening for developmental hip dysplasia: effect on management and late detected cases. A prospective survey during 1991-2006. *Pediatr Radiol* 2014;44:410-424.
34. Lorente Moltó FJ, Gregori AM, Casas LM, Perales VM. Three-year prospective study of developmental dysplasia of the hip at birth: should all dislocated or dislocatable hips be treated? *J Pediatr Orthop* 2002;22:613-621.
35. Kokavec M, Bialik V. Developmental dysplasia of the hip. Prevention and real incidence. *Bratisl Lek Listy* 2007;108:251-254.
36. Marks DS, Clegg J, al-Chalabi AN. Routine ultrasound screening for neonatal hip instability. Can it abolish late-presenting congenital dislocation of the hip? *J Bone Joint Surg [Br]* 1994;76-B:534-538.
37. Terjesen T, Holen KJ, Tegnander A. Hip abnormalities detected by ultrasound in clinically normal newborn infants. *J Bone Joint Surg [Br]* 1996;78-B:636-640.
38. Holen KJ, Terjesen T, Tegnander A, et al. Ultrasound screening for hip dysplasia in newborns. *J Pediatr Orthop* 1994;14:667-673.
39. Tegnander A, Holen KJ, Terjesen T. The natural

history of hip abnormalities detected by ultrasound in clinically normal newborns: a 6-8 year radiographic follow-up study of 93 children. *Acta Orthop Scand* 1999;70:335-337.

40. Williams D, Protopapa E, Stohr K, Hunter JB, Roposch A. The most relevant diagnostic criteria for developmental dysplasia of the hip: a study of British specialists. *BMC Musculoskelet Disord* 2016;17:38.
41. Roposch A, Liu LQ, Protopapa E. Variations in the use of diagnostic criteria for developmental dysplasia of the hip. *Clin Orthop Relat Res* 2013;471:1946-1954.
42. Roposch A, Wright JG. Increased diagnostic information and understanding disease: uncertainty in the diagnosis of developmental hip dysplasia. *Radiology* 2007;242: 355-359.
43. Shorter D, Hong T, Osborn DA. Cochrane Review: screening programmes for developmental dysplasia of the hip in newborn infants. *Evid Based Child Health* 2013; 8:11-54.

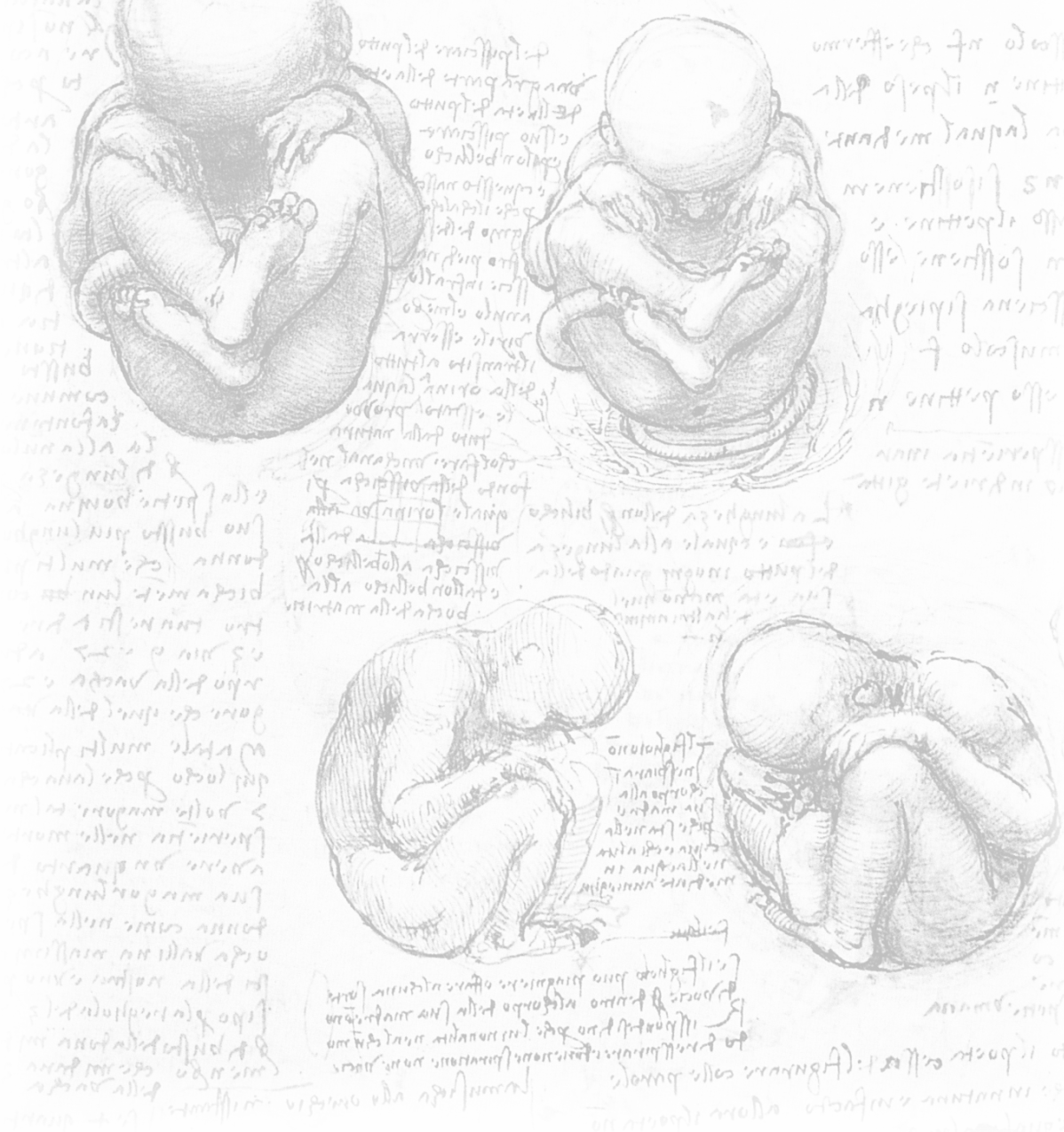
3

CHAPTER 4

Abduction treatment in stable hip dysplasia does not alter the acetabular growth: results of a randomized clinical trial

V. Pollet, R.M. Castelein, M. van de Sande, M. Witbreuk, A.K. Mostert, A. Besselaar, C van Bergen, E. Beek, CSPM Uiterwaal, R.Sakkers

Sci Rep 10, 9647 (2020)



ABSTRACT

Background

The effect of bracing over natural history of stable dysplastic hips is not well known. This multicenter randomized trial aimed at objectifying the effect of abduction treatment versus active surveillance in infants of 3 to 4 months of age.

Methods

Patients were randomized to either Pavlik harness or active surveillance group. Ultrasound was repeated at 6 and 12 weeks post randomization. The primary outcome was the degree of dysplasia using the Graf α-angle at 6 months of age. The measurement of the acetabular index (AI) on plain pelvis X-rays was used to identify persistent dysplasia after 9 months and walking age (after 18 months).

Findings

The Pavlik harness group (n=55) and active surveillance group (n=49) were comparable for predictors of outcome. At 12 weeks follow-up the mean α-angle was 60.5°±3.8° in the Pavlik harness group and 60.0°±5.6° in the active surveillance group. (p= 0.30). Analysis of secondary outcomes (standard of care) showed no treatment differences for acetabular index at age 10 months (p= 0.82) and walking age (p= 0.35).

Interpretation

Pavlik harness treatment of stable but sonographic dysplastic hips has no effect on acetabular development. Eighty percent of the patients will have a normal development of the hip after twelve weeks. Therefore, we recommend observation rather than treatment for stable dysplastic hips.

INTRODUCTION

Developmental Dysplasia of the Hip or DDH is one of the most common pediatric orthopedic problems with an incidence varying from 1- 6/1000 depending on regional predisposition and ethnic differences. [1] Hip dysplasia in the first months of life is clinically best detected by instability or dislocation of the hip. The Galeazzi test shows the leg length discrepancy due to the dislocated femoral head and the Ortolani maneuver will be positive when a hip is dislocated and can be reduced. In case of instability Barlow and Ortolani maneuvers will displace and relocate the hip joint. [2] Before the introduction of ultrasound, radiologic evaluation was used to assess acetabular development. [3] However, radiographic measurements are considered inaccurate below the age of 6 months due to a rather large variation in normal bone maturation. [3]

The introduction of sonographic imaging of the infant hip gave rise to definitions of instability and a classification of different types of severities of dysplasia of the acetabulum. [4,5] In the early 1980's, Graf and Harcke published their observations and definitions. In 1993, Graf and Harcke reached a consensus that a standard examination could be accomplished by two orthogonal views (one coronal and one sagittal) and one view should also include a stress test. The latter was used to differentiate between stable and unstable hips. [6] Others contributed to the development of US examinations such as Morin describing the percentage of Femoral Head Coverage (FHC), which was modified by Terjesen, to quantify the hip coverage, with less than 50% defined as DDH. [7,8,9]

Currently, abduction treatment, preferably started in the first months of life, is viewed as the standard of care for all types of hip dysplasia. There exists, however, a considerable geographic variation in consistency of diagnostic criteria for DDH. [10] While in some countries, clinical findings and/or risk factors will determine the need for ultrasound hip screening, in other countries all newborns are screened for DDH and receive early treatment. Some have questioned the latter as potential for over-diagnosing and therefore unnecessary treatment, as 85% of infantile DDH will resolve spontaneously by the age of 3 months. [11] The most commonly used abduction brace is the Pavlik harness. The outcome of this treatment is widely considered successful if started at a young age (less than 6 months) and in cases where the hip is not rigidly dislocated. [12] However, when studying Pavlik's original publication, the device was designed to gradually and a-traumatically reduce an unstable or dislocated hip, not for treatment of a dysplastic hip that is well centered and stable inside the acetabulum. The use of dynamic, non-rigid stirrups aim at decreasing the chances of avascular necrosis often seen in alternative rigid immobilization. [13] Until now, comparative studies in treatment of stable DDH starting treatment at 2 weeks and at 6 weeks did not show a difference in outcome nor did a randomized trial comparing treatment

versus no treatment between 6 weeks and 3 months. [14-17] The question therefore arises if well-centered stable hips that are classified as DDH by Graf (Type IIb/IIc hips) are a true pathology or merely hips within the normal spectrum of hip development. If the latter is true, what is the effect of abduction treatment on the development of well-centered stable hips? This randomized multi-center study was designed to investigate if abduction treatment, for the duration of 12 weeks, alters the sonographic development of well-centered stable hips confirmed by ultrasound at the age between 3 and 4 months.

METHODS

Participants

After Ethics board approval (08/084 - University Medical Center Utrecht, The Netherlands) of the five participating hospitals (UMC Utrecht, Leiden UMC, Amsterdam Medical University Center, Isala Hospital Zwolle, Maxima Medical Center Eindhoven) all patients between 3 and 4 months of age diagnosed with clinically stable hip dysplasia according to Graf's classification i.e. Graf type IIb and type IIc were included in the study. Calendar age was corrected for premature birth by subtracting the number of weeks prior to full term pregnancy (i.e. 38 weeks) from the calendar age. Patients with co-morbidity such as congenital deformities, previous treatment, hip instability or lack of consent were excluded from the study. Parents of eligible infants were given 7 days to consider participation in this study and a singed consent was obtained. This study was performed according to the Statement on Helsinki guidelines of 2008.

Procedures

A single independent investigator (VP), who was not involved in the treatment of the patients, randomly allocated participants to either Pavlik harness treatment versus active surveillance group by computer-generated randomization in strata for type of dysplasia and participating hospital. Pavlik harness treatment was started within one week. Parents were shown how to apply/remove the harness as they were allowed to remove the harness for bathing. The active surveillance group reviewed in clinic after 6 weeks. Parents were free to alter the treatment or request no treatment at any time for the duration of the study. All available data prior to this decision were included in the analysis.

All patients were seen in clinic with ultrasound of the hips at 6 weeks and at 12 weeks follow-up. The bony roof angle (alpha angle, α °) and Graf classification at 12 weeks follow-up were noted as primary outcome. A senior pediatric radiologist (EB) read all measurements blinded for study intervention. Applying Graf's eligibility criteria for hip ultrasound, the best image of 3 ultrasound scans was assessed to measure the alpha angle. For the active surveillance group, lack of improvement of the alpha angle and/or instability at 6 or 12 weeks ultrasound scan required treatment with Pavlik harness. Complications such as femoral nerve palsy and progression to a dislocated hip causing cessation of the Pavlik harness were noted in the medical records as safety outcome.

As standard of care in The Netherlands, X-rays of the pelvis with measurement of Acetabular Index angle (AI) are routinely taken 3 months after the 6 months ultrasound (around 9 months of age) and at least after 2 years of age (i.e. after walking age). As secondary outcome, the AI measurements were graded according to the modified Tönnis classification for residual dysplasia. [4]

Statistical analysis

The a priori hypothesis in the study protocol was that there is no difference in treatment effect between the two groups. A Two One-sided T- test (TOTS) of Equivalence showed that 50 children were needed in each group to reach a power of 90% with a significance of 5% (two-sided) and average alpha angle of 58 degrees in both groups (SD 8.2). The mean group difference ranging between -5 and + 5 degrees led to a conclusion of Equivalence. In case of bilateral stable hip dysplasia, the average of the alpha-angles was used.

For the primary outcome analysis, linear regression analysis at primary endpoint (i.e. alpha angle at 12 weeks follow-up) was used as the dependent variable and the treatment group indicator as independent variable to calculate the mean difference in alpha angle with a 95% confidence interval.

For secondary outcome analysis, as part of standard of care, Fisher exact test analysis of the Acetabular Index was used to show significance, with a p-value of less than 0.05.

RESULTS

Between 2009 and 2015, parents of 137 patients, meeting the inclusion criteria, gave preliminary consent. After randomization, the consent was withdrawn in 33 patients since parents decided to alter the allocated treatment (18 Pavlik harness treatment versus 15 active surveillance). One hundred and four patients remained for participation in this study. Fifty-five patients were allocated in the Pavlik harness treatment group and 49 patients to the active surveillance group. (Fig 1)

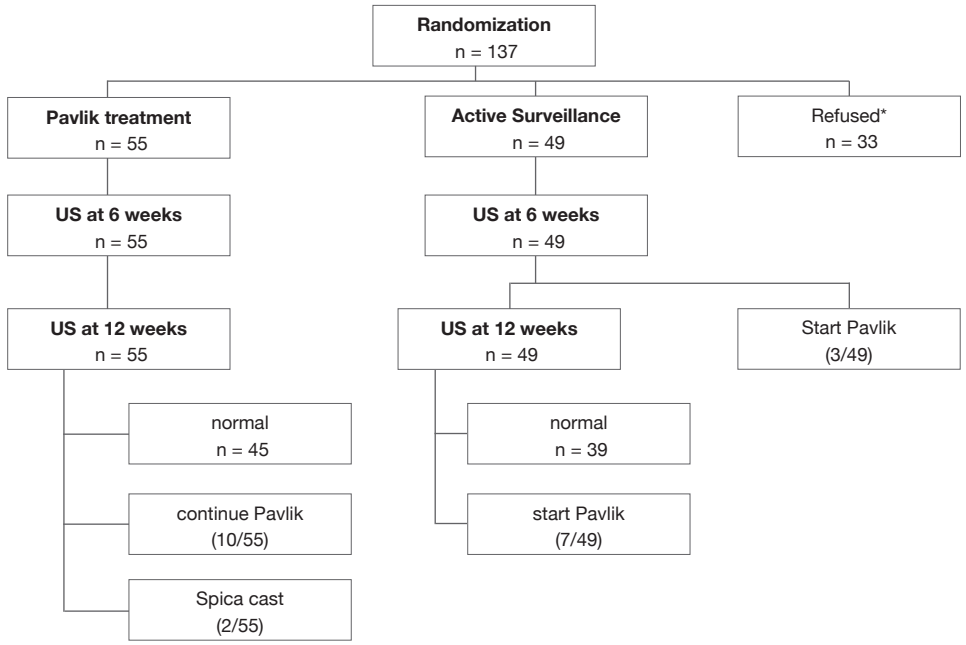


Fig 1. Study flow diagram. *After randomization, 33 hips were excluded after parents refused the allocated treatment plan. The included 104 hips were assessed by Intention-To-Treat analysis.

After 6 weeks of observation, 3 patients received a Pavlik harness in the active surveillance group because of deterioration of the alpha angle. Another 7 patients were treated after 12 weeks of observation due to persistent dysplasia (Graf IIb). Thirty-nine hips (79.6%) normalized after 3 months of active surveillance. After 12 weeks of Pavlik harness treatment, the harness was continued or switched to an abduction brace due to residual dysplasia on ultrasound in 10 patients (18.2%). Despite the prolonged treatment, two patients developed instability and were subsequently treated with closed reduction and spica cast. There were no issues with compliance and femoral nerve palsy in the Pavlik harness treated patients.

At treatment initiation, randomly allocated groups were comparable for bony roof angle, age, gender, affected side and risk factors such as breech position, positive family history and first child. (Table 1)

Characteristics of the group that withdrew after randomization were comparable to the inclusion group. Since their outcome data were not according to protocol, they were excluded from the analyses. As this may have affected the randomization, we added an analysis that was fully adjusted for covariates. All but 7 children, had Graf type IIb hips with an average α-angle of 54.2° ± 3.3° for the treated group and 55° ± 2.8° for the active surveillance group. The progression of alpha angle was calculated for both the treatment

group as the active surveillance group at 6 weeks and 12 weeks. There was no difference in treatment effect between the two groups. The alpha angle corrected over time in both groups at a similar rate. (Table 2)

Table 1. Patients' characteristics, bony roof angles (α-angle) and important predictors of outcome are comparable for both groups.

	Pavlik harness n = 55	**Active Surveillance n = 49**
age (weeks) (SD)	14.3 (1.8)	14.1 (2.1)
gender (n,%)		
female	50 (91)	43 (88)
male	5 (9)	6 (12)
side of dysplasia		
right hip	13	14
left hip	37	30
bilateral	5	5
affected hip α-angle (degrees)(SD)	54.2 (3.3)	55.0 (2.8)
Graf classification (n,%)		
mild	50 (91)	47 (96)
severe	5 (9)	2 (4)
breech (n,%)	13 (24)	14 (28)
+ fam history (n,%)	22 (40)	14 (28)
1st child (n,%)	14 (25)	10 (20)
twins (n,%)	0 (0)	1 (2) (Breech)

Table 2. Bony roof angle (α) improvement over the observed period of 12 weeks. Adjusted difference: for age, gender and measurement 1. For children with bilateral affected hips, left and right angle measurements were averaged.

	Treatment				
affected hip α (°)(SD)	**Pavlik harness treatment**	**Active Surveillance**	adjusted difference	95%CI	p-value
at 6 weeks	58.8 (±5.5)	58.0(±5.2)	-1.39	-3.46,0.67	0.18
at 12 weeks	60.5(±3.8)	60.0(±5.6)	-1.00	-2.92,0.91	0.30

As part of standard of care, we were able to identify 90 out of the 104 (86.5%) patients who received a pelvis X-ray imaging on average 3 months after ultrasound: 50 patients (= 54 hips) in the treatment group and 40 patients (= 41 hips) in the active surveillance group at 10.4 ± 4.4 months and 10.2 ± 3.2 months respectively. There was no difference in AI between the two groups. (p = 0.82) (Table 3)

Table 3. Modified Tönnis classification for degree of dysplasia (acetabular index) on pelvis X-rays at minimal 3 months after 2nd US measurement and after walking age. AI at 10 months: normal ≤ 30 °; 30° <mild dysplasia >35°; Severe dysplasia ≥35°. AI at 2 years: normal ≤25 °, 25°< mild dysplasia >30°, severe dysplasia ≥ 30°.

Modified Tönnis classification	Pavlik harness treatment	Active Surveillance	p-value
10 months - average AI	26.4° ± 4.6° (range 19° - 44°)	26.2°± 5.0° (range: 16-37°)	0.82
normal(n,%)	40 (80)	30 (75)	
mild (n,%)	8 (16)	8 (20)	
severe (n,%)	2 (4)	2 (5)	
2 years - average AI	22.9° ± 5.1° (range 8° - 33°)	23.0°± 4.4° (range 15° -30°)	0.35
normal (n,%)	24 (60)	18 (58)	
mild (n,%)	13 (33)	12 (39)	
severe (n,%)	3 (7)	1 (3)	

Furthermore, in 71 (68%) patients the hips were imaged after walking age. Forty patients of the treatment group had a latest follow-up at 30 ± 16 months. The latest follow-up for the watchful waiting group was the same at 30 ± 12.5 months. Again, there was no difference in residual dysplasia between the two groups. (p = 0.35)

DISCUSSION

This multicenter randomized-controlled study did not show differences in outcome of treatment with abduction bracing versus active surveillance in infants of 3 to 4 months of age with sonographic dysplastic but well-centered stable hips. To our knowledge, no previous trials studied the effect of abduction treatment for stable hip dysplasia beyond 3 months of age. Rozendahl and colleagues and Wood and colleagues examined the outcome of splinting versus observation in newborns during the first month of life. [14,18] (Table 4)

Table 4. Similar results in comparative studies of treatment versus sonographic surveillance. FHC% = Femoral Head Coverage - normal FHC ≥40%; AI = Acetabular index (°)

Authors	Wood et al. (FHC%) retrospective n= 44	Rosendahl et al. (α-angle) randomized n=128	This study (α-angle) randomized n=104
age at diagnosis	2-6 weeks	1-2 days	3-4 months
affected hip			
treatment	36.7 (%)	47°	54.2°
surveillance	32.8 (%)	47°	55°
at 6 weeks follow-up			
treatment	54.3 (%)	58°	58.8°
surveillance	48.6(%)	55°	58°

Table 4 continued.

Authors	Wood et al. (FHC%) retrospective n= 44	Rosendahl et al. (α-angle) randomized n=128	This study (α-angle) randomized n=104
at 12 weeks follow-up			
treatment	24.7°(AI)	61°	60.5°
surveillance	24.2°(AI)	59°	60°
10-12 months of age (AI)			
treatment	23.5°	24.2°	24.4°
surveillance	21.6°	24.2°	26.2°
after walking age (AI)			
treatment	n/a	n/a	22.9°
surveillance	n/a	n/a	23°

Wood and colleagues, examined prospectively the outcome of splinting versus observation in infants between 2 to 6 weeks of age, with stable but dysplastic hips, defined as Morin's ratio of femoral head to acetabular diameter of < 40% and less than 2mm displacement from the floor of the acetabulum during Barlow's manoeuver. More than 2 mm displacement was considered unstable and those hips were excluded. Mean acetabular coverage was 32.8% and 36.7 respectively with 54.3% after 3 months of splinting compared to 48.5% in the non-splinted group. Although this was statistically significant, the absolute percentage difference of 5.8% is not clinically relevant as both are values of normalized hips (>40%). Furthermore, the acetabular indices on radiographs after 3 months (24.8° vs 24.3°) and 24 months (21.6° vs 23.5°) did not show any difference. The authors concluded that abduction treatment has no lasting benefit and therefore recommended follow-up until the age of 3 months for stable well-centered hips with sonographic DDH rather to avoid unnecessary treatment. Our results show a similar continuation of acetabular development with or without treatment beyond the age of 3 months for stable well-centered hips with sonographic DDH (Graf type IIb/IIc). Wilkinson et al. investigated the natural history of α-angles in relation to age, gender and side and found an average of 5.0° (range 4.4° - 5.3°) of improvement during the first 3 months of life in normal hips. There was a slower increase of the alpha angles in the female patients and for the left hip. [19] In our study, we found a similar ongoing average improvement of untreated well-centered hips with sonographic DDH of 5.0° over a period of 12 weeks. Treatment with a Pavlik harness did not accelerate the hip joint development. (p = 0.30).

All but 7 children had Graf type IIb hips. The two patients with IIc hips (α-angles of 46° and 48°) that were randomized in the active surveillance group did not show residual dysplasia after 12 weeks of observation. It would be of interest to confirm this in a larger population study of severe dysplastic hips. In comparison, Rozendahl and colleagues, conducted a

randomized controlled trial of 128 newborns with stable dysplastic hips (α-angle between 43°- 49°) (Graf type IIc or mild dysplasia according to Rozendahl's modified Graf's classification) with AI at 12 months on X-rays as primary outcome. [18] Half of the children in the surveillance group received treatment during the observation period of 6 months because of persistent dysplasia on ultrasound i.e. α-angle less than 50° after 6 weeks or less than 55° at 3 months follow-up. There was no increase in treatment duration due to the surveillance. Both groups showed similar results at one year follow-up (AI of 24.2° in both groups). The authors concluded that active sonographic surveillance halved the number of children requiring treatment with important implications for families and health care costs. In our study, a decrease or cease in progression of the α-angle led to treatment in only 3 patients (6.1%) during the active surveillance period of 3 months. After 12 weeks of follow-up, another 7 patients were treated with the Pavlik harness due to persistent Graf IIb dysplasia. In total, 10 out of 49 patients (20.4%) in the active surveillance group received treatment. This is in accordance to our recently published findings on the natural history of sonographic stable hips under six months of age where more than 80% will normalize without treatment. [20] This implies that even less patients will need treatment and the sonographic surveillance period can be extended until 6 months of age for Graf type IIb hips. Furthermore, this questions the sensitivity of ultrasonography distinguishing between true pathological hip morphology and normal ongoing development in stable hips. The current classifications based merely on bony-roof angles and instability testing aren't able to identify those hips that will do poorly later in life and leads to overtreatment.

While not all patients received further follow-up as standard of care, analysis of the rate of further acetabular growth by measuring the acetabular indices showed no added effect of treatment even after more than 2 years. We believe this is the only study, in which patients with stable hip dysplasia are randomized for treatment or observation, that describes acetabular development beyond walking age. Pruszczynski and colleagues studied the natural history of acetabular growth in 48 hips with neonatal instability without dislocation/ subluxation on ultrasound, i.e. reduced in rest and no dislocation on Barlow. [21] Acetabular indices progressively normalized (i.e AI ≤25°) in 100% of the cases at 3 years of age. Interestingly, they identified two groups: one with normal hips at 7 months, and a second group that normalizes after 7 months with 81% being normal by 24 months of age. The latter was significantly correlated with breech position and caesarean delivery. We also found the same percentage of normal hips (AI ≤25°) at 2y follow-up, 80% and 75% respectively. At 30 months, 2 hips were still severely dysplastic according to the Tonnis criteria (AI ≥ 30°) and will need further follow-up.

Despite Pavlik harness treatment started at 3 to 4 months of age, two hips developed instability. Both patients were successfully treated with closed reduction and spica casting

for 3 months and did not present residual dysplasia at walking age. Sibinski and colleagues analyzed long-term results of abduction treatment for Graf type IIb hips. [22] After 9 years, they found 20% to have residual dysplasia despite 66% of this subgroup having normal ultrasounds after treatment as an infant. Furthermore, Gardiner and colleagues, confirmed that some ultrasonographic unstable hips can be mistaken for normal on Graf's static exam and therefor progress to instability during follow-up. Reversely, a Graf III hip can be stable on Harcke dynamic examination. [23] This could explain why two hips progressed further despite treatment, as they could have been more severely dysplastic than initially diagnosed on ultrasound.

The findings in this study make us reflect on the usefulness of current ultrasound classifications for stable hip dysplasia as they are not able to distinguish between normal developing hips and true pathologic hip dysplasia. Since the majority of hips that are classified as sonographic stable dysplastic hips show spontaneous normalization, more specific methods and definitions are needed to distinguish between normal developing hips and true hip dysplasia. Until we have better methods for the diagnosis of true hip dysplasia, we recommend observation, rather than treatment, of all well-centered stable hips according to the current ultrasound classifications. This would also avoid significant overtreatment (80%) with a burden to both the families and health care systems. Identifying true DDH cases will show insufficient improvement in time and might need some form of treatment at follow-up.

CONCLUSION

Pavlik harness treatment in 55 three to four months old infants with well-centered, stable but dysplastic hips on ultrasound showed no difference compared to active surveillance in 49 infants with identical hip dysplasia after 12 weeks of observation. Furthermore, treatment with Pavlik harness did not accelerate the improvement of the bony roof angle (α-angle). To avoid overtreatment, observation of well-centered sonographic stable hips up to the age of 6 months seems sufficient in order to identify those hips that fail to improve spontaneously.

REFERENCES

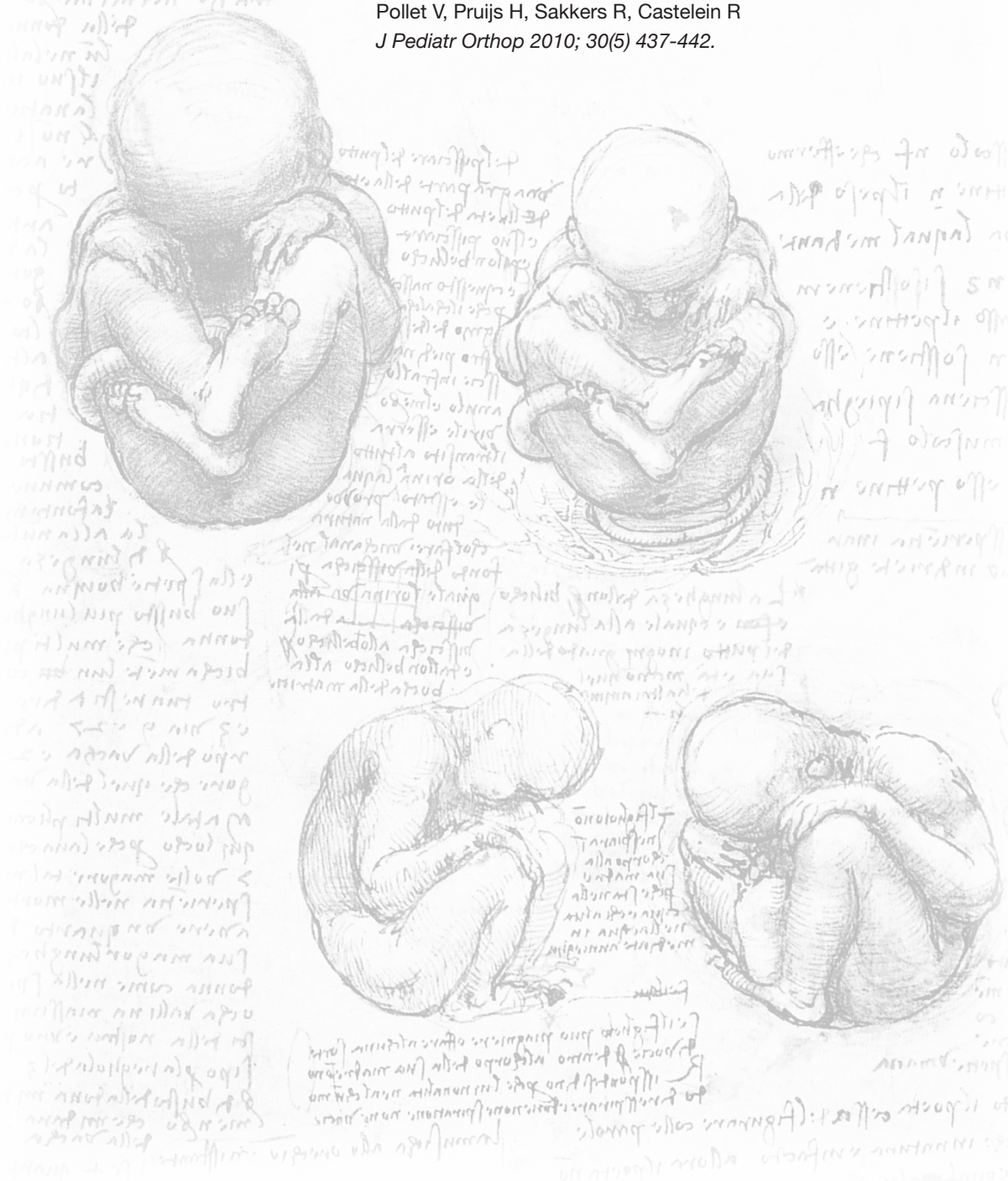
1. Patel H. Preventive health care, 2001 update: screening and management of developmental dysplasia of the hip in newborns. *CAMJ*. 164, 1669 - 77 (2011)
2. Dezateux C, Rosendahl K. Developmental dysplasia of the hip. *Lancet* 369,1541-52 (2007)
3. Tonnis D. Congenital dysplasia and dislocation of the hip in children and adults. Berlin, Springer-Verlag 1987.
4. Graf R. The diagnosis of congenital hip-joint dislocation by ultrasonic Combound treatment. *Arch Orthop Trauma Surg.* 97, 117-33 (1980)
5. Harcke HT. Hip ultrasonography in clinical practice. *Pediatr Radiol.* 47,1155-59 (2017)
6. Harcke HT. Personal email communication to corresponding author, 12 October 2018.
7. Morin C, Harcke HT, MacEwen GD. The infant hip: real-time US assessment of acetabular development. *Radiology.*157, 673-7 (1985)
8. Terjesen T, Bredland T, Berg V. Ultrasound of hip assessment in the newborn. *Bone Joint Surg Br.* 71,767-73 (1989)
9. Harcke HT, Clarke NM, Lee MS, Borns PF, MacEwen GD. Examination of the infant hip with real- time ultrasonography. *J Ultrasound Med.* 3, 131-7 (1984)
10. Roposch A, Liu L, Protopapa E. Variations of diagnostic criteria for developmental dysplasia of the hip. *Clin Orthop Relat Res*.471,1946–54 (2013)
11. Roovers EA et al. The natural history of developmental dysplasia of the hip: sonographic findings in infants of 1-3 months of age. J *Pedi Orthop B.* 14, 325-30 (2005)
12. Schaeffer EK, IHDI Study group, Mulpuri K. Developmental dysplasia of the hip: addressing evidence gaps with a multicentre prospective international study. *Med J Aust*. 208,359-64 (2018)
13. Pavlik A. The functional method of treatment using a harness with stirrups as the primary method of conservative therapy for infants with congenital dislocation of the hip. 1957. *Clin Orthop Relat Res*. 281,4-10 (1992)
14. Wood MK, Conby C, Benson MK. Does early treatment by abduction splintage improve the development of dysplastic but stable neonatal hips? *J Ped Orthop.* 20, 302-5 (2000)
15. Riad JP, Cundy P, Gent R et al. Longitudinal study of normal hip development by ultrasound. *J Ped Orthop*. 25, 5-9 (2005)
16. Sucato DJ, Johnston CE, Birch JG, Herring JA, Mack P. Outcome of ultrsonographic hip abnormalities in clinically stable hips. *J Ped Orthop*. 19,754-59 (1999)
17. Bilgili F et al. Treatment of Graf type IIa hip dysplasia: a cutoff value for decision making. *Balkan Med J*. 15, 427-30 (2018)
18. Rosendahl K, Dezateux C, Fosse K et al. Immediate treatment versus sonographic surveillance for mild dysplasia in newborns. *Pediatrics*. 125,9-16 (2010)
19. Wilkinson AG, Wilkinson S, Elton R. Values for bony acetabular roof angle and percentage femoral head cover in a selective ultrasound neonatal hip-screening programme: effect of age, sex and side. *J Pediatr Orthop-B.* 27,236-43 (2018)
20. Sakkers R, Pollet V. The natural history of abnormal ultrasound findings in hips of infants under six months of age. *J Child Orthop*.12,302-7 (2018)
21. Pruszczynski B, Harke HT, Holmes L, Bowen JR. Natural history of hip instability in infants (without subluxation or dislocation): a three year follow-up. *BMC Musculoskeletal Disorders.* 15,355-62 (2014)
22. Sibinski M, Adamczyk E, Higgs Z, Synder M. Hip joint development in children with type IIb developmental dysplasia. Int Orthop. 36,1243-46 (2012)
23. Gardiner HM, Duncan AW. Radiological assessment of the effects of splinting on early hip development: results from a randomised controlled trial of abduction splinting vs sonographic surveillance. *Pediatr Radiol*. 22,159-62 (1992)

CHAPTER 5

Results of pavlik harness treatment in children with dislocated hips between the age of six and twenty-four months.

Pollet V, Pruijs H, Sakkers R, Castelein R

J Pediatr Orthop 2010; 30(5) 437-442.



ABSTRACT

Background

We retrospectively studied the outcome of Pavlik harness treatment in late-diagnosed hip dislocation in infants between 6 and 24 months of age (Graf type 3 and 4 or dislocated hips on radiographs) treated in our hospital between 1984 and 2004. The Pavlik harness was progressively applied to improve both flexion and abduction of the dislocated hip. In case of persistent adduction contracture, an abduction splint was added temporarily to improve the abduction.

Methods

We included 24 patients (26 hips) treated in our hospital between 1984 and 2004. The mean age at diagnosis was 9 months (range 6-23 months). The average follow-up was 6y6m (2-12y). Ultrasounds and radiographs were assessed at the time of diagnosis, one year after reposition and at last follow-up.

Results

Twelve of the twenty-six hips (46%) were successfully reduced with Pavlik harness after an average treatment of 14 weeks (4 – 28 weeks). One patient (9%) needed a secondary procedure 1y9m after reposition because of residual dysplasia (Pelvis osteotomy). None of the successfully treated hips developed an avascular necrosis (AVN). Three (11%) hips showed signs of AVN, 1 after closed reposition and 2 after closed reposition.
17 of the 26 hips were primary diagnosed by Ultrasound recording the Graf classification. Ten had a Graf type 3 hip and 7 hips were classified as Graf type 4. There was a 60% success rate for the type 3 hips. None of the type 4 hips were successfully reduced. The success rate between both groups was significantly different. (p = 0,035)

Conclusion

The use of a Pavlik harness in the late-diagnosed hip dislocation can be a successful treatment option in the older infant. We have noticed very few complications in these patients may be due to progressive and gentle increase of abduction and flexion, with or without temporary use of an abduction splint. None of the Graf IV hips were able to be reduced successfully by Pavlik harness. This was significantly different from the success rate for the Graf type 3 hips.

INTRODUCTION

Late diagnosed hip dislocation has become a rare entity because of early screening and ultrasound diagnosis in newborns at risk or when clinical exam warrants it. The common treatment of these hips consists of closed reduction and spica cast application under anesthesia all or not after a period of traction. This necessitates sometimes long hospitalization, general anesthetics and often a CT-scan to confirm the reposition of the hip. The Pavlik harness has become the method of choice to treat DDH in infants younger than 6 months. Harris et al described when to abandon the Pavlik harness. (1) They looked at the results of 550 patients (720 hips) with (sub)luxation of the hip in infants younger than 1 year. The mean age of their patients was 8 weeks (1-53 weeks) at time of treatment. They achieved reduction in 89% by means of Pavlik harness. The rate of avascular necrosis was low (0,7%). Based on their results they recommend to abandon the treatment in case there is no adequate sense of reduction, hips that need excessive flexion to maintain reduction, hips that re-dislocate with slightest adduction and in larger children, older than eight months of age.

In late-presenting DDH, the hips have limited abduction and are not reducible at clinical exam because of soft tissue contractures.

The objective of our study was to analyze the results of the Pavlik harness treatment in the late-diagnosed hip dislocation in infants between 6 and 24 months of age treated at our hospital between 1984 – 2004. We also looked if adding an abduction brace increased the success rate of the Pavlik harness treatment.

METHODS

We included all patients older than 6 months and younger than 24 months, who were treated in our hospital for hip dislocation (Graf type 3 and 4 or hip dislocation on pelvis X-rays) between 1984 and 2004 with a minimal follow-up of 1 year after reposition.

Over 6 months of age, we use the Pavlik harness with metal clips and buckles (Stiefeneder – Germany) to withstand the forces of adduction and extension generated by the older infant. The Pavlik harness is progressively adjusted to achieve good flexion (100°) and abduction (full abduction. The outline of the treatment as performed in our hospital is giving in the flowchart (Fig. 1). Ultrasounds and pelvic radiographs were assessed at initial diagnosis, 1 year after reposition and at latest follow-up. Graf's classification was used to assess the severity of the dislocation in ultrasounds as well as Tönnis classification for those patients

who had only pelvic X-rays at initial diagnosis. The AC index, Shenton line, the migration percentage and center edge angle were measured on pelvis radiographs for evaluating residual dysplasia. Both the Salter and Kalamchi-McEwen classification were used to diagnosis avascular necrosis (AVN).

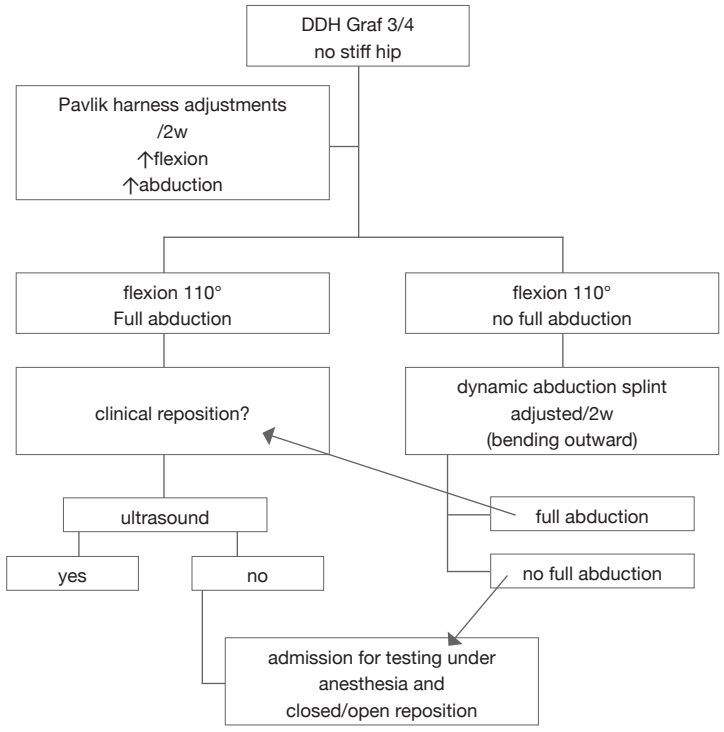


Fig 1. Guideline of extended Pavlik harness treatment in infants older than 6 months of age as used in our hospital. Stiff hip = severe adduction contracture not allowing sufficient abduction to start the Pavlik harness treatment.

Statistic analysis

The Fisher's Exact test was used to look at the success rate between Graf type 3 and type 4 and the use of the abduction brace.

A 2 sided p-value < 0.05 was considered significant.

RESULTS

Twenty-four patients (26 hips, 22 girls, 2 bilateral, Right/Left = 7/19) were included that were primary treated with the Pavlik harness. Ten patients were treated by traction and spica cast and were excluded for this study. Patients were also excluded if primary treatment was started elsewhere (92 patients), in case of teratologic hip dysplasia (25 patients), and when the child was younger than 6 months or older than 24 months (125 patients). Of 37 patients, the medical records were incomplete. The average age at the start of the Pavlik treatment was 9 months (range, 6-23months). The average follow-up was 6y6m (2-12y). Twelve out of 26 hips (46%) were successfully reduced with the Pavlik harness after an average treatment duration of 14 weeks (4-28 weeks). The average time to reposition was 4 weeks (range 2-7 weeks).

Fourteen hips (54%), that failed Pavlik treatment, were reduced either with closed or open reposition. (Table 1)

Table 1. Patients overview and successful reposition in relation to age, type of dislocation and use of abduction brace. (DVO = derotation varisation osteotomy) Avascular necrosis (AVN) was diagnosed using both Salter and Kalamchi/McEwen classification.

Case	Age(m)	side	Graf type	Tönnis type	Successful reposition	Abduction orthosis	Closed/open reposition	2nd procedure	AVN
1	8	L	3		0	Yes	Closed		
2	7	R	3	2	0	Yes	Open		yes
3	6	L		3	1	No			
4	8,5	R/L	3/3	3/3	0/1	Yes/Yes	Closed	Pemberton	
5	10,5	R		2	0	Yes	Closed		
6	7	L	4		0	No	Open	DVO	
7	9,5	L	4		0	Yes	Closed		
8	7	L	3		1	Yes			
9	7	L	4		0	Yes	Open		yes
10	8	R/L	4/4		0/0	No/No	Open/open		
11	6,5	L	4		0	No	Closed		
12	6,5	R		3	1	No			
13	16	L	3		1	Yes			
14	7	L	3	3	0	Yes	Closed		
15	15,5	R		2	0	Yes	Closed		yes
16	9	L		2	1	No			
17	7	L	3	2	1	No			
18	12	L		2	1	Yes			
19	23	R		4	1	Yes			
20	7,5	R	4	4	0	Yes	Open		
21	10	L	3		1	Yes			
22	8	L		4	1	Yes		Pemberton	
23	7	L		4	0	Yes	Closed		
24	8,5	L	3		1	No			

In 16 out of 24 (66%) patients, an abduction splint (Dynamic hip abduction splint – Basko–Germany) was added after an initial period of Pavlik treatment to improve abduction after achieving good flexion. (Fig 2) There was no significant difference in successful reposition, when the abduction brace was added to the Pavlik (p = 0.57).

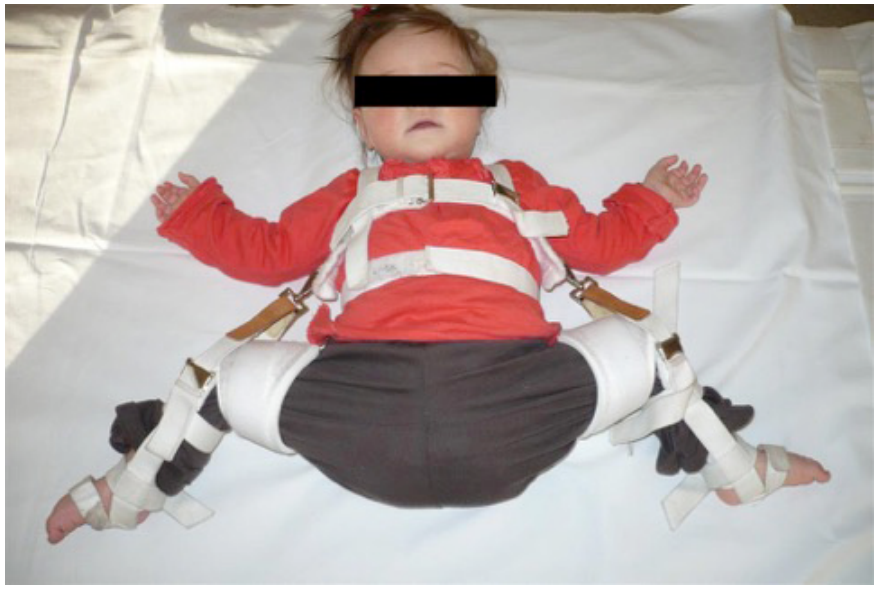


Fig 2. Dynamic abduction splint added to Pavlik harness to improve abduction after obtaining sufficient flexion to descent the femoral head in the acetabulum.

Three patients developed an AVN (11%). All had failed Pavlik harness treatment with added abduction orthosis and were subsequently reduced by closed or open reposition. At latest follow-up, two of these hips had developed a coxa magna. One patient developed a neuropraxia of the femoral nerve, which resolved spontaneously after temporarily discontinuation of the Pavlik harness. One successful reduced hip needed a secondary procedure (Pelvis osteotomy) because of residual dysplasia. Two hips after failed Pavlik treatment and subsequent closed or open reposition, needed a Derotation Varisation Osteotomy (DVO) and a Pelvis osteotomy respectively, within 2 years after reposition.

DDH was diagnosed by Ultrasound recording to Graf's method in 17 hips in 15 patients. Ten patients presented with a Graf type III and 7 patients with Graf type IV. The other 9 patients had only pelvis x-rays at the time of diagnosis. On these X-rays, 3 hips were classified recording the Commission for the Study of hip Dysplasia of the German society for Orthopaedics and Traumatology (CSHD) as Tönnis type II, one as type III and 5 hips as type IV.

There was a significant difference in outcome of Pavlik treatment between Graf type 3 and type 4 hips. (p= 0,035) Six out of 10 (60%) Graf type 3 hips had a successful reposition compared to none of the Graf type 4 hips (0%). Of the 9 hips classified recording the CSHD, six were successfully treated by Pavlik harness. (66%) Statistically, it was not possible to correlate the severity of the lateralization and the treatment outcome because of the low number of hips. There was a successful reposition in 1/3 for type 2; 1/1for type 3 and 4/5 for type 4.

Looking at the pelvis X-rays one year after reposition, the average AC index was 29° (range, 20-36°). The migration percentage was 23% (range, 0-100%). At latest follow-up, the AC index improved to 22 degrees (range 11-36 degrees) and the migration percentage was 8 % (range 0-42%). In two patients, who had a 100% migration at 1 year after reposition, a Pemberton osteotomy was performed less than 2 years after reposition. Both hips normalized almost completely to a migration percentage of 0% and 10% with an AC index of 22 and 24 degrees respectively. When the patient was older than 5 year at latest follow-up, we measured the CE-angle. The average CE-angle was 24 degrees in 17 hips (range, 8-37 degrees).

DISCUSSION

In 1957 Arnold Pavlik published his functional method of the treatment of congenital dislocation of the hip because of the disappointingly high rate of avascular necrosis of dislocated hips when immobilized in abduction. [2] He described a harness with stirrups that permitted motion in the affected hip. More than 50 years later, this has become the method of choice to treat DDH in infants. In order to improve the abduction and flexion and hereby increase the possibility of hip relocation, we applied the Pavlik harness with regular follow-up and progressive adjustment of the harness. When sufficient flexion was achieved to descent the femoral head in the acetabulum, an abduction orthosis was added in those hips where the Pavlik harness couldn't obtain sufficient gradual abduction. This could be because of the older age of the infants that are stronger to withstand the abduction imposed by the Pavlik harness.

We use the ultrasound to confirm reposition described by Van Douveren et.[5] This is a transinguinal approach in a transverse plane showing the femoral head, acetabulum, ramus superior of the pubic bone and the femoral neck (metaphysis) in one plane. (Fig 3)

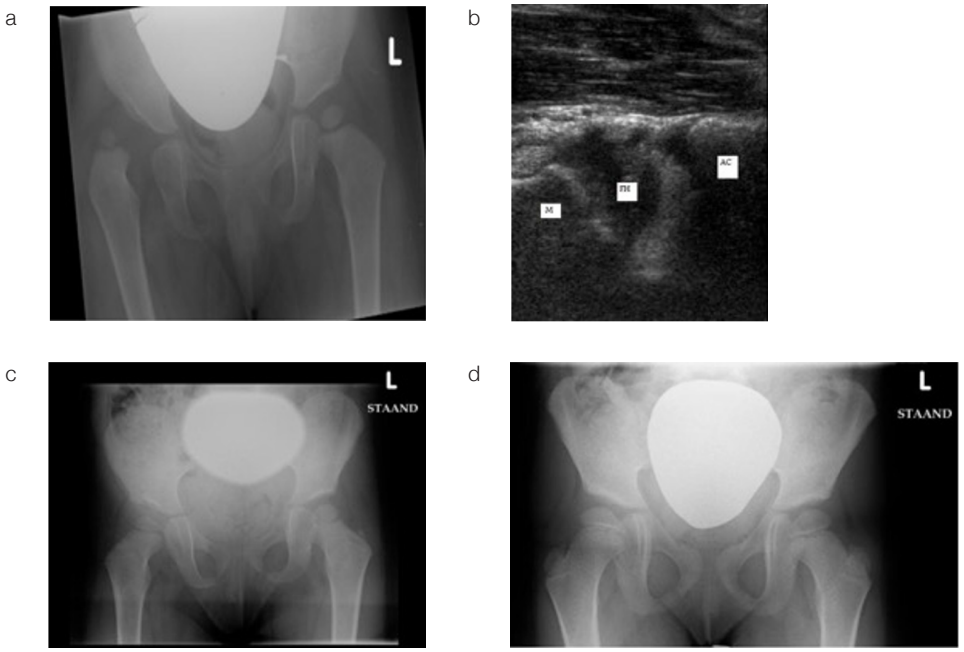


Fig 3. Patient 19: Successful Pavlik treatment in late-diagnosed dislocated right hip in a 23 months old girl. a. Pelvis X-rays at initial diagnosis (at 23 m). b. Transinguinal ultrasound to confirm the reposition of the right hip after 8 weeks of Pavlik treatment. (M= metaphysis, FH= Femoral head, AC = acetabulum). c. Pelvis X-rays at 1 y after reposition (at 2 y 1m) and d. final follow-up (at 5y3m).

Only 4 out of 14 hips with failed Pavlik treatment had traction before closed reposition under anaesthesia was attempted. It is unclear from this study if the success rate of closed reduction would be higher if all failed Pavlik treated hips had preliminary traction. Based on our results, we question the indication of the Pavlik harness treatment in Graf type 4 hips. None of these hips were successfully reduced. In Graf type 4 hips, the labrum is caudally displaced, blocking a successful reposition. While in Graf type 3 hips, the cartilage roof is pushed upwards by the femoral head. Mostert et al also found a significant difference in outcome between Graf type 3 (97%) and Graf type 4 (50%) hips treated by Pavlik harness in infants younger than 6 months. [20] Looking at the X-rays, we couldn't make the same conclusion depending on the type of Tönnis classification, which is based on the severity of lateralization of the femoral head rather than "the pathoanatomical deformation of the cartilage roof" as described by Graf.[16]

This suggests that the Graf classification has a better predictive value for the outcome of the Pavlik harness treatment. Those hips that failed Pavlik treatment, had similar results (success rate of 53%) after closed reduction as mentioned in the literature (57 – 94%). [3,4,7,8,9,10] The 3 cases of AVN developed in this group though. One Graf type 3 hip, one Graf type 4 hip and one Tönnis type 2 hip developed AVN. They were initially treated by Pavlik harness and the abduction orthosis was added. One hip was reduced by closed reposition (Tönnis type 2). Both Graf 3 and 4 hips needed open reposition. Papadimitriou et al used the modified Hoffmann-Daimler functional method to treat late-presenting DDH.[6] In a similar way, they first apply a flexion harness to gradually reduce the femoral head, followed by an abduction splint, to remodel the reduced hips. The average age was sixteen months (6-44m). Osteonecrosis was noted in 6%. After reduction was obtained, 16 hips (17%) were treated by hip spica cast during 6 weeks because of re-dislocation or very unstable hips. At latest follow-up, eighty-eight dislocated hips were classified as satisfactory (Severin class I and II). They reported no secondary procedures for residual dysplasia. Our results were less favourable. Maybe because we did not use a spica cast to improve the stability nor we used the abduction brace in all of our patients to enhance acetabular remodeling.

In the study of Ward et al, the intra- and inter-observer reliability of the Severin classification showed only poor to moderate agreement. [10] Also Ali et al found a poor inter-observer reliability, but had a better result for the intra-observer reliability. [12] We agree that in order to assess the outcome of treated DDH, there is a need for a more objective description based on reliable measurements which also includes the functional outcome. Therefore we did not use the Severin classification to describe our outcome. Instead, we described residual dysplasia as a combination of increased migration percentage, decreased CE angle and increased Acetabular Index. All 3 measurements have proven good inter- and intra-observer reliability. [13, 14,15] Three patients treated primary by Pavlik harness showed residual dysplasia, but all 3 were only 5 years of age at the latest follow-up. Since remodeling of the acetabulum can still improve the dysplasia, they are followed-up closely. The weakness of this study is the small number of patients that have been studied retrospectively, although late-presenting DDH is not frequently seen in daily practice. Also, comparing ultrasound with pelvis X-rays in determining the severity of the disease seemed to be difficult. Therefore, we included both Graf type III and IV - severely dysplastic decentered hips- in comparison with dislocated hips on radiographs (Tönnis type 2, 3 and 4) in the overall assessment of outcome. Since all successful Pavlik harness treated hips were reduced in less than 7 weeks of treatment, we believe that the treatment can be abandoned if the hip is not reduced after 6 weeks of treatment. A good compliance of the parents, regular follow-up and availability of the surgeon are mandatory for a successful treatment with Pavlik harness, even more so in this age group.

CONCLUSION

Although controversy exists on the use of the Pavlik harness in infants with dislocated hips over the age of 6 months, it can be successful, especially for Graf type 3 hips, and can

reduce the rate of closed or open reposition in this age group. The treatment should be abandoned if the hip is not reduced after 6 weeks. Graf type IV hips showed a significantly worse success rate in reposition when treated by Pavlik harness. These hips are better treated by means of closed or open reposition.

REFERENCES

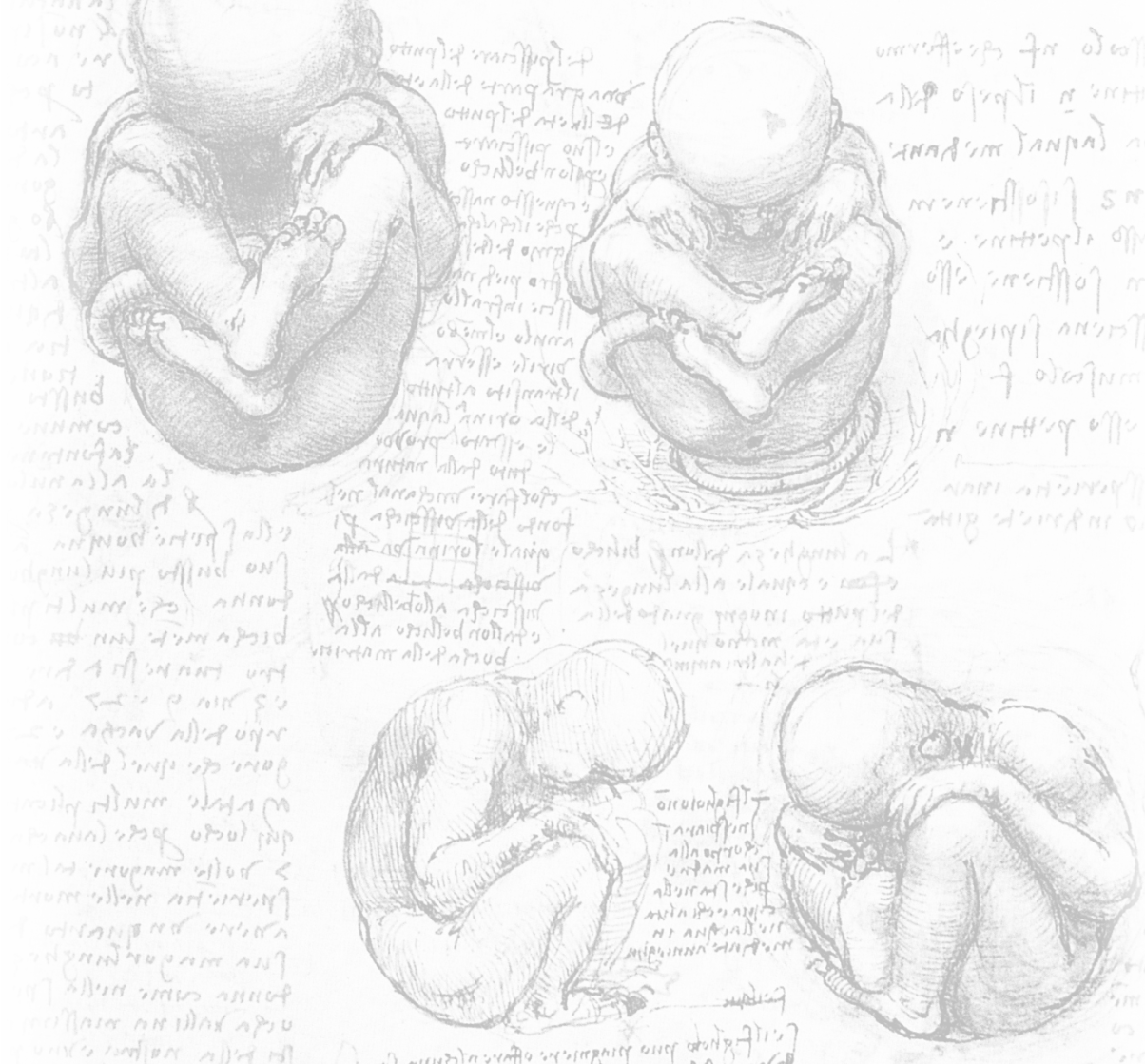
1. Harris IE, Dickens R, Malcolm BM. Use of the Pavlik Harness for Hip displacement: when to abandon treatment. *Clin Orthop Relat Res.* 1992;281:29-33.
2. Pavlik A. The functional method of treatment using a harness with stirrups as the primary method of conservative therapy for infants with congenital dislocation of the hip. 1957. *Clin Orthop Relat Res.* 1992; 281:4-10.
3. Schoenecker PL, Dollard PA, Sheridan JJ, Strecker WB. Closed reduction of developmental dislocation of the hip in children older than 18 months. *J Pediatr Orthop*. 1995;15:763-767.
4. Zionts LE, MacEwen GD. Treatment of congenital dislocation of the hip in children between the ages of one and three years. *J Bone Joint Surg Am*. 1986 ;68:829-846
5. van Douveren FQMP, Pruijs HEH, Sakkers RJB, Nievelstein RAJ, Beek FJA. Ultrasound in the management of the position of the femoral head during treatment in a spica cast after reduction of the hip dislocation in developmental dysplasia of the hip. *J Bone Joint Surg Br.* 2003; 85:117-120.
6. Papadimitriou NG, Papadimitriou A, Christophorides JE, Beslikas TA, Panagopoulos PF. Late-presenting developmental dysplasia of the hip treated with the modified Hoffmann-Daimler functional method*. J Bone Joint Surg Am*. 2007; 89: 1258-1268.
7. Murray T, Cooperman DR, Thompson GH, Ballock T. Closed reduction for treatment of development dysplasia of the hip in children. *Am J Orthop*. 2007;36:82-84.
8. Kokavec M, Makai F, Olos M, Bialik V. Pavlik's method: a retrospective study. *Arch Orthop Trauma Surg*. 2006;126:73-76.
9. Nakamura J, Kamegaya M, Saisu T, Someya M, Koizumi W, Moriya H. Treatment for developmental dysplasia of the hip using the Pavlik harness: long-term results. *J Bone Joint Surg Br*. 2007;89:230-235.
10. Terjesen T, Halvorsen V. Long-term results after closed reduction of late-detected hips dislocation. *Acta Orthopaedica* 2007;78: 236-246.
11. Ward WT, Vogt M, Grudziak JS, Tümer Y, Cook PC, Fitch RD. Severin classification system for evaluation of the results of operative treatment of congenital dislocation of the hip. A study of intraobserver and interobserver reliability. *J Bone Joint Surg* Am. 1997;79:656-663.
12. Ali AM, Angliss R, Fujii G, Smith DM, Benson MK. Reliability of the Severin classification in the assessment of developmental dysplasia of the hip. *J Pediatr Orthop B*. 2001 Oct;10:293-297.
13. Faraj S, Atherton WG, Stott NS. Inter- and intra-measurer error in the measurement of Reimers' hip migration percentage. *J Bone Joint Surg Br*. 2004; 86: 434-437
14. Broughton NS, Brougham DI, Cole WG, Menelaus MB. Reliability of radiological measurements in the assessment of the child's hip. *J Bone Joint Surg Br*. 1989 ;71:6-8.
15. Spatz DK, Reiger M, Klaumann M, Miller F, Stanton RP, Lipton GE. Measurement of acetabular index interobserver and interobserver vatiation. *J Pediatr Orthop* 1997;17:174-175.
16. Graf R. The use of ultrasonography in developmental dysplasia of the hip. *Acta Orthop Traumatol Turc* 2007; 41 suppl 1:6-13.
17. Wirth T, Stratmann L, Hinrichs F. Evolution of late presenting developmental dysplasia of the hip and associated surgical procedures after 14 years of neonatal ultrasound screening. *J Bone Joint Surg Br.* 2004;86:585-589

18. Salter RB, Kostiuk J, Dallas S, Avascular necrosis of the femoral head as a complication of treatment for congenital dislocation of the hip in young children: a clinical and experimental investigation. *Can J Surg*. 1969;12:44-61.
19. Kalamchi A, MacEwen GD. Avascular necrosis following treatment of congenital dislocation of the hip. *J Bone Joint Surg Am*. 1980 ;62:876-888.
20. Mostert.AK, Tulp, NJA, Castelein RM. Results of Pavlik harness treatment for neonatal hips dislocation as related to Graf's sonographic classification. *J Pediatr Orthop*. 2000; 20:306-310.

CHAPTER 6

Long-term outcomes following the medial approach for open reduction of the hip in children with developmental dysplasia.

Pollet V, Van Dijk L, Reijman M, Castelein RMC, Sakkers RJB
Bone Joint J. 2018;100-B(6):822-827



ABSTRACT

Aims

Open reduction is required following failed conservative treatment of developmental dysplasia of the hip (DDH). The Ludloff medial approach is a commonly used, but poor results have been reported, with rates of the development of avascular necrosis (AVN) varying between 8% and 54%. This retrospective cohort study evaluates the long-term radiographic and clinical outcome of dislocated hips treated using this approach.

Patients and Methods

Children with a dislocated hip, younger than one year of age at the time of surgery, who were treated using a medial approach were eligible for the study. Radiographs were evaluated for the degree of dislocation and the presence of an ossific nucleus preoperatively, and for the degree of AVN and residual dysplasia at one and five years and at a mean of 12.7 years (4.6 to 20.8) postoperatively. Radiographic outcome was assessed using the Severin classification, after five years of age. Further surgical procedures were recorded. Functional outcome was assessed using the Pediatric Outcomes Data Collection Instrument (PODCI) or the Hip disability and Osteoarthritis Outcome Score (HOOS), depending on the patient's age.

Results

A total of 52 children (58 hips) were included. At the latest follow-up, 11 hips (19%) showed signs of AVN. Further surgery was undertaken in 13 hips (22.%). A total of 13 hips also had a poor radiological outcome with Severin type III or higher. Of these, the age at the time of surgery was significantly higher ($p < 0.05$) than in those with a good Severin type (I or II). The patient-reported outcomes were significantly worse ($p < 0.05$) in children with a poor Severin classification.

Conclusion

This retrospective long-term follow-up study shows that one in five children with DDH who undergo open reduction using a medial surgical approach has poor clinical and/or radiological outcome. The poor outcome is not related to the presence of AVN (19%), but due to residual dysplasia.

INTRODUCTION

Between 1% and 3% of newborns have developmental dysplasia of the hip (DDH).[1] This condition includes a spectrum of hip problems in children, ranging from dysplasia to frank dislocation. In the child with an early diagnosis of DDH, the current routine treatment involves the use of a Pavlik harness or a brace. If this treatment fails, closed reduction will usually be the next step. This can be undertaken with or without preliminary traction. If this fails, open reduction is undertaken. Medial or anterior approaches are commonly used. Avascular necrosis (AVN) of the femoral head is a well-documented complication of both approaches.[2,3] The anterior approach is usually used at an older age, about nine months of age, after the ossific nucleus of the epiphysis becomes visible on plain radiographs. This has a probable protective effect against AVN.[4] The medial approach was introduced by Ludloff and later adapted by Ferguson and Weinstein and Ponseti.[5,6,7] However, the results have been questioned, due to the risks of damage to the medial femoral circumflex artery and subsequent AVN.[8,9] The medial approach has been routinely used in our hospital (Sophia's Children's Hospital, Erasmus Medical Center, Rotterdam, The Netherlands) for many years. In this study, we investigate the long-term radiological and clinical outcomes following its use in children with a dislocated hip.

PATIENTS AND METHODS

Following approval from the institutional review board at Sophia's Children's Hospital, we reviewed the clinical and radiological records of all children with dislocation of the hip aged less than one year at the time of surgery, and who underwent surgery using a medial approach between 1985 and 2010. All procedures were performed by one surgeon. Children aged over one year at the time of surgery and those with a teratologic or neuromuscular dislocation were excluded. Those with follow-up of less than four years were also excluded. A total of 60 children fulfilled the inclusion criteria. Eight children had incomplete medical or radiological records and were excluded, leaving 52 patients with 58 hips for inclusion in the study (Table 1).

Table 1. Baseline characteristics of the children in the study

Characteristic	Total n = 52 (hips, n = 58)
Female gender, n (%)	47 (*90*)
Side, n (%)	
Left	42 (*73*)
Right	10 (*17*)
Bilateral	6 (*10*)
Mean age at surgery, months (SD)	6.3 (2.5)
Mean age at final follow-up, years (range)	13.1 (4.7 to 21.5)
Mean follow-up time, years (range)	12.7 (4.6 to 20.8)

An arthrogram was performed per-operatively prior to open reduction. Postoperatively, a spica was retained for four months. When available, a CT scan was used to assess reduction if there was doubt at the end of the procedure, and was undertaken within 24 hours. CT scans were undertaken routinely between 2001 and 2010; the frequency with which CT scans were undertaken between 1985 and 2001 is uncertain, as records for this period were not available. An abduction brace was used to treat residual dysplasia for a duration of two to three months following removal of the spica cast. Bilateral dislocations were treated at the same sitting.

Radiological outcome

The following were noted on a preoperative anteroposterior (AP) pelvic radiograph: the International Hip Dysplasia Institute (IHDI) classification, the presence of an ossific nuleus, and the acetabular index (AI).[10] The Bucholz and Ogden classification was used to assess AVN at one and five years postoperatively, and at the latest follow-up.[11] Although hard evidence does not yet exist to support this hypothesis, Bucholz and Ogden type I is not currently thought to affect the radiological outcome at skeletal maturity; we therefore considered that types II, III, and IV would be correlated to disturbances of proximal femoral growth. The centre-edge (CE) angle was measured five years postoperatively and at the latest follow-up, to allow classification of the hips according to the Severin grade.[12-14] Severin types I and II were considered to represent a good result and types III, IV, V, and VI were considered to represent a poor result. All classifications were determined by two authors (LD and VP) with a consensus. The requirement for further surgical treatment, including pelvic osteotomy, femoral osteotomy, and repeat open reduction, was noted from the records, as was the amount of abduction of the hip (in degrees) in the spica cast when stated in the operation notes. The functional outcome was assessed using the Pediatric Outcomes Data Collection Instrument (PODCI) or the Hip Disability and Osteoarthritis Outcome Score (HOOS) questionnaire.[15,16] The validated Dutch version of the PODCI was used for patients up to 18 years of age.[16] For patients aged ten years or under, the questionnaire was filled out by the patient's parents; for patients aged between 11 and 18 years, the questionnaire was filled out by the patient. This assesses six outcomes: upper limb and physical function, transfer and basic mobility, sports/physical functioning, pain/comfort, happiness, and global functioning. For patients aged 19 years or over, the Dutch HOOS questionnaire was used. This records five measures including pain, other symptoms, activities of daily living (ADL), sports and recreation, and hip-related quality of life. Each has a score ranging from 0 to 100, with 0 being the worst outcome.

Statistical analysis

Continuous variables were tested for normality using the Shapiro–Wilk test. Mean and standard deviations were obtained for normally distributed variables; median and interquartile range (IQR) were obtained for non-parametric distributed variables. The non-parametric Mann–Whitney U test was used to answer secondary questions for non-normally distributed variables. When data were presented as numbers and percentages, the Fisher's exact test was used. The level of significance was set at $p < 0.05$. Statistical analysis was performed using SPSS 21.0 for Windows (IBM Corp., Armonk, New York).

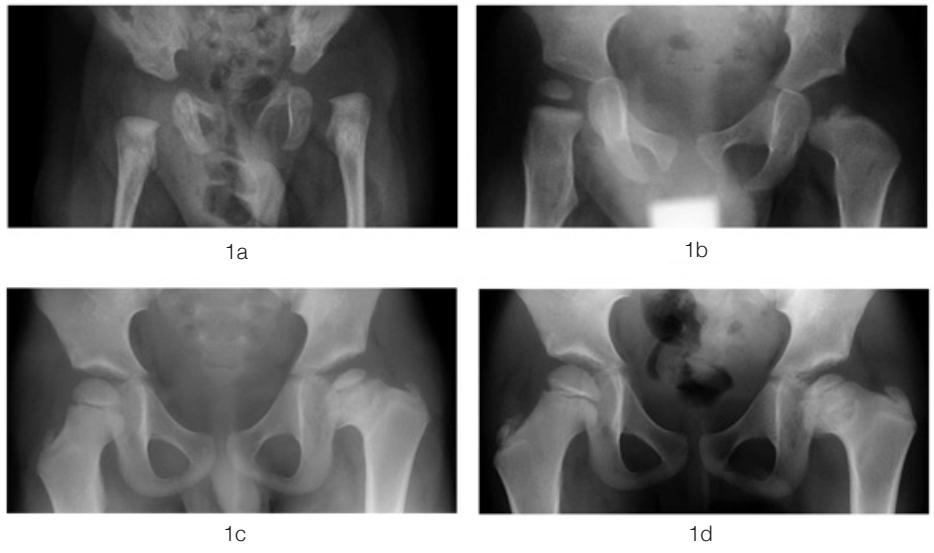
RESULTS

A total of 20 children (38%) had previous failed conservative treatment involving a Pavlik harness in three, an abduction brace in ten, and closed reduction in seven; 32 had no previous treatment. The mean follow-up was 12.7 years (4.6 to 20.8). There was insufficient information for 12 children (23.1%; 14 hips) as the initial radiographs were not available. The preoperative radiological characteristics of the remaining 40 children (44 hips) are shown in Table 2.

Table 2. Preoperative radiological characteristics in 40 children (44 hips)
*Information missing for 12 children (14 hips) IHDI, International Hip Dysplasia Institute; AI, acetabular index

Characteristic	No. of hips
IHDI classification*	
Grade II	10
Grade III	27
Grade IV	7
Presence of ossified nucleus*	
Yes	12
No	32
Mean AI, ° (range)*	
Affected hip	38 (24 to 52)
Contralateral stable hip	27 (11 to 42)

The mean AI of the affected hip was higher preoperatively and remained significantly higher than that of the unaffected side five years postoperatively ($p < 0.001$). The mean CE angle was significantly lower on the affected side at the final follow-up ($p = 0.023$), and was within normal limits.(13) A total of 45 hips (78%) were Severin type I (33 hips; 57%) and type II (12 hips; 21%), thus had an excellent or good outcome at the final follow-up. A total of 13 hips (22%) were Severin type III or higher and thus had a poor result; two (3%) were type III, nine (16%) were type IV, and two (3%) were type V. The median age at the time of surgery for the Severin type I and II groups was significantly lower than that of the poorer Severin outcome groups: 5.2 months (IQR 1.9 to 8.5) and 8.6 months (IQR 5.2 to 12.0), respectively ($p = 0.047$). AVN was present in 31 hips (53%) postoperatively. Of these hips, 11 (19%) had developed Bucholz and Ogden type II, III, or IV AVN. (Table 3; Fig. 1)



1a 1b 1c 1d

Fig 1. a) An antero-posterior radiograph of a four-month-old boy with dysplasia and dislocation of the left hip. b) One year after open reduction, there is type IV avascular necrosis of the femoral head. c) Significant growth disturbance of the medial plate is seen five years after treatment, leading to coxa vara. d) At 6.5 years after surgery, there remains coxa vara and the greater trochanter is starting to overgrow. The right hip is developing normally.

Table 3. Presence of avascular necrosis (AVN) in relation to the outcome (Severin classification) (p = 0.750). Type II or more AVN hips were all Severin type I or II.

AVN group	No. of hips (%)	No AVN, n (%)	No. of hips (%)
Total AVN	**30 (*100*)**	**Total no AVN,**	**28 (*100*)**
Severin ≤ II	20 (*66*)	Severin ≤ II	25 (*89*)
Severin ≥ III	10 (*34*)	Severin ≥ III	3 (*11*)
AVN type I	**19 (*63*)**		
Severin ≤ II	9 (*30*)		
Severin ≥ III	10 (*33*)		
AVN type ≥ II	**11 (*37*)**		
AVN type II	5 (*17*)		
AVN type III	4 (*13*)		
AVN type IV	2 (*7*)		
Severin ≤ II	11 (*37*)		
Severin ≥ III	0 (*0*)		

For the whole study group, the operation notes did not specifically record the preservation or damage to the medial circumflex femoral artery. There was no significant correlation between the presence of AVN and the degree of dislocation (IHDI grade) (p = 0.31), the presence of an ossified nucleus at the time of surgery (p = 0.72), or the age at the time of surgery (p = 0.24). The range of abduction of the hip that was required to maintain reduction was recorded in the operation notes in 48 patients (92.3%). The rate of AVN was lower with hips abducted to < 60° than those abducted to > 60° (25% *vs* 50%), although this did not reach significance (p = 0.06). The development of AVN did not correlate with a poor radiological outcome (Severin classification) at the final follow-up (p = 0.75). It is notable that type II or more severe AVN was not associated with severe residual dysplasia. All of the poorest outcomes (Severin Type III or more) were associated with type I AVN (Table III). Further surgery was necessary in 13 hips. One child had a recurrent dislocation requiring a further open reduction through an anterior approach and a Salter pelvic osteotomy. One child with type II AVN underwent a Salter osteotomy at the age of five years, followed by a derotation/varus proximal femoral osteotomy at the age of ten years. A Salter osteotomy was performed in nine children in isolation. Finally, two required a greater trochanteric osteotomy. Further surgery was undertaken in 13 hips (22%) for residual dysplasia. Older age at the time of the initial surgery was a significant predictive factor for the need for further surgery, 8.7 months (IQR 7.3 to 10.1) for children requiring further surgery compared with 5.1 months for those who did not (IQR 1.8 to 8.4) (p = 0.002). At the final follow-up, there was a trend towards the requirement for further surgery and poorer outcome, though this did not reach significance (p = 0.053). Eight of the 13 hips requiring further surgery had AVN. The need for further surgery and the presence of AVN were not associated with a poor outcome (p = 1.00). The families of 32 children (62%) completed questionnaires; 17 completed the PODCI questionnaire and 15 completed the HOOS questionnaire. AVN was present in 11 of these children (34%). The functional outcome, for all of the subscales of the PODCI and the HOOS questionnaires, did not correlate with the presence or absence of AVN (p > 0.25). Conversely, subscales for 'pain/comfort' (p = 0.04) and 'global functioning' (p = 0.04) for the PODCI and subscales for 'pain' (p = 0.01), 'symptoms' (p = 0.01), and 'activities of daily living' (p = 0.01) for the HOOS were significantly worse in those with a poorer radiological outcome (Severin type III to V).

DISCUSSION

Avascular necrosis, as a complication of treatment of DDH, may lead to early osteoarthritis of the hip. Our results show that following open reduction of the hip through the medial approach, more than half of the hips (53%) showed some epiphyseal abnormality; 19% of hips developed significant AVN with proximal growth disturbance. In general, the rate of AVN is exponential to the severity of the dislocation and the extent of the surgery. 5-10% could be considered acceptable but there is no outspoken number about this as there are too many variables contributing to AVN. Several studies have analyzed the rate of AVN using the medial approach, and previous authors have also questioned the safety of the

medial approach and the correlation with the rate of AVN (Table IV).[3,17-24] The reported rate of significant AVN (types II to IV) may be as high as 43%.[17,18] Other studies, however, have reported an acceptably low rate of AVN, which would render the medial approach safe for treating the dislocated hip.[19,20] Our results are well within the reported range of AVN.

Table IV. Previously reported outcomes after open reduction using a medial approach compared with the current study (AVN, avascular necrosis)

Author (year)	Hips(n)	Mean age at surgery, mths	Mean follow-up, yrs	Significant AVN, n (%)	Severin ≥ III, n (%)	Additional surgeries, n (%)
Castillo and Sherman[21] (1990)	26	19	7	4 (15)	7(27)	9(35)
Koizumi et al[17] (1996)	35	14	19.4	15(43)	19(54)	16(46)
Morcuende et al[18] (1997)	93	14	11	40(43)	27 (29)	16(17)
Konigsberg et al[3] (2003)	40	7.7	10.3	7(18)	9(23)	9(23)
Kiely et al[19] (2003)	49	12.3	6.8	3(6)	4(8)	11(22
Ucar et al[22] (2004)	44	10.7	19.8	8(18)	9 (21)	11(25)
Di Mascio et al[20] (2008)	24	4.8	4.9	0	3(13)	2 (8)
Okano et al[23] (2009)	45	14	16.4	13 (29)	27(53)	3(7)
Yamada et al [24] (2013)	115	8.5	20.3	32(28)	46(40)	74(64)
Current study (2016)	**58**	**6.3**	**12.7**	**11(19)**	**13(22)**	**13(22)**

Although all operations were performed by a single senior surgeon, whether the medial circumflex artery was always seen and preserved was not recorded in the operation notes. Therefore, we cannot comment on this aspect of the approach in relation to the presence of AVN. All the children were aged < 12 months at the time of surgery. We did not find any significant relationship between age (older or younger than six months) at the time of surgery and the development of AVN (p = 0.239). Some authors have reported a lower risk of AVN in younger patients.[18,21,23,25] Morcuende at al reported a higher rate of AVN when the child was aged over two years at the time of surgery, while there was no difference when the child was younger than this. [18] A recently published meta-analysis did not show any difference in the rate of AVN if the child was treated on before or after 12 months of age.[26] The relationship between the presence of an ossified nucleus and the development of AVN following open reduction is controversial. Segal et al have reported that the presence of an ossific nucleus at the time of reduction is protective against AVN.[4] We found that that the presence of an ossific nucleus did not influence the rate of development of AVN (p = 0.722). It has also been shown that abduction in a cast of > 60° is a risk factor for the development of AVN.[8,9,27] We were not able to show that immobilization of the reduced hip in a spica cast with > 60° of abduction increased the risk of AVN (p = 0.059). The study was,

however, limited by small numbers, by being retrospective, and by the fact that objective measurements of abduction were not made but only retrieved from operative reports

We found that 13 hips (22%) had a poor outcome, being Severin types III, IV, V, or VI at final follow-up of 12.7 years (4.6 to 20.8). This is comparable to previous studies, in which rates ranged from 8% to 54%, (Table IV). The median age at the time of reduction in those with a good outcome was 5.2 months (IQR 1.9 to 8.5) and the median age of those with a poor outcome was 8.6 months (IQR 5.2 to 12.0). An older age at the time of reduction has a significant negative effect on the radiological outcome (p = 0.047). A total of 13 hips (22%) also required further surgery. Those who required further surgery were older (8.7 months (IQR 7.3 to 10.1)) at the time of the initial surgery than those who did not (5.1 months (IQR 1.8 to 8.4)) (p = 0.002). These results confirm the importance of age in relation to outcome and need for secondary surgery in medial approach open reduction where eight months would be an acceptable upper age limit for this procedure. Di Mascio et al, Castillo and Sherman, and Okano et al also demonstrated the importance of young age for this approach.[20, 21, 23]

Persistent pain and difficulties with ADLs were related to a poor radiological outcome. AVN on its own was not related to poorer function (p > 0.248). However, significant AVN (i.e. types II to IV) was related to a subsequent proximal growth disturbance and a worse Severin classification. We found that residual dysplasia, without AVN, was also associated with a poor outcome. Most of the secondary operations were Salter osteotomies for residual dysplasia and were not related to the presence of AVN. The Severin classification becomes more reliable with increasing age, thus reassessment at maturity seems necessary for a more accurate evaluation.[14] The age at the time of final evaluation of the hips is a limitation of our study. The mean follow-up was 12.7 years (4.3 to 23.3), with some thus not having reached skeletal maturity. Proximal growth disturbance due to AVN will not appear until over the age of eight years. The results could alter when the younger patients reach maturity.[17,18,22] AVN may lead to loss of congruency of the hip.[28] The aims of all forms of treatment are a stable, well-centred hip with minimal residual dysplasia at maturity. As AVN is iatrogenic and a consequence of invasive treatment, future research should investigate the early detection of morphological changes due to AVN, in order to predict which hips will develop early deterioration.

In conclusion, we found in this retrospective cohort study that one in five children had a poor radiological outcome (Severin type III or more) at a mean follow-up of 12.7 years (4.6 to 20.8) after open hip reduction for DDH using a medial approach. The rate of AVN was 19%, similar to that in previous studies. The development of AVN was not related to the severity of the dislocation, the age at the time of surgery, the amount of abduction of

the hip during postoperative splintage, or the presence of an ossific nucleus at the time of surgery. While there was no association between poor outcome and development of AVN, children younger than 8.6 months at time of surgery had a better radiological outcome and needed fewer secondary procedures. One in five children had pain or limitations of ADLs, and these were significantly worse when there was persistent dysplasia, subluxation, or recurrent dislocation regardless of age.

REFERENCES

1. Sewell MD, Rosendahl K, Eastwood DM. Developmental dysplasia of the hip. BMJ 2009; 339: b4454
2. Hoellwarth JS, Kim YJ, Millis MB, et al. Medial versus anterior open reduction for developmental hip dislocation in age-matched patients. *J Pediatr Orthop* 2015;35:50-56.
3. Konigsberg DE, Karol LA, Colby S, O'Brien S. Results of medial open reduction of the hip in infants with developmental dislocation of the hip. *J Pediatr Orthop* 2003;23:1-9.
4. Segal LS, Boal DK, Borthwick L, et al. Avascular necrosis after treatment of DDH: the protective influence of the ossific nucleus. *J Pediatr Orthop* 1999;19:177-184.
5. Ludloff K. The open reduction of the congenital hip dislocation by an anterior incision. Am J Orthop Surg 1913; 10: 438.
6. Ferguson AB Jr. Primary open reduction of congenital dislocation of the hip using a median adductor approach. *J Bone Joint Surg [Am]* 1973;55-A:671-689.
7. Weinstein SL, Ponseti IV. Congenital dislocation of the hip. *J Bone Joint Surg [Am]* 1979;61-A:119-124.
8. Gardner ROE, Bradley CS, Howard A, et al. The incidence of avascular necrosis and the radiographic outcome following medial open reduction in children with developmental dysplasia of the hip: a systematic review. *Bone Joint J* 2014;96-B:279-286.
9. Akilapa O. The medial approach open reduction for developmental dysplasia of the hip: do the long-term outcomes validate this approach? A systematic review of the literature. *J Child Orthop* 2014;8:387-397.
10. Narayanan U, Mulpuri K, Sankar WN, et al. Reliability of a new radiographic classification for developmental dysplasia of the hip. *J Pediatr Orthop* 2015;35:478-484.
11. Roposch A, Wedge JH, Riedl G. Reliability of Bucholz and Ogden classification for osteonecrosis secondary to developmental dysplasia of the hip. *Clin Orthop Relat Res* 2012;470:3499-3505.
12. Wiberg G. Studies on dysplastic acetabula and congenital subluxation of the hip joint. *Acta Chir Scand* 1939;83(Suppl 58):53-68.
13. Fredensborg N. The CE angle of normal hips. *Acta Orthop Scand* 1976;47:403-405.
14. Ali AM, Angliss R, Fujii G, Smith DM, Benson MK. Reliability of the Severin classification in the assessment of developmental dysplasia of the hip. *J Pediatr Orthop B* 2001;10:293-297.
15. Daltroy LH, Liang MH, Fossel AH, Goldberg MJ. The POSNA pediatric musculoskeletal functional health questionnaire: report on reliability, validity, and sensitivity to change. Pediatric Outcomes Instrument Development Group. Pediatric Orthopaedic Society of North America. *J Pediatr Orthop* 1998;18:561-571.
16. van der Holst M, Vlieland TP, van de Sande MA, et al. Translation and adaptation of the Pediatric Outcome Data Collecting Instrument (PODCI) into the Dutch language and preliminary validation in children with Neonatal Brachial Plexus Palsy. *J Pediatr Rehabil Med* 2015;8:219-226.
17. Koizumi W, Moriya H, Tsuchiya K, et al. Ludloff's medial approach for open reduction of congenital dislocation of the hip. A 20-year follow-up. *J Bone Joint Surg [Br]* 1996;78-B:924–929.
18. Morcuende JA, Meyer MD, Dolan LA, Weinstein SL. Long-term outcome after open reduction through an anteromedial approach for congenital dislocation of the hip. *J Bone Joint Surg [Am]*

1997;79-A:810–817.

19. Kiely N, Younis U, Day JB, Meadows TM. The Ferguson medial approach for open reduction of developmental dysplasia of the hip. A clinical and radiological review of 49 hips. *J Bone Joint Surg [Br]* 2004;86-B:430-433.
20. Di Mascio L, Carey-Smith R, Tucker K. Open reduction of developmental hip dysplasia using a medial approach. *Acta Orthop Belg* 2008;74:343-348.
21. Castillo R, Sherman FC. Medial adductor open reduction for congenital dislocation of the hip. *J Pediatr Orthop* 1990;10:335-340.
22. Ucar DH, Isiklar ZU, Stanitski CL, Kandemir U, Tumer Y. Open reduction through a medial approach in developmental dislocation of the hip: a follow-up study to skeletal maturity. *J Pediatr Orthop* 2004;24:493–500.
23. Okano K, Yamada K, Takahashi K, et al. Long-term outcome of Ludloff's medial approach for open reduction of developmental dislocation of the hip in relation to the age at operation. *Int Orthop* 2009;33:1391-1396.
24. Yamada K, Mihara H, Fujii H, Hachiya M. A long-term follow-up study of open reduction using Ludloff's approach for congenital or developmental dislocation of the hip. *Bone Joint Res* 2014;3:1-6.
25. Holman J, Carroll KL, Murray KA, Macleod LM, Roach JW. Long-term follow-up of open reduction surgery for developmental dislocation of the hip. *J Pediatr Orthop* 2012;32:121-124.
26. Novais EN, Hill MK, Carry PM, Heyn PC. Is age or surgical approach associated with osteonecrosis in patients with Developmental Dysplasia of the Hip? A meta-analysis. *Clin Orthop Relat Res* 2016;474:1166-1177.
27. Bache CE, Graham HK, Dickens DR, et al. Ligamentum teres tenodesis in medial approach open reduction for developmental dislocation of the hip. *J Pediatr Orthop* 2008;28:607-613.
28. Wedge JH, Kelly SP. Strategies to improve outcomes from operative childhood management of DDH. *Orthop Clin North Am* 2012;43:291-299.

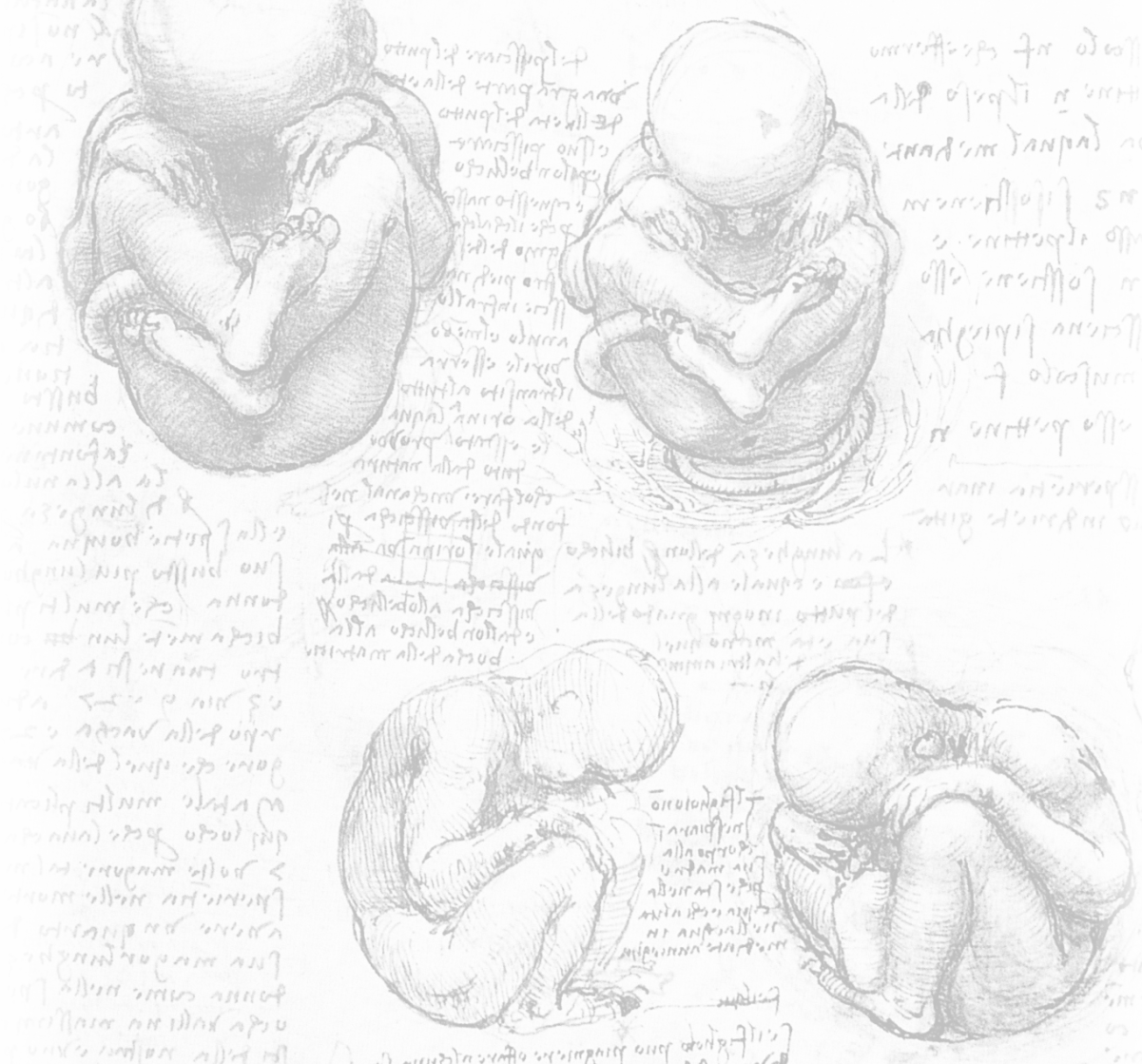
6

CHAPTER 7

Morphological variants to predict outcome of avascular necrosis in developmental dysplasia of the hip.

V. Pollet, J. Bonsel, B. Ganzeboom, R. Sakkers, J. Waarsing

Accepted Bone Joint J (2020)



ABSTRACT

Purpose

The most important complication of treatment of developmental dysplasia of the hip (DDH) is avascular necrosis (AVN) of the femoral head. Consequently, proximal femoral growth disturbances can cause pain and dysfunction and eventually lead to early onset osteoarthritis. We aimed to identify morphological variants in hip joint development that are predictive for poor outcome.

Methods

Patients who developed AVN after DDH treatment (closed and/or open reduction) in a single institution between 1984 and 2007 with a minimal follow-up of 8 years were retrospectively included. Standard Pelvis X-rays obtained at one, two, three, five and eight years of age and at latest follow-up were retrieved. The Bucholz-Ogden classification was used to determine the type of AVN on all X-rays. Poor outcome was defined by Severin classification Grade 3 or above on latest follow-up X-rays and/or the need for secondary surgery. With Statistical Shape Modeling (SSM) we identified the different shape variants of the hip at each age. Logistic regression analysis was used to associate the different modes or shape variants with poor outcome.

Results

One hundred thirty-five patients with AVN were identified with sufficient follow-up. Mean age at time of surgery was 7.0 ± 0.45 months. Mean follow-up was 13.3 ± 3.7 years. Forty-six percent had AVN type 1 while 54% type 2 or higher. More than half of the patients (52.6%) had a poor outcome. We found 11 shape variants that were significant associated to poor outcome. These shape variants were predominantly linked to AVN type 2 or higher.

Conclusion

Specific morphological characteristics on pelvis X-rays of AVN hips were predictive for poor outcome, already at a very young age. There was an overall stronger association to Bucholz-Ogden type 2-3-4 with the exception of two modes at age 2 and 5, linked to AVN type 1.

INTRODUCTION

Avascular necrosis (AVN) is a common complication in treatment of Developmental Dysplasia of the Hip (DDH). The incidence of AVN after closed or open hip reposition varies between 0-28% and 4-66% respectively. [1,2] The (temporary) lack of blood supply during the manipulation of the hip joint will cause growth disturbance of the epiphysis, physis and/or metaphysis. This will alter the normal hip morphology. The existing classifications of AVN type, such as Bucholz-Ogden classification, mainly describe the abnormal hip joint morphology but have limited prognostic value. [3,4] In particular type 2 AVN, the coxa valga does not present till after 5 to 8 years of age, when the acetabulum is almost fully developed, leaving minimal remaining hip remodeling. [3,5,6] Furthermore, the inter- and intra-reliability is poor to moderate. [5,7,8] The Severin classification is widely used to grade the outcome of a dysplastic hip on a pelvis X-ray combining radiographic measurement (Center-Edge (CE) angle of Wiberg) for residual dysplasia and morphological characteristics describing changes to the femoral head and acetabulum. Grade 1 and 2 are considered a good outcome, while grade 3 and above as poor. The extent of the damage and the subsequent growth disturbance of the hip resulting from AVN are directly correlated to a poor outcome. To improve hip remodeling and outcome at skeletal maturity, early intervention aims at restoring hip joint congruency. Roposch et al. compared the rate of acetabular remodeling in hips complicated with AVN compared to hips without signs of osteonecrosis in the same cohort of patients treated for DDH. [9] The acetabular index (AI) improved at a significant slower rate for the hips with AVN. ($p < 0.001$) A comparative small sample size study by Bar-On et al showed indeed that early pelvic osteotomy (between 5 and 10 years after index surgery causing AVN) improved the radiographic outcome and hip function. [10] Mahieu et al studied the inter-shape correspondence of the femoral shape using Statistical Shape Modeling (SSM) on CT scans of 40 dysplastic hips in adults compared to 43 normal hips. [11] Increase in acetabular dysplasia (low CE-angle) was reflected in proximal femoral morphology changes, including shortening of the femoral neck and flattening of the head. Although their study was cross-sectional, they suggested that adequate acetabular coverage would contribute to better (radiographic) outcome in adult life. In absence of predictive value of current classification systems for AVN and outcome, we hypothesized that certain hip morphologies can predict the outcome of AVN. We conducted a retrospective cohort study using SSM to identify shape variants in AVN hips that were positively correlated to poor Severin outcome at different ages during growth. Furthermore, we studied the correlation between the Bucholz-Ogden classification and the identified morphological shape variants.

METHODS

Study population

Following ethical approval from the institutional review board, all patients treated at a single institution between 1984 and 2007 for Developmental Dysplasia of the hip were identified. Patients older than 24 months at time of treatment, less than 7 years follow-up, teratological dislocation, neuromuscular co-morbidity and incomplete/missing data were excluded. Patients' characteristics and type of treatment were collected. Radiographic reports and images were revised by two trained medical students for any signs of AVN according to the classification by Bucholz-Ogden. [3,8] Debatable cases were discussed with a pediatric orthopedic surgeon.

Radiographic assessment

After patient inclusion, conventional radiographs of the pelvis at ages 1, 2, 3, 5, 8 and latest follow-up were reviewed and graded according to Bucholz-Ogden classification. Physical radiographs were digitalized using the VIDAR Film Digitizer (Vidar Systems Corporation, USA). Bucholz-Ogden classification consists of 4 Types depending on the location of the damage to the proximal femur: Type 1, epiphyseal changes; Type 2, lateral physeal/metaphyseal changes; Type 3, complete physeal/metaphyseal changes; Type 4, medial physeal/metaphyseal changes. [3] As the hip develops, AVN grade can change over time, especially type 1 at early age can become a higher grade or remodel to a normal joint. We considered the latest follow-up radiographs, as representative of the grade for AVN. In case of bilateral AVN, one hip was selected using a random number generator with 1 for the right hip and 2 for the left hip.

To classify the outcome, grading of the latest Follow-up pelvis radiograph according to Severin classification was assessed. Severin classification is based on a combination of CE-angle and morphologic dysplastic description of the proximal femur. A grade higher or equal to 3 is considered a poor outcome. [12] Since surgeries changing the hip joint morphology, such as pelvis or femoral osteotomies, are performed when a poor outcome is expected, we defined a "poor outcome", as Severin score ≥3 or the need for shape correction surgery. Severin type ≤ 2 without the need of secondary surgery was rated as a good outcome.

Statistical Shape Model (SSM)

To analyze the shape of the AVN hips on radiographs, the Active Shape Tool Kit (Manchester University, Manchester) was used to construct the SSM of the hips. [13,14,15] With SSM, the variation of anatomical shapes is mathematically modeled. We placed important identifiable points to delineate the outline of the femur and the pelvis to describe the shape. Using Principal Component Analysis, the set of outline points was decomposed into a set of principal components or modes. The modes were ranked according to the amount of variance in shape they described. Thus, each mode represents a specific shape variant present in the population. [15] The modes explaining 80% of the variation in the study population were analyzed.

An incremental number of landmarks, with increasing age and growth of the patients, was applied (age 1: 79 landmarks; age 2: 88 landmarks; age 3: 98 landmarks; age 5 and 8: 101 landmarks), 5 different shape models were created. (Fig 1) Two trained medical students (JB and BG) applied these shape models to each radiograph at the corresponding age. An inter-observer reliability at each age was assessed by comparing modes of each SSM of a subset of 16 hip radiographs. The Interclass Correlation Coefficient (ICC) proved to be good to excellent.

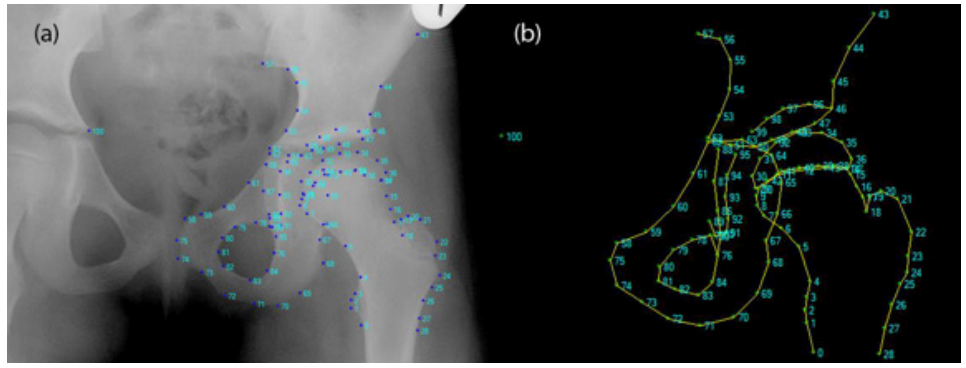


Fig 1. Illustration of the point set of year 8 (a), which subsequently form the shape model of year 8 (b)

Statistical analysis

The association between the various shape modes and the outcome was tested using logistic regression analysis. P-value of less than 0.05 was considered significant.

For the primary analysis, a mode was considered predictive of poor outcome if the association with the combined outcome was significant. For each mode, the Odds-Ratio (ORs) with 95% confidence intervals (95%CI) for the outcome was calculated. To assess whether the found associations were not due to surgery only, we performed a sensitivity analysis by recalculating the ORs for the predictive modes in the group without secondary surgery. Secondary analysis studied the association between the identified predictive modes and the outcome stratified for the grades of AVN. Type 2, 3 and 4 were combined, as the incidence of type 3 and 4 are low. These calculated ORs (95% CI) indicate whether a mode has a comparable or different predictive value in type 1 or type 2-4.

RESULTS

Characteristics of the study population

We identified 174 patients with signs of AVN on pelvis X-rays out of 495 patients treated for DDH between 1984 and 2007 in our hospital. Thirty-nine patients were excluded due to insufficient follow-up, missing data or no clear consensus on AVN presence. Patient characteristics of the remaining 135 patients are summarized in Table 1.

Table 1. Patient characteristics. Avascular necrosis (AVN) classification according to Bucholz-Ogden.
* Secondary surgeries unknown in 6 cases.

Gender	
female (n (%))	122 (90.4%)
male (n (%))	13 (9.6%)
Age at 1st reposition (y (SD))*	0.7 (0.45)
closed (n (%))	72 (53.3%)
open (n(%))	57(42.2%)
Number of repositions*	
successful first reposition	96 (71.1%)
second reposition	33 (24.4%)
Age at latest F/U (y (SD))	13.1 (3.9)
Type of AVN at last FU (n (%))	
Type 1	60 (44.4%)
Type 2	38 (28.1%)
Type 3	18 (13.3%)
Type 4	19 (14.1%)

Overall, at latest follow-up, 56 hips (41.5%) were treated with pelvic and/or femoral osteotomy after the moment of the open or closed hip reposition surgery. Overall, 88 (65%) hips had a good outcome according to Severin classification (Grade ≤ 2). This outcome decreased to 47% (64 hips) when we applied the combined outcome with 71 hips (53%) rated as poor. Seventy-two percent (14/18 hips) of the AVN type 3 hips received secondary surgery. Interestingly, despite having classified 60 hips as type 1 AVN, 32 hips (53%) had a poor outcome in this group, mainly due to need for secondary surgery.

Shape modes

Eight shape variants per age described 80% of the variation in shape. Furthermore, we identified 11 modes of shape variation significantly associated with a poor combined outcome. The first mode, representing the largest amount of shape variance, was significantly associated to the outcome in each age specific model, with exception of the model of age two. The relevant modes and association with poor outcome defined by OR, p-value and 95% CI are depicted in Table 2. When ORs were recalculated only for the group of hips without secondary surgery (n= 79), as part of a sensitivity analysis looking at the effect of secondary surgery, the ORs were similar for the majority of the modes. The modes at age 1 and 8 showed an increased association. Figure 2 subsequently shows the outlines of some of the identified shape variants at age 1, 3, 5 and 8.

Table 2. Relevant modes and adjusted association on the "combined outcome".
(OR= Odds Ratio; CI = Confidence Interval)

	OR	p-value	95% CI
Age 1 mode 1	2.28	0.01	1.22; 4.29
Age 1 mode 7	1.91	0.05	1.02; 3.61
Age 1 mode 8	0.47	0.03	0.24; 0.92
Age 2 mode 6	0.54	0.02	0.32; 0.91
Age 3 mode 1	2.22	0.01	1.21; 4.06
Age 5 mode 1	2.20	0.02	1.16; 4.18
Age 5 mode 2	0.51	0.05	0.27; 0.99
Age 5 mode 8	0.50	0.03	0.27; 0.93
Age 8 mode 1	0.35	0.01	0.16; 0.73
Age 8 mode 2	2.76	0.01	1.31; 5.82
Age 8 mode 8	1.76	0.05	1.01; 3.06

Morphological characteristics of the most relevant modes are delayed ossification and lateralization in mode 1 of age 1, a flattened femoral epiphysis, shortened femoral neck and small major trochanter with some overgrowth in mode 1 at age 3, 5 and 8.

In a secondary analysis, we repeated the calculations for the identified significant modes after stratification for type of AVN. Type 1 AVN hips (n = 60) were separately assessed from the type 2-3-4 AVN hips (n = 75). Due to high correlation between the type of reduction and number of reductions in type 1 hips, we removed the number of reductions variable out of the model in the stratified analysis. The ORs were similar to the overall primary analysis for most of the modes. Mode 6 at age 2 and Mode 2 at age 5 were more strongly associated to poor outcome in AVN type 1 hips than type 2-3-4 hips, while Mode 1 at age 1-8, Mode 8 at age 5 were associated to poor outcome in AVN type 2-3-4. (Table 3)

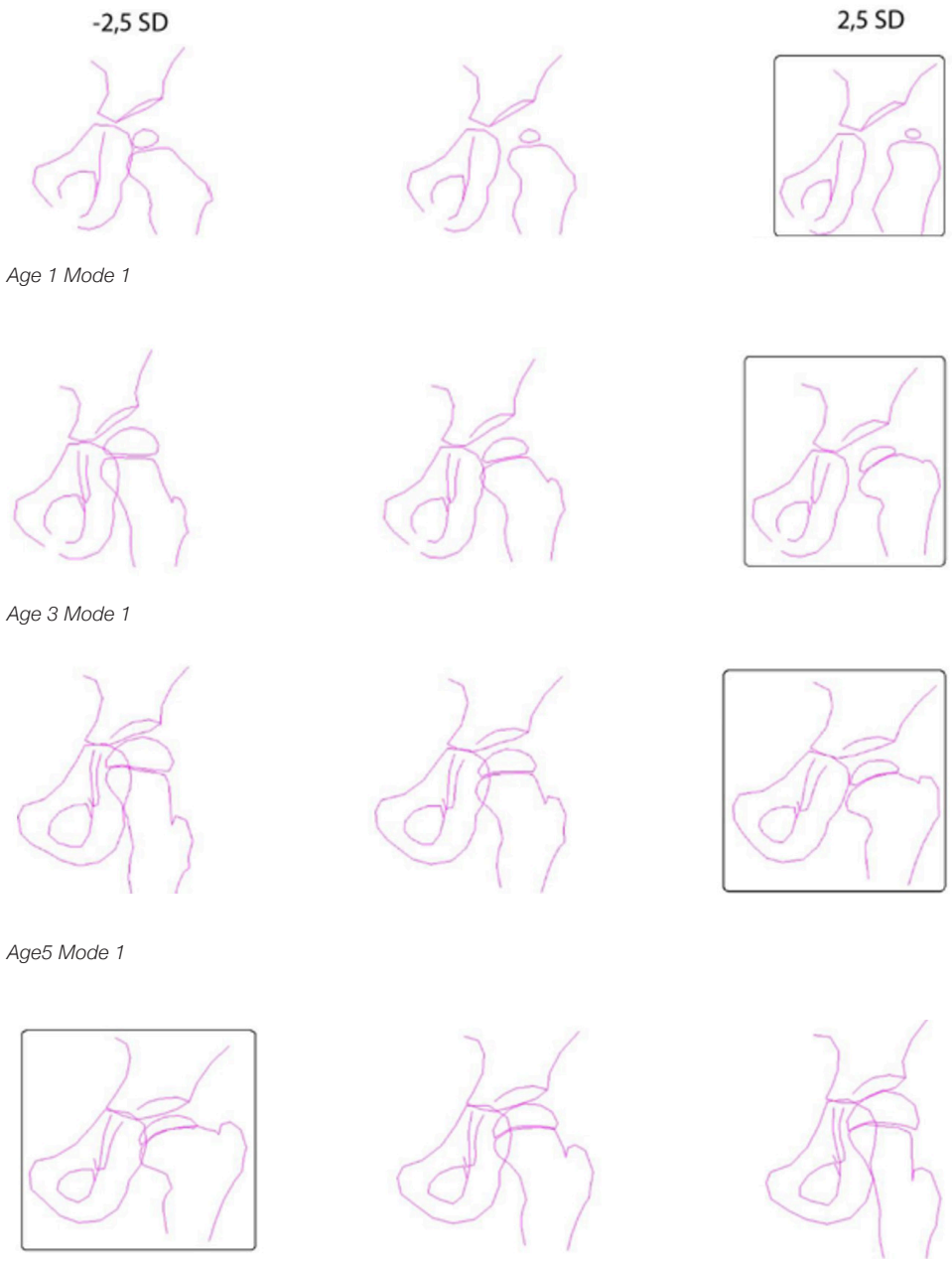


Fig 2. Examples at Age 1, 3, 5 and 8 of outlines of the modes: the center outline represents the mean. The variation in the studied sample is represented by the outer outlines (+/- 2.5 SD). The shape associated with a poor outcome is visualized in the boxed outline.

Table 3. Significant modes for AVN grade 1 versus 2-3-4. (*the model became unstable due to collinearity problems involving mode 2)

	Type 1			Type 2-3-4		
	OR	95%CI	p-value	OR	95%CI	p-value
Age 1 mode 1	1,28	0.4; 4.95	0.68	2.50	1.17; 5.32	0.02
Age 1 mode 7	1.73	0.42; 7.15	0.45	2.17	0.97; 4.88	0.61
Age 1 mode 8	0.52	0.16; 1.7	0.28	0.74	0.39; 1.39	0.34
Age 2 mode 6	0.16	0.02; 1.18	0.07	0.59	0.29; 1.12	0.15
Age 3 mode 1	2.00	0.35; 11.38	0.44	2.12	1.15; 3.93	0.02
Age 5 mode 1	2.77	0.52; 14.84	0.24	2.56	1.24; 5.24	0.01
Age 5 mode 2	0.16	0.03; 0.76	0.02	0.53	0.24; 1.16	0.11
Age 5 mode 8	1.20	0.31; 4.58	0.79	0.41	0.18; 0.96	0.04
Age 8 mode 1	0.72	0.15; 3.51	0.69	0.38	0.17; 0.83	0.02
Age 8 mode 2	293*	0.2; 420497*	0.13	2.55	1.09; 5.95	0.03
Age 8 mode 8	0.96	0.41; 2.23	0.93	1.76	0.89; 3.50	0.10

DISCUSSION

Classifications of AVN hips are mainly describing growth disturbances but fail to give any prognostic value. [16] Therefore, our study is of great interest as we identified specific morphological characteristics as prediction of outcome. Eleven shape variants of AVN hips were linked with poor outcome using Statistical Shape Modeling. At all ages, except for age 2, the first mode, which described the largest variation in shape, was significantly associated with a poor outcome.

Mode 1 and 8 at age 1 show characteristics of delayed ossification and lateralization, consistent with persistent subluxation and fragmented ossification of the nucleus. On the other hand, Mode 7 at age 1 and Mode 6 at age 2 outline epiphyseal overgrowth (coxa magna). These changes are often seen on X-rays within the first two years of closed or open reposition and have the potential to remodel over time. Furthermore, they are consistent with residual subluxation and incongruent joint with the potential to progress into re-dislocation (or to normalize) rather than growth disturbance.

Interestingly, Mode 1 at age 3, 5 and 8 all showed similar features of shortened femoral neck, flattened epiphysis and short greater trochanter at the level of the epiphysis (coxa breva et plana). This is an important finding as, already at age 3, we can identify the shape variant predictive for poor outcome, the same changes we find at age 5 and age 8. The clinical implication of early detection means that preventive shape modifying surgery could already be performed at a young age.

Furthermore, Mode 2 at age 5 and 8 was characterized by coxa valga and some degree of lateralization. This supports the clinical observation that AVN type 2 (lateral physeal arrest with progressive development of coxa valga) is often not present before 5 years of age.

Separating type 1 AVN hips from type 2-3-4, showed some different shape variants associated with AVN type 1 compared to AVN type 2 or higher. The two morphological outlines more likely to be seen with AVN type 1 that are of interest are Mode 6 at age 2 and Mode 2 at age 5. Mode 6 at age 2 shows features of coxa magna, a result of epiphyseal growth disturbance. As we found a high rate of poor outcome in the AVN type 1 group - contrarily to the general belief AVN type 1 will remodel, we wonder if the current classification of Bucholz-Ogden is maybe missing a type of AVN or requires a subtype of AVN type 1 hips? Kruczynski described 5 grades of AVN as he subdivided Bucholz-Ogden Grade 1 into type 1 and 2, both describing epiphyseal involvement, with type 1 showing minimal changes and no fragmentation compared to type 2 representing moderate changes with fragmentation of the epiphysis. Especially when he measured the sphericity using the Mose rings, he noticed the difference was most visible at a young age of 4 to 6 years, similar to our finding of coxa magna as a subtype of AVN linked to poor outcome. On the other hand, Mode 2 at age 5 represents a coxa valga with some lateralization. Not all hips with AVN type 1 will remodel fully and we have noticed while reviewing all X-rays at different ages, some hips will develop into a type 2 around 5 years of age. This could be a possible explanation for the coxa valga outline at age 5. For AVN type 2, 3 and 4, a coxa breva et plana with some trochanter overgrowth were associated shape variants of Mode 1 at all ages except for year 2.

Early intervention with shape improving surgery, such as acetabuloplasty, could lead to better outcome. Roposh et al concluded that acetabular development is slower in hips with AVN. [9] A subgroup analysis of their results, although somewhat limited due to low sample size, showed that type 2 and type 3 of Bucholz-Ogden classification were the most affected with slow acetabular index improvement. These hips are characterized by morphological changes of coxa breva with flattened femoral head (type 3) and coxa valga with decreased acetabular coverage (type 2). Coxa breva (et plana) and coxa valga are two shape variants that we have found associated with poor outcome already at a young age of 3. Combining our results with the finding of slower acetabular improvement by Roposh et al could justify the argument for early surgical intervention. Our study has some limitations. We used a combined outcome score in order to take “shape influencing” surgery into consideration as this will affect the outcome. The choice of secondary surgery was based not on protocol but surgeon’s decision. This may have impacted our Severin score. Furthermore, Severin classification is limited as a measure for outcome after DDH treatment, as this is a scoring system for hip dysplasia. Unfortunately, there is no specific outcome score for AVN hips in DDH treatment, which ideally measures the shape of the femoral head (sphericity), the relation of the femoral neck to the shaft/ head and assesses the congruency of the joint beyond the acetabular dysplasia (CE-angle).

Previous studies demonstrated that avascular necrosis in DDH has a 20% poor outcome based on radiographic criteria and self-reported measures. [17] Unfortunately, AVN develops over time and can’t be identified during primary surgery of closed or open reduction. Signs of morphological changes linked to poor outcome, as detected by SSM, can help with early recognition of the hips that are at risk of failing. Surgeries, such as guided growth, acetabuloplasty or proximal femoral osteotomies, have all been described improving joint congruency and stability. [10,18] Consequently, this can lead to an improved hip function at skeletal maturity. Long-term follow-up prospective studies combining identification of AVN hips using SSM and early surgical intervention can lead to a better understanding of the best timing of surgery in relation to outcome.

CONCLUSION

Specific morphological characteristics on pelvis X-rays of DDH hips with AVN were identified by SSM. While at 1 year the modes are morphologically consistent with subluxation rather than growth disturbance, already at the age of 3, shape variants predictive for poor outcome, similar to age 5 and 8, can be identified. There was a stronger association within Bucholz-Ogden type 2-3-4. This early recognition can help to decide on indication for shape influencing intervention to modify the outcome.

7

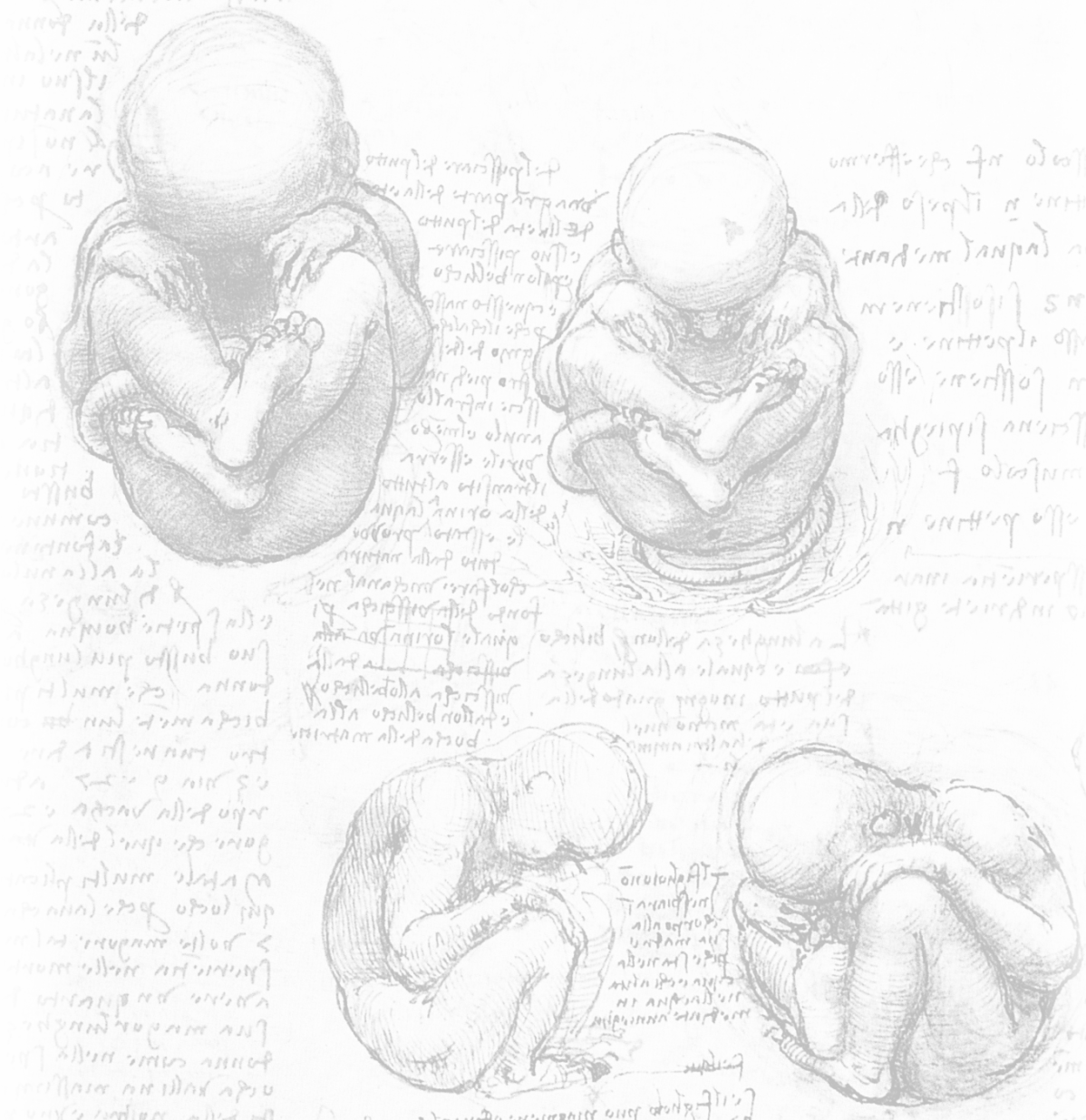
REFERENCES

1. Gulati V, Eseonu K, Sayani J, Ismail N, Uzoigwe C, Choudhury MZ, et al. Developmental dysplasia of the hip in the newborn: A systematic review. World J Orthop. 2013;4(2):32-41
2. Wang YJ, Yang F, Wu QJ, Pan SN, Li LY. Association between open or closed reduction and avascular necrosis in developmental dysplasia of the hip: A PRISMA-compliant meta-analysis of observational studies. Medicine (Baltimore). 2016;95(29):e4276
3. Bucholz RW OJ. Patterns of ischemic necrosis of the proximal femur in nonoperatively treated congenital hip disease in the hip. Proc 6th Open Scientific Meeting of the Hip Society. 1978;Volume 2:43-63.
4. Kalamchi A, MacEwen GD. Avascular necrosis following treatment of congenital dislocation of the hip. J Bone Joint Surg Am. 1980;62(6):876-88
5. Gardner RO, Bradley CS, Howard A, Narayanan UG, Wedge JH, Kelley SP. The incidence of avascular necrosis and the radiographic outcome following medial open reduction in children with developmental dysplasia of the hip: a systematic review. Bone Joint J. 2014;96-B(2):279-86.
6. Morcuende JA, Meyer MD, Dolan LA, Weinstein SL. Long-term outcome after open reduction through an anteromedial approach for congenital dislocation of the hip. J Bone Joint Surg Am. 1997;79(6):810-7
7. Roposch A, Liu LQ, Offiah AC, Wedge JH. Functional outcomes in children with osteonecrosis secondary to treatment of developmental dysplasia of the hip. J Bone Joint Surg Am. 2011;93(24):e145.
8. Roposch A, Wedge JH, Riedl G. Reliability of Bucholz and Ogden classification for osteonecrosis secondary to developmental dysplasia of the hip. Clin Orthop Relat Res. 2012;470(12):3499-505.
9. Roposch A, Ridout D, Protopapa E, Nicolaou N, Gelfer Y. Osteonecrosis complicating developmental dysplasia of the hip compromises subsequent acetabular remodeling. Clin Orthop Relat Res. 2013;471(7):2318-26.
10. Bar-On E, Huo MH, DeLuca PA. Early innominate osteotomy as a treatment for avascular necrosis complicating developmental hip dysplasia. J Pediatr Orthop B. 1997;6(2):138-45.
11. Mahieu P, Hananouchi T, Watanabe N, Claes P, Li H, Audenaert E. Morphological abnormalities of the femur in the dysplastic hip. Relation between femur and acetabulum. Act Orthop Belg. 2018; 84 (3): 307-315.
12. Kruczynski J. Avascular necrosis after nonoperative treatment of developmental hips dislocation: Prognosis in 36 patients followed 17-26 years. Acto Orthop. 1995; 66(#):239-244.
13. Agricola R, Leyland KM, Bierma-Zeinstra SM, Thomas GE, Emans PJ, Spector TD, et al. Validation of statistical shape modelling to predict hip osteoarthritis in females: data from two prospective cohort studies (Cohort Hip and Cohort Knee and Chingford). Rheumatology (Oxford). 2015;54(11):2033-41.
14. Cootes TF, Taylor CJ. Anatomical Statistical models and the role in feature extraction. Br J Radiol 2004; 77; 2: S133-9
15. Stegeman MB, Gomez DD. A brief introduction to statistical shape analysis. Lecture note. 2002. Available at https://graphics.stanford.edu/courses/cs164-09-spring/Handouts/paper_shape_spaces_imm403.pdf
16. Luedtke L, Flynn J, Pill S. A Reveiw of avascular necrosis in developmental dysplasia of the hip and contemporary efforst at prevention. UPOJ. 2000;13:22-28.
17. Pollet V, Van Dijk L, Reijman M, Castelein RMC, Sakkers RJB. Long-term outcomes following the medial approach for open reduction of the hip in children with developmental dysplasia. Bone Joint J. 2018 Jun 1;100-B(6):822-827.
18. Agus H, Önvural B, Kazimoglu C, Reisoglu A, Kalenderer O. Medial percutaneous hemi-epiphysiodesis improves the valgus tilt of the femoral head in developmental dysplasia of the hip (DDH) Type II avascular necrosis. Acta Orthop. 2015; 86(4):506-510.

7

CHAPTER 8

General discussion, answers to the questions, future perspectives and conclusion



GENERAL DISCUSSION, ANSWERS TO QUESTIONS

Over the past decennia, many positive developments in diagnosis and treatment of DDH have led to improved outcome of this complex disease. Early detection of hip abnormalities with ultrasound, a change to a more dynamic treatment with the Pavlik harness and a better understanding of vascularity and subsequent growth disturbances are only a few examples. Nevertheless, a number of questions still remain unanswered. Interestingly, Sommerville wrote already in 1953: "*The development of congenital dislocation of the hip in one of those fascinating puzzles in orthopaedics in which the pieces are relatively complete but the picture which results presents some flaw, suggesting that minor adjustments here and there might give a better results"* [(1)] This sums up nicely what this thesis was aimed at: trying to improve the overall picture of DDH.

In **Chapter 2**, the incidence and risk factors of DDH in a multi-cultural population in the province of Manitoba, Canada, without universal screening was studied to help with creating screening guidelines. Using the Manitoba Centre for Health Policy's (MCHP) data repository, using ICD diagnosis codes and billing tariffs we identified 1716 cases out of 258 499 newborns between 1995 and 2012. The incidence was calculated at 6.6/1000 newborns and 2.2/1000 presented late (after 6 months). We identified increased Relative Risk for firstborn, female, breech birth and associated clubfoot. The age at diagnosis differed significantly for rural areas (12.3 months CI 95% 10. -14.0) compared to urban areas (6.4 months CI95% 4.9 - 7.8). Furthermore, diagnosis after walking age (i.e. 18 months) was almost 3x higher in rural areas compared to children who live in the cities. ($p<0.0001$) Manitoba has a large First Nation Cree-Ojibwa community of 15% of the total population of the province. This increases to 25% for the Interlake-Eastern to 75% in the Northern Regional Health Authorities (RHA). Although less frequently now, swaddling the child with the legs in extension on a cradle board is still a cultural custom often till 1 year of age. This is promoted by the harsh weather conditions in these regions where baby carriages are not an option. Our results showed a high incidence, especially of late presenting and in rural areas. Introduction of selective screening by clinical examination in combination with Ultrasound would decrease these numbers of late-presenting DDH and improve the overall outcome as we know Pavlik harness treatment in the first 6 months of life has a high success rate. Several countries have introduced screening tools that lead to decreased numbers of late DDH and fewer surgeries. A prospective study implementing a screening programme based on the identified risk factors and regions would be of interest to improve early detection of hip dysplasia.

In **Chapter 3**, a literature-based analysis of abnormal hip ultrasounds in children younger than 6 months of age was conducted as current screening tools lead to overtreatment due to the high sensitivity and low specificity of hip US. The aim was to identify and quantify those hips that will become normal over time in order to improve screening specificity. In a Pubmed search for "DDH and "ultrasound", all hips were identified that were abnormal on ultrasound and were left untreated. Data of 13 561 hips were collected and analysed. Normal development within the first 6 months in stable hips was 89-98% for Graf IIa, 80-100% for Graf IIc and 80 -97% in a clustered group of Graf IIa to IIC. Interestingly, more than 50% of Graf III hips were reported as normal over time but less so for Graf IV DDH. Normalization of Femoral Head Coverage (FHC) of less than 50% followed in 78 - 100%. There was not enough clinical information to extract why the dislocated hips were left untreated. These results show a high potential for abnormal US findings to have a benign course over time. This questions the ability of US screening to differentiate between benign natural history and relevant DDH.

In **Chapter 4**, we studied the effect of bracing over natural history of stable dysplastic hips in 3 to 4 month old infants, in a multi-center randomized trial. Patients were randomized to either Pavlik harness (n = 55) or active surveillance group (n = 49). The improvement of the bony roof angle, α, was the primary outcome was the degree of dysplasia at 12 weeks follow-up. Both groups showed a similar improvement with mean α-angle of 60.5° ±3.8° in the Pavlik group and 60.0°±5.6° in the active surveillance group. (p=0.30) Furthermore, analysis of secondary outcome (Acetabular Index (AI) as standard of care on Pelvis X-rays) showed no difference at age of 10 months and at walking age. Our findings are of importance as Pavlik harness treatment is current practice for Graf type IIb/IIc hips. We demonstrated that there was no added benefit of bracing in stable well-centered hips. Our results are in line with findings by Wood et al. and Rosendahl et al. [(2,3)] We found an overall improvement of α-angle of 5° over a period of 12 weeks. During the active surveillance period of 3 months(at 6 weeks follow-up), 3 patients (6.1%) were treated due to decrease of α-angle. At 12 weeks, 7 patients more patients needed treatment in the surveillance group but equally, 7 patients in the Pavlik harness group still showed dysplasia at 12 weeks. This is conforming the natural history presented in **chapter 3**, where 80% will have a benign course and don't need treatment. Ultrasound is not able to differentiate between the benign hip abnormality and true hip pathology leading to overtreatment. Our study showed active surveillance of well-centered stable dysplastic hips is justified rather than treatment.

After the age of 6 months, the conservative treatment of DDH with bracing becomes more challenging as the child develops and becomes more active. The aim of **chapter 5** was to study if there was still a place for abduction bracing in late DDH. We conducted a retrospective analysis of the success rate of abduction treatment in 24 patients (26 hips) with a mean age of 9 months (range 6-23 months) and average follow-up of 6.5 years (range 2-12 years). Twelve out of 26 hips (46%) were successfully reduced with an average time

to reduction of 4 weeks (range 2- 7 weeks). Fourteen hips (54%) of failed Pavlik harness treatment were reduced either with closed or open reduction. A current practice in our hospital was to add a rigid abduction brace once good flexion was achieved in the Pavlik harness to withstand the forces of adduction in these older children. There was no added value of this method as adding the brace didn't improve the chances of reduction (p = 0.57). This practice was abandoned after this study. Of the 17 hips that were diagnosed with US, 10 presented with a Graf type III and 7 with Graf type IV. Six out of 10 (60%) Graf type III hips had a successful reduction compared to none of the Graf type 4 hips (0%). (p = 0.035) None of the Graf type III hips were reduced after 6 weeks of treatment. We therefore recommend Pavlik harness treatment for late DDH, especially in Graf type III hips. The treatment should be abandoned if the hip is not reduced after 6 weeks. Graf type IV should probably be treated with closed/open reduction.

After failed closed reduction, open reduction will be the next step in the treatment for persistent hip dislocation. In **Chapter 6**, we studied the long-term outcome of the medial approach as described by Ludloff. The open reduction is linked with a high rate of AVN (8%-54%) and potentially poor results. We aimed at assessing the radiographic outcome and patient reported outcome with a minimal of 4 years follow-up. Of the 58 hips included, 31 hips showed signs of AVN post-operatively with 11 hips (19%) developing to Bucholz-Ogden type II-IV at latest follow-up. Poor outcome defined by Severin type III or higher was seen in 22%. The median age at time of surgery was 5.2 months(IQR 1.9 - 8.5) for Severin type I and II and was significant lower that in the poor outcome group, 8.6 months (IQR 5.2 - 12.0). (p = 0.047) The latter was also a significant predictive factor for the need for secondary surgery. (p = 000.2) To assess patient reported outcome, we used the PODCI and HOOS questionnaires depending on the patient's age. The response was 62% with 17 completed PODCI and 15 HOOS questionnaires. Surprisingly, there was no correlation between poor outcome and the presence of AVN. However, subscales for pain and global functioning for both questionnaires were worse in patients with poor Severin outcome. As Severin grades residual hip dysplasia, the loss of normal joint morphology/ congruency is more reflective of poor functional outcome rather than the type of AVN.

If the type of AVN cannot predict poor outcome, we hypothesized in **Chapter 7** that certain shapes of the hip joint should be more predictive. In order to identify these shapes, we used Statistical Shape Modeling (SSM) and linked the shape variants to poor outcome defined by Severin at latest follow-up (minimal 8 years). Standard X-rays at 1, 2, 3, 5 and 8 years of children who developed AVN after closed or open hip reduction in the Sophia Children's Hospital of the EMC between 1984 and 2007 were included. The Bucholz-Ogden classification was used to determine the presence and type of AVN. SSM models the variation of the anatomical model mathematically by outlining the femur and pelvis to describe the shape. We found 11 Modes of shape variation significantly associated with a poor outcome. Stratification for type of AVN was done in a secondary analysis, we found Mode 6 at age 2 and Mode 2 at age 5 more strongly associated to poor outcome in AVN type 1 hips while Mode 1 at age 1-8 and Mode 8 at age 5 were associated to AVN type 2-3-4. We described the morphologic characteristics of the identified modes as this could be useful to identify these abnormalities in hip development at a young age. This early recognition can help to decide on shape influencing surgery in order to improve the outcome.

FUTURE PERSPECTIVES

With this thesis, we have found some more pieces of the puzzle and improved the picture of DDH as quoted by Sommerville. However, still various questions remain unanswered and some new ones have arisen from this thesis.

Firstly, there is an urgent need for universal terminology to improve diagnostics and outcomes in DDH. Too often, several definitions are used across the literature. Taking the above into consideration and based on this thesis, DDH terminology should be based on the various causes of DDH, namely genetic dysplasia, mechanical fetal and post-natal postural dislocation as suggested by Avisse.[4] It would be of interest to explore this further and create a classification system for DDH combining etio-pathogenic, clinical and sonographic features as only by combining this 3 aspects of DDH, in relation to the child's age, will we be able to separate the benign abnormalities from the true/relevant hip pathologies. Table 1 provides an overview of a proposed differentiation of "positive" developmental hip dysplasia with a trend to normalization from "negative" developmental dysplasia that deteriorates if left untreated. Based on these criteria, further research should focus on establishing clinically workable definitions of DDH.

Table 1. Proposed differentiation of "developmental" aspect of hip dysplasia in "positive" and "negative" based on age, etio-pathogenesis and clinical/US findings.

BENIGN DYSPLASIA OF THE HIP (BDH) ("Positive" developmental)	TRUE DYSPLASIA OF THE HIP (TDH) ("Negative" developmental)
neonatal	any age
secondary	primary
external factors	genetic
biomechanical	family history
stable/dysplastic	unstable/dysplastic
immature	progressive
normalization	dislocation

Furthermore, ultrasound as diagnostic tool is valuable compared to clinical screening, as shown in chapter 2. Physical examination is very much examiner dependent and will miss DDH cases. However, US according to Graf as a screening tool has limitations and is highly sensitive leading to over-diagnosed hip abnormalities that will spontaneous improve over time without treatment. [5,6] The timing of diagnosis is also important as shown in chapter 3. Many ultrasound abnormalities in children younger than 6 months, will improve without treatment. Lussier et al concluded that screening newborns after 28 days improved accuracy.[7] Roposch et al. also showed the importance of aligning diagnostic practices as the consistency was overall poor, especially for ultrasonographic criteria.[8] Stability of the hip is the most important requirement for good acetabular growth. Hence, stability testing during ultrasound will allow for identification of those hips at risk of progression to dislocation. In spite of a universal accepted quantification of hip instability, FHC seems to be used most commonly. However, FHC requires several linear measurements and percentage calculation. There is some conflicting data in the literature on the cut-off value ranging between 33%-50%. Of interest is the study by Salut et al who assessed all females at 1 month of age measuring the pubo-femoral distance (PFD) or acetabular depth ('fond du cotyloïdien") as quantification of instability, defined by Couture and Tréguier et al. [9,10] The PFD is measured in supine position on the same dynamic lateral coronal view as the Harcke view for FHC. (Fig 1)

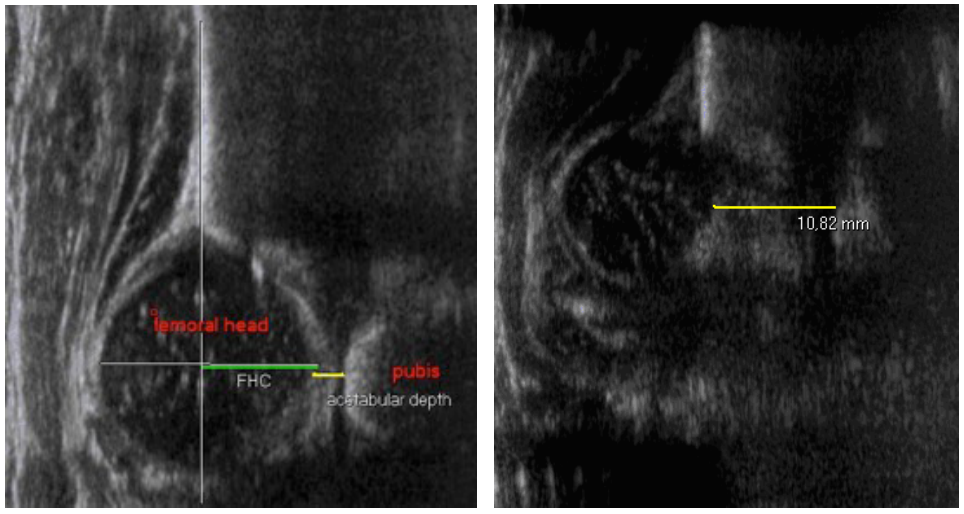


Fig 1. Measurement of femoral head coverage (FHC) and Pubo-femoral distance (Acetabular depth) on ultrasound in a normal hip (left); in a dislocated hip (right) with PFD > 6mm.

It is less prone to error as the accuracy of the plane is less relevant and only measures a distance between two points, namely the medial border of the epiphysis and the ossification of the nucleus of the pubic bone, easily identified on ultrasound. Normal PFD in stable hips is 4-5mm (with 6 mm being unstable) and a difference of less than 1.5 mm between both hips. There were no cases of late DDH, except for 2 boys with male gender being an exclusion criterion. In unpublished data presented during the IFPOS/POSNA meeting in 2013 by the author of this thesis, the reliability of this measurement showed the same moderate to good agreement as the femoral head coverage. Furthermore, single leg stress in supine position showed superior quantification of instability than simultaneously stress on both legs. More recently, Husum at al found a PFD value above 4.4mm as the cut-off value for hip instability, but in lateral position, with a sensitivity of 100% and specificity of 93%. The PFD is promising as a quick, highly sensitive and specific quantification tool for instability. Combining instability with hip morphology and acetabular dysplasia is a sine qua non in ultrasound screening and diagnostics. Further research should focus on quantification tools and algorithm identifying relevant abnormal hip morphology and instability on ultrasound.

Finally, the use of SSM to identify shape variants linked with poor outcome has also shown to be of interest in chapter 7. The unpredicted value of the current classification systems (with also poor to moderate reliability) for AVN and outcome, makes the decision for surgery at a young age difficult with often a wait-and-see policy, repeat X-rays and frequent clinic visits. [11,12,13,14,15] A prospective trial in a larger population identifying shapes linked with poor outcome and early surgical intervention with long-term follow-up would be the next step. The main challenge remains the growth of the child and thus the remodeling potential of the hip joint. Whitlock at al measured hip parameters in different age groups till skeletal maturity.[16] These values are of interest to quantify normal hip development and set goals for treatment of dysplastic hips. (Fig2)

Age group	Variables	Acetabular index (degrees ± SD)	Pelvic width index (ratio ± SD)	Lateral center edge angle (degrees ± SD)	Tönnis angle (degrees ± SD)	Acetabular -femoral head distance (mm ± SD)	Femoral head diameter (mm ± SD)
6 months-3 years (*n* = 30)	Combination	28.7 ± 4.8 (20-41)	0.51 ± 0.05 (0.41-0.64)	14.2 ± 5.2 (2-23)	22.5 ± 3.9 (13-30)	7.14 ± 1.22 (5.18-10.38)	13.9 ± 3.7 (7.4-22.3)
	Female	28.8 ± 4.1 (20-36)	0.52 ± 0.06 (0.41-0.64)	13.0 ± 5.5 (2-22)	22.6 ± 3.9 (13-30)	7.05 ± 1.22 (5.30-10.38)	14.0 ± 4.0 (7.4-22.3)
	Male	28.5 ± 5.53 (21-41)	0.51 ± 0.04 (0.43-0.60)	15.4 ± 4.7 (5-23)	22.3 ± 4.0 (14-29)	7.24 ± 1.23 (5.18-9.70)	13.7 ± 3.4 (8.2-21.9)
3-6 years (*n* = 30)	Combination	21.2 ± 3.7 (14-27)	0.53 ± 0.04 (0.46-0.60)	22.0 ± 4.7 (5-31)	14.2 ± 3.4 (8-23)	6.63 ± 1.36 (3.48-10.69)	25.0 ± 4.2 (17.2-32.9)
	Female	20.3 ± 3.8 (15-27)	0.54 ± 0.04 (0.47-0.60)	22.1 ± 5.1 (5-28)	13.5 ± 3.6 (8-23)	6.20 ± 1.29 (3.48-8.88)	24.8 ± 3.6 (20.5-31.4)
	Male	22.0 ± 3.4 (14-27)	0.51 ± 0.04 (0.46-0.60)	21.9 ± 4.3 (12-31)	15.0 ± 3.1 (11-21)	7.07 ± 1.30 (5.10-10.69)	25.2 ± 4.7 (17.2-32.9)
6-10 years (*n* = 40)	Combination	17.5 ± 3.4 (9-24)	0.53 ± 0.03 (0.46-0.64)	23.4 ± 4.4 (13-33)	11.9 ± 3.0 (4-17)	6.80 ± 1.26 (4.82-11.28)	35.5 ± 5.4 (24.2-48.4)
	Female	17.6 ± 3.5 (9-24)	0.53 ± 0.04 (0.46-0.64)	23.5 ± 4.8 (13-33)	11.9 ± 3.3 (4-17)	6.53 ± 0.95 (4.86-9.35)	35.3 ± 4.0 (26.1-41.4)
	Male	17.4 ± 3.3 (10-23)	0.53 ± 0.03 (0.47-0.60)	23.3 ± 4.0 (15-32)	12.0 ±2.7 (7-17)	7.07 ± 1.48 (4.82-11.28)	35.7 ± 6.5 (24.2-48.4)
10-13 years (*n* = 30)	Combination	43.6 ± 4.0 (35-53)	0.50 ± 0.04 (0.43-0.57)	24.5 ± 5.2 (12-36)	9.4 ± 4.2 (2-21)	7.20 ± 1.09 (5.10-10.35)	41.7 ± 4.1 (33.1-52.2)
	Female	44.6 ± 4.7 (35-53)	0.51 ± 0.04 (0.42-0.57)	24.1 ± 5.0 (15-32)	10.1 ± 5.2 (2-21)	7.08 ± 1.04 (5.10-9.78)	39.8 ± 3.8 (33.1-46.2)
	Male	42.6 ± 3.0 (37-49)	0.49 ± 0.03 (0.42-0.53)	24.9 ± 5.3 (12-36)	8.7 ± 2.9 (3-15)	7.32 ± 1.14 (5.50-10.35)	43.5 ± 3.4 (37.8-52.2)
13-16 years (*n* = 28)	Combination	46.1 ± 4.6 (36-56)	0.53 ± 0.05 (0.43-0.67)	28.3 ± 6.3 (15-47)	10.4 ± 4.2 (3-22)	7.95 ± 1.42 (5.50-12.50)	45.2 ± 4.5 (35.1-51.2)
	Female	47.0 ± 3.9 (41-56)	0.56 ± 0.04 (0.50-0.67)	27.6 ± 5.3 (16-40)	10.2 ± 3.9 (3-20)	7.70 ± 1.39 (5.50-10.80)	43.1 ± 4.3 (35.1-51.2)
	Male	45.4 ± 5.0 (34-54)	0.51 ± 0.04 (0.43-0.61)	28.8 ± 6.9 (15-47)	10.5 ± 4.4 (5-22)	8.14 ± 1.44 (5.70-12.50)	46.7 ± 4.0 (39.0-53.9)

Fig 2. Standardized values for continuous hip parameters during growth.
(ref: Whitlock P, Salari K, Blumstein G, Zhang B, Arkader A, Choi P. Reliability and normative values of common adult radiographic parameters for hip preservation in the developing pelvis. J Hip Preserv Surg 2019; 6(3): 189-198.)

However, DDH is a 3-Dimensional (3-D) deformity with both acetabular and femoral dysplasia, where X-rays merely describes the contours of the bony joint. MRI scan as pre-operative planning has proven to be useful in decision-making process for surgery. [17] Quantification of both bony and cartilage deficiencies, as the latter will be missed on X-rays, allows the surgeon to decide in favor or not of surgery. Figure 3 shows a schematic representation of the MRI images with assessment of the position of the labrum in relation to the femoral head.

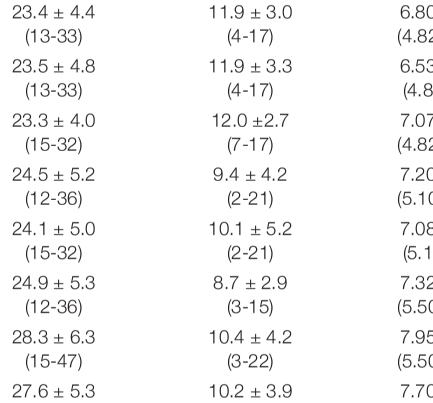


Fig 3. Measurement of labral angle (LA). LA is defined as the angle that the labrum makes with the acetabulum (that is, with the line that is used for measurement of acetabular index [AI]). Line A is the midline of the labrum: that is, it passes through a point midway between the outer and inner attachment points of the labrum (points B and C) and the distal apex of the labrum. Line H is Hilgenreiner's line. The figure shows a dysplastic hip in neutral; such hips have LA values that are high in neutral and low in abduction
(ref: Kim HT, Kim IB, Lee JS. MR-based parameters as a supplement to radiographs in managing Developmental Dysplasia of the hip. Clin Orthop Surg 2011; 3: 202 - 210.)

Combining normative values on X-rays as reference during growth with MRI findings quantified by SSM, would allow to study the bony and cartilage coverage and possibly help with determination of timing of surgery. The shape influencing surgery in combination with the remaining remodeling in the child would improve overall outcome and hopefully protect the hip joint from further degeneration in adulthood.

GENERAL CONCLUSION

In this thesis, we showed that the incidence of (late) DDH increases in regions such as the province of Manitoba (Canada), where there is no screening programme in place, as (selective) ultrasound programmes in other countries have shown to decrease the rate of

late presenting DDH. Improved access to health care and well baby clinics in rural areas, including clinical assessment of the hips beyond walking age, can improve diagnosis and overall outcome. It is unclear from our study if the late DDH is due to family predisposition and inbreeding or mechanically induced due to swaddling/restricted hip movements, a regional custom. Screening should also take into consideration risk factors for the province such as first female, breech and presence of clubfoot deformity. The latter is somewhat controversial, and could again be a regional entity, as current screening programmes no longer include clubfoot as a risk factor.[18,19] On the other hand, ultrasound has also its limitations in identifying relevant DDH. Despite abnormal findings on ultrasound suggestive for DDH within the first 6 months of life, many of these abnormalities will improve over time without treatment. Furthermore, abduction treatment of stable well-centered hips in 3 to 4 months old will not alter acetabular development, as 80% will become normal without treatment. Again, this questions the specificity of US as diagnostic tool to identify true hip disease based on Graf Classification alone. The role of Pavlik harness treatment over 6 months of age is questionable but can still be successful in 60% of the cases in moderate dislocation (≤ Graf type III). Prolongation of the Pavlik harness beyond 6 weeks of treatment did not alter the success rate. After failed Pavlik harness, medial approach lead to poor results in 20% of the patients for both radiographic and functional outcomes. The medial approach in patients younger than 6 months showed better results. Thus, the medial approach should probably be reserved to this age group. AVN rate was high, with almost 1/2 showing some changes during growth but eventually only 1/6 developed more severe proximal growth disturbance. The patient's observed outcome was not linked to the type of AVN but the severity of residual dysplasia. Finally, shape variants of AVN hips using SSM can identify early radiographic changes linked to poor outcome. This has the potential to develop as a tool for decision-making process at already a very young age and therefore improving the outcome.

REFERENCES

1. Sommerville E. Development of congenital dislocation of the hip. J Bone Joint Surg - Br. 1953 35(4): 568 - 577.
2. Wood MK, Conby C, Benson MK. Does early treatment by abduction splintage improve the development of dysplastic but stable neonatal hips? *J Ped Orthop.* 20, 302-5 (2000)
3. Rosendahl K, Dezateux C, Fosse K et al. Immediate treatment versus sonographic surveillance for mild dysplasia in newborns. *Pediatrics*. 125,9-16 (2010)
4. Avisse C, Gomes C, Delvinquiere V, Ouedraogo T, Lallemand A, Delattre J, Flament J. Anatomic study of the pre-and neonatal hip. Physiopathogenic considerations on dysplasia and congenital dislocation of the hip. Surg Radiol Anat 1997; 19: 155-159.
5. Screening programmes for developmental dysplasia of the hip in newborn infants**.** Shorter, Damon; Hong, Timothy; Osborn, David AThe Cochrane database of systematic reviews; 2011 (9)
6. Ultrasound in the diagnosis of developmental dysplasia of the hip in newborns. The European approach. A review of methods, accuracy and clinical validity. Rosendahl, Karen; Toma, Paolo European radiology. 2007; 17 (8):1960-1967.
7. Lussier E, Sun Y, Chen H, Chang T, Chang C. Ultrasound screening for developmental dysplasia of the hip after 4 weeks increases exam accuracy and decreases follow-up visits. Pediatr Neonatol 2019; 60:270-277.
8. Roposch A, Liu L, Protopapa E. Variations in the use of diagnostic criteria for developmental dysplasia of the hip. Clin Orthop Relat Res 2013; 471:1946-1954.
9. Salut C, Moriau D, Pascaud E, Layré B, Peyrou P, Maubon A. Résultats initiaux d'une expérience de dépistage échographique systématique de la luxation congénitale de hanche chez la fille . J Radiol. 2011;92(10):920-929
10. Tréguier C, Chapuis M, Branger B et al. Dépistage echographique de la luxation congenitale de hanche centre sur la mesure du fond cotyloidien. J Radiol 2006; 87(10): 1240.
11. Bucholz RW OJ. Patterns of ischemic necrosis of the proximal femur in nonoperatively treated congenital hip disease in the hip. Proc 6th Open Scientific Meeting of the Hip Society. 1978;Volume 2:43-63.
12. Kalamchi A, MacEwen GD. Avascular necrosis following treatment of congenital dislocation of the hip. J Bone Joint Surg Am. 1980;62(6):876-88
13. Gardner RO, Bradley CS, Howard A, Narayanan UG, Wedge JH, Kelley SP. The incidence of avascular necrosis and the radiographic outcome following medial open reduction in children with developmental dysplasia of the hip: a systematic review. Bone Joint J. 2014;96-B(2):279-86.
14. Roposch A, Liu LQ, Offiah AC, Wedge JH. Functional outcomes in children with osteonecrosis secondary to treatment of developmental dysplasia of the hip. J Bone Joint Surg Am. 2011;93(24):e145.
15. Roposch A, Wedge JH, Riedl G. Reliability of Bucholz and Ogden classification for osteonecrosis secondary to developmental dysplasia of the hip. Clin Orthop Relat Res. 2012;470(12):3499-505.
16. Whitlock P, Salari K, Blumstein G, Zhang B, Arkader A, Choi P. Reliability and normative values of common adult radiographic parameters for hip preservation in the developing pelvis. J Hip Preserv Surg 2019; 6(3): 189-198.
17. Kim HT, Kim IB, Lee JS. MR-based parameters

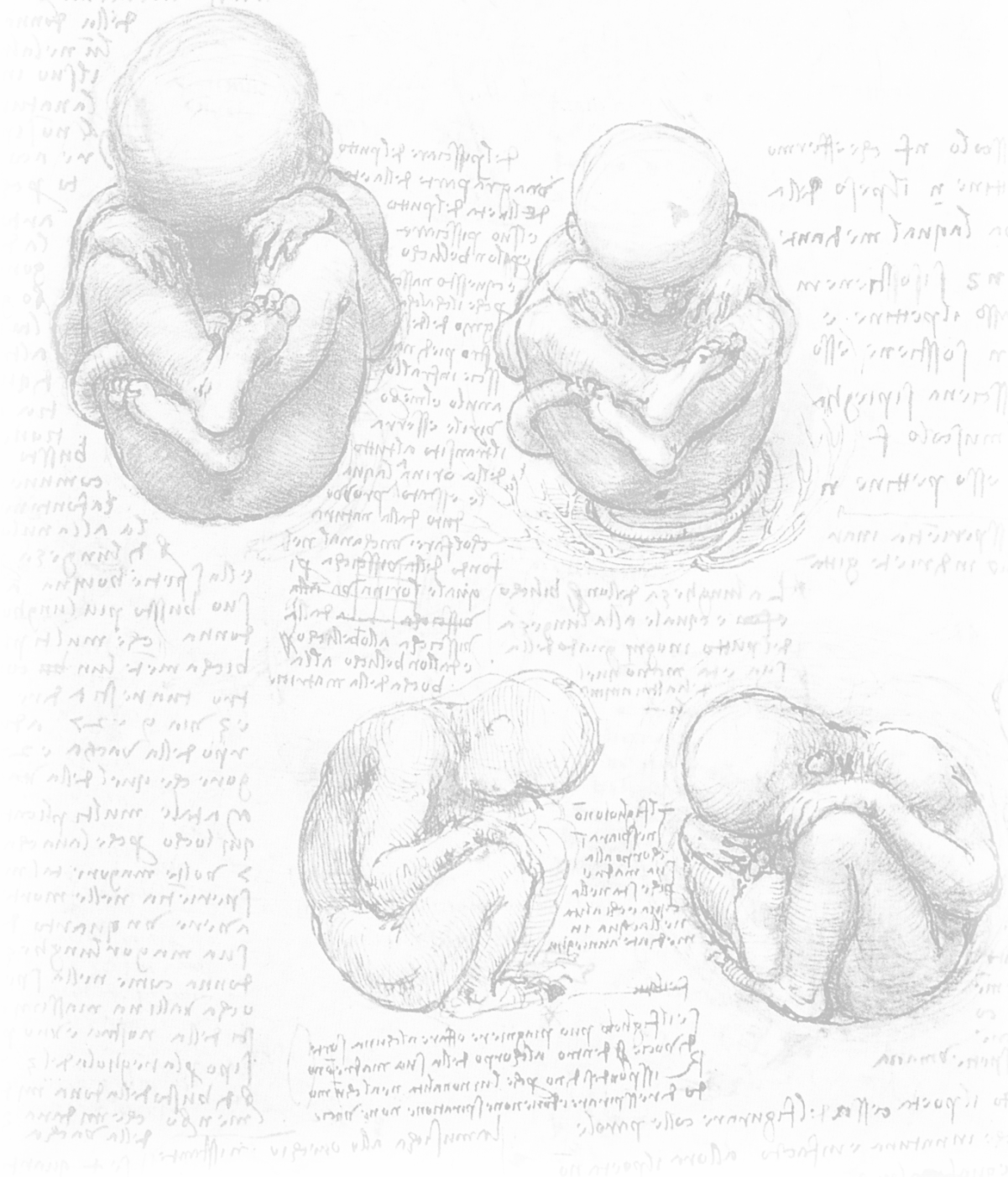
as a supplement to radiographs in managing Developmental Dysplasia of the hip. Clin Orthop Surg 2011; 3: 202 - 210.

18. Paton RW, Choudry Q. Neonatal foot deformities and their relationship to DDH: and 11-year prospective longitudinal observational study. JBJS-Br. 2009; 91(5): 655-658.
19. Mulpuri K, Schaeffer E, Andrade J, Sankar W, Williams N, Mathaney T, Mubarak S, Cundy P, Price C. What risk factors and characteristics are associated with late-presenting dislocations of the hip in infants? Clin Orthop Relat Res 2016; 474:1131-1137.

8

CHAPTER 9

Nederlandse samenvatting



ALGEMENE DISCUSSIE, ANTWOORDEN OP DE VRAGEN.

In de afgelopen decennia hebben positieve ontwikkelingen in de diagnose en behandeling van DDH geleid tot een beter resultaat van deze complexe ziekte. Vroegtijdige opsporing van heupafwijkingen met echografie, een overstap naar een meer dynamische behandeling door middel van het Pavlik-harnas en een beter begrip van de heup vasculariteit en groeistoornissen zijn slechts enkele voorbeelden. Toch blijven een aantal vragen onbeantwoord. Interessant genoeg schreef Sommerville al in 1953: “De ontwikkeling van een aangeboren heupluxatie is één van die fascinerende puzzels in de orthopedie waarin de stukjes relatief compleet zijn, maar het beeld dat eruit voortvloeit een fout vertoont, suggererend dat kleine aanpassingen hier en daar tot een beter resultaat leiden”[1] Dit vat mooi samen waar dit proefschrift op gericht was: proberen het totaalbeeld van DDH te verbeteren.

In **hoofdstuk 2** zijn de incidentie en risicofactoren van DDH in een multiculturele populatie zonder universele screening in de provincie Manitoba, Canada, bestudeerd om te helpen bij het opstellen van screeningsrichtlijnen. Gebruikmakend van de database van het Manitoba Center for Health Policy (MCHP), met behulp van ICD-diagnosecodes en factureringstarieven, identificeerden we 1716 gevallen van DDH van de 258 499 pasgeborenen tussen 1995 en 2012. De incidentie werd berekend op 6,6 / 1000 pasgeborenen en 2,2 / 1000 met laattijdige presentatie (na 6 maanden). We identificeerden een verhoogd relatief risico voor eerstgeborenen, meisjes, geboorte in stuitligging en aanwezigheid van een klompvoet afwijking. De leeftijd bij diagnose verschilde significant voor landelijke gebieden (12.3 maanden CI 95% 10.0-14.0) vergeleken met stedelijke gebieden (6.4 maanden CI 95% 4.9 - 7.8). Bovendien was de diagnose na loopleeftijd (d.w.z. 18 maanden) bijna 3x zo hoog op het platteland als bij kinderen die in de steden wonen. (p <0.0001) Manitoba heeft een grote First Nation Cree-Ojibwa-gemeenschap van 15% van de totale bevolking van de provincie. Dit stijgt tot 25% voor de Interlake-Eastern en tot 75% in de Northern Regional Health Authorities (RHA). Hoewel nu minder vaak, is het nog steeds een culturele gewoonte om het kind in te bakeren met gestrekte benen op een wiegplank tot de leeftijd van 1 jaar. Dit wordt bevorderd door de barre weersomstandigheden in deze streken waar kinderwagens geen optie zijn. Onze resultaten lieten een hoge incidentie zien, vooral van late presentaties en in landelijke gebieden. Introductie van selectieve screening door klinisch onderzoek in combinatie met echografie zou dit aantal laat-presenterende DDH verminderen en het algehele resultaat verbeteren, aangezien we weten dat Pavlik harnas behandeling in de eerste 6 maanden van het leven een hoog slagingspercentage heeft. Verschillende landen hebben screeningstools geïntroduceerd die leiden tot een afname van het aantal late DDH en minder operaties. Een prospectieve studie waarin een screeningprogramma wordt geïmplementeerd op basis van de geïdentificeerde risicofactoren en regio’s, zou van belang zijn om de vroege detectie van heupdysplasie te verbeteren.

In **hoofdstuk 3** werd een literatuuranalyse uitgevoerd van abnormale heup echo’s bij kinderen jonger dan 6 maanden, aangezien de huidige screeningsinstrumenten tot overbehandeling leiden vanwege de hoge sensitiviteit en lage specificiteit van heup US. Het doel was om die heupen te identificeren en te kwantificeren die in de loop van de tijd normaal zullen worden om de screening-specificiteit te verbeteren. In een Pubmed-zoektocht naar “DDH en “echografie” werden alle heupen geïdentificeerd die abnormaal waren op echografie en werden onbehandeld gelaten. Gegevens van 13 561 heupen werden verzameld en geanalyseerd. De normale ontwikkeling binnen de eerste 6 maanden in stabiele heupen was 89-98 % voor Graf IIa, 80-100% voor Graf IIc en 80-97% in een geclusterde groep van Graf IIa tot IIC. Interessant genoeg werd meer dan 50% van Graf III-heupen in de loop van de tijd als normaal gerapporteerd, maar minder voor Graf IV DDH. Normalisatie van femurkopbedekking (FHC) van minder dan 50% volgde in 78 - 100%. Er was niet genoeg klinische informatie om erachter te komen waarom de ontwrichte heupen onbehandeld bleven. Deze resultaten laten een groot potentieel zien voor abnormale echografie bevindingen om na verloop van tijd een goedaardig beloop te hebben. Dit stelt het vermogen van US screening om onderscheid te maken tussen goedaardige natuurlijke historie en relevante DDH in twijfel.

In **hoofdstuk 4** hebben we het effect van bracing op de natuurlijke verloop van stabiele dysplastische heupen bij zuigelingen van 3 tot 4 maanden bestudeerd in een gerandomiseerde multicenter studie. Patiënten werden gerandomiseerd naar Pavlik-harnas (n = 55) of actieve surveillancegroep (n = 49). De verbetering van de hoek van het benige dak, α, was de primaire uitkomstmaat na 12 weken follow-up. Beide groepen vertoonden een vergelijkbare verbetering met een gemiddelde α-hoek van 60.5 ° ± 3.8 ° in de Pavlik-groep en 60.0 ° ± 5.6 ° in de actieve surveillancegroep. (p = 0,30) Bovendien toonde analyse van de secundaire uitkomst (acetabulaire index (AI) als standaardzorg op bekkenröntgenfoto’s) geen verschil op de leeftijd van 10 maanden en op loopleeftijd. Onze bevindingen zijn van belang omdat Pavlik harnas behandeling de huidige praktijk is voor Graf type IIb / IIc-heupen. We hebben aangetoond dat bracing geen bijkomend voordeel heeft in stabiele, goed gecentreerde heupen. Onze resultaten zijn in overeenstemming met de bevindingen van Wood et al. en Rosendahl et al. [2,3] We vonden een algehele verbetering van de α-hoek van 5 ° over een periode van 12 weken. Tijdens de actieve surveillance periode werden 3 patiënten (6,1%) behandeld na 6 weken follow-up vanwege afname van de α-hoek. Na 12 weken hadden 7 patiënten behandeling nodig in de surveillancegroep, maar evenzo vertoonden 7 patiënten in de Pavlik-harnasgroep na 12 weken nog steeds dysplasie waarvoor de behandeling doorgezet werd. Dit komt overeen met het natuurlijk beloop dat werd gepresenteerd in hoofdstuk 3, waar 80% van abnormale heup echo een goedaardig beloop kent en geen behandeling nodig heeft. Echografie kan geen onderscheid maken tussen de goedaardige heupafwijking en echte heuppathologie die tot overbehandeling leidt. Onze studie toonde

aan dat actief surveillance van gecentreerde stabiele dysplastische heupen gerechtvaardigd is in plaats van behandeling.

Na de leeftijd van 6 maanden wordt de conservatieve behandeling van DDH met bracing uitdagender naarmate het kind zich ontwikkelt en actiever wordt. Het doel van **hoofdstuk 5** was om te onderzoeken of er in de late DDH nog plaats was voor abductiebehandeling. We voerden een retrospectieve analyse uit van het slagingspercentage van abductiebehandeling bij 24 patiënten (26 heupen) met een gemiddelde leeftijd van 9 maanden (spreiding 6-23 maanden) en een gemiddelde follow-up van 6.5 jaar (spreiding 2-12 jaar). Twaalf van de 26 heupen (46%) werden met succes gereponeerd met een gemiddelde tijd tot repositie van 4 weken (2 tot 7 weken). De overige 14 heupen (54%) van de gefaalde Pavlik harnas behandeling werden gereponeerd met gesloten of open repositie. Een gangbare praktijk in ons ziekenhuis was om een stevige abductiebrace toe te voegen zodra een goede flexie werd bereikt in de Pavlik harnas om de krachten van adductie bij deze oudere kinderen te weerstaan. Deze methode had geen toegevoegde waarde (p = 0,57). Deze praktijk werd na deze studie verlaten. Van de 17 heupen die werden gediagnosticeerd met US hadden 10 een Graf type III en 7 Graf type IV. Zes van de 10 (60%) Graf type III heupen hadden een succesvolle repositie vergeleken met alle Graf type 4 heupen (0%). (p = 0,035) Geen van de Graf type III-heupen reponeerde na 6 weken behandeling. We raden daarom Pavlik harnas behandeling aan voor late DDH, vooral bij Graf type III heupen. De behandeling moet worden stopgezet als het heup na 6 weken nog niet gereponeerd is. Graf type IV heupen kunnen beter behandeld worden met gesloten/open repositie.

Na een mislukte gesloten repositie zal een chirurgische ingreep de volgende stap zijn in de behandeling van aanhoudende heup luxatie. In **hoofdstuk 6** hebben we de lange termijn resultaten van de mediale benadering bestudeerd, zoals beschreven door Ludloff. De open repositie via deze benadering heeft een gekend hoge kans op botnecrose of avasculaire necrose (AVN) (8% -54%) met mogelijks slechte resultaten. We hebben ons gericht op het beoordelen van de radiografische uitkomst en de door de patiënt gerapporteerde uitkomst met een follow-up van minimaal 4 jaar. Van de 58 heupen geïncludeerd, vertoonden 31 heupen postoperatief tekenen van AVN, waarbij 11 heupen (19%) zich ontwikkelden tot Bucholz-Ogden type II-IV bij de laatste follow-up. Een slecht resultaat gedefinieerd door Severin type III of hoger werd gezien bij 22%. De mediane leeftijd ten tijde van de operatie was 5.2 maanden (IQR 1.9 - 8.5) voor Severin type I en II en was significant lager dan in de groep met slechte resultaten, 8.6 maanden (IQR 5.2 - 12.0). (p = 0,047) De leeftijd op moment van de ingreep was ook een significante voorspellende factor voor de noodzaak aan bijkomende ingrepen. (p = 0.002) Om de door de patiënt gerapporteerde uitkomst te beoordelen, hebben we de PODCI- en HOOS-vragenlijsten gebruikt, afhankelijk van de leeftijd van de patiënt. De respons was 62% met 17 ingevulde PODCI- en 15 HOOS-vragenlijsten. Verrassend genoeg was er geen verband tussen een slechte uitkomst en de aanwezigheid van AVN. De schalen voor pijn en globaal functioneren voor beide vragenlijsten waren echter slechter bij patiënten met een slechte Severin-uitkomst. Aangezien Severin resterende heupdysplasie beoordeelt, is het verlies van normale gewrichtsmorfologie / congruentie meer een weerspiegeling van een slecht functioneel resultaat dan van het type AVN.

Aangezien we in hoofdstuk 6 hebben aangetoond dat het type AVN een slechte uitkomst niet kan voorspellen, stelden we in **hoofdstuk 7** de hypothese op dat bepaalde vormen van het heupgewricht meer voorspellend zouden moeten zijn. Om deze vormen te identificeren, hebben we “Statistical Shape Modeling” (SSM) gebruikt en de vormvarianten gekoppeld aan een slecht resultaat gedefinieerd door Severin bij de laatste follow-up (minimaal 8 jaar). Standaard röntgenfoto’s op 1, 2, 3, 5 en 8 jaar van kinderen die AVN ontwikkelden na gesloten of open heup repositie in het Sophia Kinderziekenhuis van het EMC tussen 1984 en 2007 werden opgenomen. De Bucholz-Ogden-classificatie werd gebruikt om de aanwezigheid en het type AVN te bepalen. SSM is een wiskundige berekening waarbij het heup gewricht gemodelleerd wordt en de variatie van het anatomische model beschreven wordt door middel van de contouren van het dijbeen en bekken te herleiden tot punten. We vonden 11 vormen van vormvariatie significant geassocieerd met een slecht resultaat. Stratificatie voor type AVN werd uitgevoerd in een secundaire analyse. We vonden Mode 6 op 2-jarige leeftijd en Mode 2 op 5-jarige leeftijd sterker geassocieerd met een slechte uitkomst in AVN-type 1 heupen, terwijl Mode 1 op 1- en 8-jarige leeftijd en Mode 8 op 5-jarige leeftijd werden geassocieerd met AVN type 2-3-4. We hebben de morfologische kenmerken van de geïdentificeerde modi beschreven, om deze afwijkingen in de heupontwikkeling op jonge leeftijd te kunnen identificeren. Deze vroege herkenning kan helpen bij het beslissen over chirurgie die de vorm van het heup gewricht kan beïnvloeden met het oog op verbeteren van het resultaat.

TOEKOMSTPERSPECTIEVEN

Met dit proefschrift hebben we wat meer stukjes van de puzzel gevonden en het beeld van DDH verbeterd, zoals geciteerd door Sommerville. Er blijven nog steeds vragen onbeantwoord en er zijn ook enkele nieuwe vragen naar voren gekomen uit ons onderzoek. Ten eerste hebben we gemerkt dat er dringend behoefte is aan universele terminologie om de diagnostiek en uitkomsten bij DDH te verbeteren. Te vaak worden in de literatuur verschillende definities gebruikt. Rekening houdend met het bovenstaande, zou DDH-terminologie gebaseerd moeten zijn op de verschillende oorzaken van DDH, namelijk genetische dysplasie, mechanische foetale en postnatale posturele dislocatie zoals gesuggereerd door Avisse. [4]

Het zou interessant zijn om dit verder te onderzoeken en een classificatiesysteem voor DDH dat etiologie, klinische en echografische kenmerken combineert, want alleen door deze 3 aspecten van DDH te combineren in relatie tot de leeftijd van het kind, zullen we in staat zijn om de goedaardige afwijkingen te kunnen scheiden van de echte / relevante heup pathologie. Ten tweede is echografie als diagnostisch hulpmiddel waardevol in vergelijking met klinische screening, zoals aangetoond in hoofdstuk 2. Lichamelijk onderzoek is sterk afhankelijk van de onderzoeker en zal DDH-gevallen missen. De heup echografie volgens Graf heeft echter ook beperkingen en is zeer gevoelig, wat leidt tot over diagnose van heupafwijkingen die na verloop van tijd spontaan verbeteren zonder behandeling. [5,6] Het tijdstip waarop de diagnose wordt gesteld is ook belangrijk, zoals blijkt uit hoofdstuk 3. Veel echografische afwijkingen bij kinderen jonger dan 6 maanden zullen zonder behandeling verbeteren. Zo besloten ook Lussier et al. dat screening van pasgeborenen na 28 dagen de nauwkeurigheid verbeterde.[7] Roposh et al. benadrukten ook het belang van goed afgestemde afspraken in diagnostistiek, aangezien de consistentie over het algemeen slecht was, vooral voor echografische criteria.[8] Stabiliteit van de heup is misschien wel de belangrijkste vereiste voor een goede heupkom ontwikkeling. Daarom zijn stabiliteitstesten tijdens echografie belangrijk om die heupen te identificeren die het risico lopen op progressie en dus luxatie. Ondanks het gebrek aan een algemeen aanvaarde kwantificering van heupinstabiliteit, lijkt de “Femoral Head Coverage” (FHC) het meest gebruikt te worden. FHC vereist echter verschillende lineaire metingen en percentageberekeningen. Er zijn enkele tegenstrijdige gegevens in de literatuur over de afkapwaarde tussen 33% en 50% en de reproduceerbaarheid van de test is maar matig. Salut et al in Frankrijk beoordeelden alle heupen van pasgeboren meisjes op 1 maand oud door de pubofemorale afstand (PFD) of acetabulaire diepte (‘fond du cotyloïdien) te meten als kwantificering van instabiliteit, gedefinieerd door Couture and Tréguier et al. [9,10] De PFD is gemeten in rugligging in het zelfde dynamische laterale coronale vlak als de Harcke-weergave voor FHC. Het is minder foutgevoelig omdat de nauwkeurigheid van het vlak minder relevant is en alleen een afstand meet tussen twee punten, namelijk de mediale rand van de epifyse (ronde structuur) en de ossificatie van de kern van het schaambeen, gemakkelijk te identificeren op echografie. Normale PFD in stabiele heupen is 4-5 mm (waarbij 6 mm per definitie onstabiel is) en een verschil van minder dan 1,5 mm tussen beide heupen. Er waren geen enkele gevallen van late DDH, behalve bij 2 jongens die niet geincludeerd waren op basis van hun geslacht. Ongepubliceerd onderzoek die door de auteur van dit proefschrift tijdens de IFPOS / POSNA-bijeenkomst in 2013 gepresenteerd werd, toonde de betrouwbaarheid van deze PFD meting matige tot goede overeenstemming, gelijkaardig als de FHC. Van belang was dat de luxeerbaardeidstest (druk op de heup met gebogen knie) van één been in rugligging een betere kwantificering van instabiliteit gaf dan gelijktijdige belasting van beide benen. Meer recent vonden Husum et al een PFD-waarde van meer dan 4,4 mm als de afkapwaarde voor heupinstabiliteit, maar dit was in laterale positie, met een gevoeligheid van 100% en

specificiteit van 93%. De PFD is veelbelovend als een snelle, zeer gevoelige en specifieke kwantificeringstest voor instabiliteit. Het combineren van instabiliteit met heupmorfologie en acetabulaire dysplasie is een conditio sine qua non bij echografie en diagnostiek. Verder onderzoek zou zich moeten richten op kwantificeringstesten en algoritmen die relevante abnormale heupmorfologie en instabiliteit op echografie identificeren. Ten slotte is de inzetbaarheid van SSM om vormvarianten te identificeren, die verband houden met een slechte uitkomst, een interessante vaststelling in hoofdstuk 7. De onvoorspelbare waarde van de huidige classificatiesystemen (met ook een slechte tot matige betrouwbaarheid) voor AVN en uitkomst, maakt de beslissing voor chirurgie op jonge leeftijd moeilijk met vaak een afwachtend beleid, herhaalde röntgenfoto’s en frequente klinische afspraken. [11,12,13,14,15] Een prospectieve studie in een grotere populatie die vormen identificeert die verband houden met een slechte uitkomst en vroege chirurgische interventie met follow-up op de lange termijn, zou een volgende stap kunnen zijn. De belangrijkste uitdaging blijft de groei van het kind en daarmee gaande mogelijkheid tot remodellering van het heupgewricht. Whitlock heeft in verschillende leeftijdsgroepen heupparameters gemeten tot volgroeid skelet. [16] Deze waarden zijn van belang om de normale heupontwikkeling te kwantificeren en doelen te stellen voor de behandeling van dysplastische heupen. DDH is echter een 3D-afwijking met zowel acetabulaire als femorale dysplasie, waarbij röntgenfoto’s alleen de contouren van het botgewricht beschrijven. MRI-scan als preoperatieve planning blijkt nuttig te zijn bij het beslissen omtrent wel of niet overgaan tot chirurgie. [17] Door kwantificering van zowel bot- als kraakbeendeficiënties, aangezien deze laatste op röntgenfoto’s gemist zullen worden, kan de chirurg beslissen al dan niet in te grijpen. Een andere rol van SSM zou kunnen zijn om bot- en kraakbeendekking te bestuderen op MRI-beelden in correlatie met bekkenröntgenfoto’s om ook het kraakbenig aspect van de heup ontwikkeling mee te nemen. Een betere timing van de operatie zal het algehele resultaat verbeteren en hopelijk het heupgewricht beschermen tegen verdere degeneratie op volwassen leeftijd.

ALGEMENE CONCLUSIE

In dit proefschrift hebben we laten zien dat de incidentie van (late) DDH toeneemt in regio’s zoals de provincie Manitoba (Canada), waar geen screeningsprogramma bestaat, terwijl (selectieve) echografische screening in andere landen heeft aangetoond de incidentie van late presentatie van DDH te verminderen. Verbeterde toegang tot gezondheidszorg en consultatiebureaus in landelijke gebieden, inclusief klinische beoordeling van de heupen na de loopleeftijd, kan de diagnose en de resultaten verbeteren. Het is echter uit onze studie niet duidelijk of de late DDH te wijten is aan familiale voorbeschiktheid/inteelt of mechanisch geïnduceerd wordt door inbakeren / beperkte heupbewegingen, een regionaal gebruik. Bij het screening zal ook rekening worden gehouden met risicofactoren voor de provincie, zoals

eerste meisje, stuitligging en de aanwezigheid van een klompvoet. Dit laatste is enigszins controversieel en zou opnieuw een regionale entiteit kunnen zijn, aangezien de huidige screeningprogramma's klompvoeten niet langer als risicofactor bevatten. [18,19] Anderzijds heeft de echografie ook zijn beperkingen bij het identificeren van relevante DDH. Ondanks abnormale bevindingen op echografie die wijzen op DDH binnen de eerste 6 maanden van het leven, zullen veel van deze afwijkingen in de loop van de tijd verbeteren zonder behandeling. Bovendien zal abductiebehandeling van stabiele, goed gecentreerde heupen bij 3 tot 4 maanden oud de ontwikkeling van de heupkom niet veranderen, aangezien 80% normaal zal worden zonder behandeling. Nogmaals, dit stelt de specificiteit van de VS als diagnostisch hulpmiddel ter discussie om ware heup dysplasie te identificeren uitsluitend gebaseerd op de Graf-classificatie. De rol van Pavlik-harnas behandeling bij na de leeftijd van 6 maanden is twijfelachtig, maar kan nog steeds succesvol zijn in 60% van de gevallen bij matige luxatie (≤ Graf type III). De behandeling doorzetten na 6 weken heeft geen bijkomende effect en kan beter gestaakt worden als de heup dan nog niet gereponeerd is. Na het falen van het Pavlik-harnas leidde mediale benadering tot slechte resultaten bij 20% van de patiënten voor zowel radiografische als functionele uitkomsten. De mediale benadering bij patiënten jonger dan 6 maanden liet betere resultaten zien. Daarom is het aan te bevelen dat de mediale benadering beter wordt voorbehouden aan deze leeftijdsgroep. Het AVN-percentage was hoog, waarbij bijna de helft veranderingen vertoonde aan de vorm van de heupkop tijdens de groei, maar uiteindelijk ontwikkelde slechts 1/6 een ernstigere proximale groeistoornis. Het waargenomen resultaat van de patiënt was niet gekoppeld aan het type AVN, maar aan de ernst van resterende dysplasie. Ten slotte kunnen vorm-varianten van AVN-heupen met behulp van SSM vroege radiografische veranderingen identificeren die verband houden met een slechte uitkomst. Dit heeft de mogelijkheid om reeds op zeer jonge leeftijd in te zetten als een hulpmiddel bij de besluitvorming tot wel of niet ingrepen en daardoor het uiteindelijke resultaat te verbeteren.

REFERENTIES

1. Sommerville E. Development of congenital dislocation of the hip. J Bone Joint Surg - Br. 1953 35(4): 568 - 577.
2. Wood MK, Conby C, Benson MK. Does early treatment by abduction splintage improve the development of dysplastic but stable neonatal hips? *J Ped Orthop.* 20, 302-5 (2000)
3. Rosendahl K, Dezateux C, Fosse K et al. Immediate treatment versus sonographic surveillance for mild dysplasia in newborns. *Pediatrics*. 125,9-16 (2010)
4. Avisse C, Gomes C, Delvinquiere V, Ouedraogo T, Lallemand A, Delattre J, Flament J. Anatomic study of the pre-and neonatal hip. Physiopathogenic considerations on dysplasia and congenital dislocation of the hip. Surg Radiol Anat 1997; 19: 155-159.
5. Screening programmes for developmental dysplasia of the hip in newborn infants**.** Shorter, Damon; Hong, Timothy; Osborn, David AThe Cochrane database of systematic reviews; 2011 (9)
6. Ultrasound in the diagnosis of developmental dysplasia of the hip in newborns. The European approach. A review of methods, accuracy and clinical validity. Rosendahl, Karen; Toma, Paolo European radiology. 2007; 17 (8):1960-1967.
7. Lussier E, Sun Y, Chen H, Chang T, Chang C. Ultrasound screening for developmental dysplasia of the hip after 4 weeks increases exam accuracy and decreases follow-up visits. Pediatr Neonatol 2019; 60:270-277.
8. Roposch A, Liu L, Protopapa E. Variations in the use of diagnostic criteria for developmental dysplasia of the hip. Clin Orthop Relat Res 2013; 471:1946-1954.
9. Salut C, Moriau D, Pascaud E, Layré B, Peyrou P, Maubon A. Résultats initiaux d'une expérience de dépistage échographique systématique de la luxation congénitale de hanche chez la fille . J Radiol. 2011;92(10):920-929
10. Tréguier C, Chapuis M, Branger B et al. Dépistage echographique de la luxation congenitale de hanche centre sur la mesure du fond cotyloidien. J Radiol 2006; 87(10): 1240.
11. Bucholz RW OJ. Patterns of ischemic necrosis of the proximal femur in nonoperatively treated congenital hip disease in the hip. Proc 6th Open Scientific Meeting of the Hip Society. 1978;Volume 2:43-63.
12. Kalamchi A, MacEwen GD. Avascular necrosis following treatment of congenital dislocation of the hip. J Bone Joint Surg Am. 1980;62(6):876-88
13. Gardner RO, Bradley CS, Howard A, Narayanan UG, Wedge JH, Kelley SP. The incidence of avascular necrosis and the radiographic outcome following medial open reduction in children with developmental dysplasia of the hip: a systematic review. Bone Joint J. 2014;96-B(2):279-86.
14. Roposch A, Liu LQ, Offiah AC, Wedge JH. Functional outcomes in children with osteonecrosis secondary to treatment of developmental dysplasia of the hip. J Bone Joint Surg Am. 2011;93(24):e145.
15. Roposch A, Wedge JH, Riedl G. Reliability of Bucholz and Ogden classification for osteonecrosis secondary to developmental dysplasia of the hip. Clin Orthop Relat Res. 2012;470(12):3499-505.
16. Whitlock P, Salari K, Blumstein G, Zhang B, Arkader A, Choi P. Reliability and normative values of common adult radiographic parameters for hip preservation in the developing pelvis. J Hip Preserv Surg 2019; 6(3): 189-198.
17. Kim HT, Kim IB, Lee JS. MR-based parameters

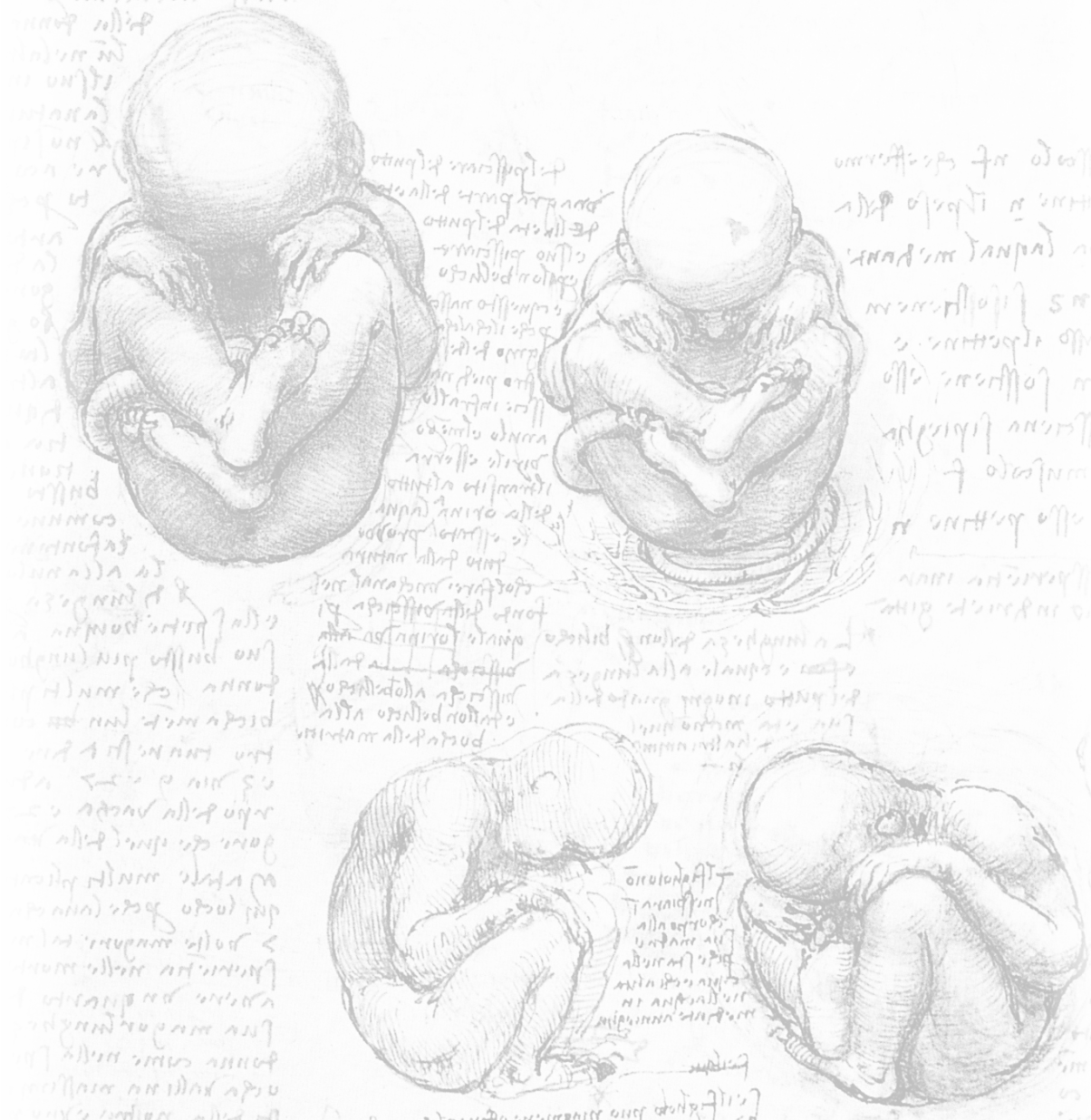
as a supplement to radiographs in managing Developmental Dysplasia of the hip. Clin Orthop Surg 2011; 3: 202 - 210.

18. Paton RW, Choudry Q. Neonatal foot deformities and their relationship to DDH: and 11-year prospective longitudinal observational study. JBJS-Br. 2009; 91(5): 655-658.
19. Mulpuri K, Schaeffer E, Andrade J, Sankar W, Williams N, Mathaney T, Mubarak S, Cundy P, Price C. What risk factors and characteristics are associated with late-presenting dislocations of the hip in infants? Clin Orthop Relat Res 2016; 474:1131-1137.

9

CHAPTER 10

PhD portofolio
List of publications
Curriculum vitae
Acknowledgements



PORTOFOLIO

1. PhD training

	Year	Workload hrs/ ECTS
General academic/Research skills		
– Tri-council policy statement (TCPS) 2: course on Research Ethics(Core), Winnipeg, Canada	2012	0.5
– ORS-OREF-AAOS new investigator workshop, Baltimore, USA	2013	1.5
– Biostatistical methods 1: Basic Principles part A (CCO2) (NIHES), Rotterdam, The Netherlands	2017	2
Presentations and (inter)national conferences		
– EPOS meeting Lisbon, Portugal. "Results of Pavlik harness treatment in children with dislocated hips between 6 and 24 months" - poster	2009	0.5
– Grand round "Developmental Dysplasia of the hip" - University of Manitoba, Canada - presentation	2011	1
– Manitoba Orthopaedic Symposium, Winnipeg, Canada. "Pediatric sports injuries". - Presentation.	2011	1
– POSNA annual meeting, Denver, USA: "Reliability of acetabular depth measurement by ultrasound in diagnosis of DDH in newborns"- Presentation	2012	1
– AAP National conference, San Diego, USA: "Relative risk and incidence in Developmental Dysplasia of the hip" - Presentation (by Co-author Vanessa Percy)	2014	1
– EPOS annual meeting, Rome: "Abduction Bracing versus Natural History in Hip Dysplasia: Multicenter Randomized Controlled Trial." - Presentation (***Awarded best clinical paper***)	2016	1
– POSNA annual meeting, Indianapolis, USA: "Abduction Bracing versus Natural History in Hip Dysplasia: Multicenter Randomized Controlled Trial." (*nomination for best clinical paper*) - Presentation	2016	1
– POSNA annual meeting, Indianapolis, USA: "Long-term Radiographic and Functional Outcome of Medial Approach in Open Hip Reduction for DDH"- Presentation	2016	1
– EPOS annual meeting, Oslo: " Shape of the hip joint in avascular necrosis to predict outcome." - presentation	2018	1
– EPOS annual meeting, Tel Aviv: "ACL injuries in the female adolescent athlete". - presentation	2019	1
Other		
– Writing Grant proposal - "Incidence of DDH in children for the province of Manitoba" - Alexander Gibson Grant University of Manitoba - awarded 15.000 CAD$	2012	0.5

2. Teaching activities

	Year	Workload hrs/ECTS
Supervising practicals		
– Supervising practical assignment for medical students attending the minor "orthopaedic Sports Traumatology" EMC, the Netherlands	2016-2017	1
– Supervising practical assignment of medical students musculoskelatal block - Aston University, Birmingham, UK	2018-2019	0.5
Supervising Master's theses		
– Supervising medical students (Lisa van Dijk, Brit Ganzeboom, Joshua Bonsel) in their scientific master project.	2015-2018	6
Teaching		
– Teaching Residents & Medical students, University of Manitoba	2011-2014	4
– Mentor medical students, University of Manitoba	2013-2014	1
– Teaching MSK block - medical students, Erasmus University of Rotterdam	2016-2017	1
– Aston University MBChB programme, musculoskeletal block - lectures	2018-2019	1

LIST OF PUBLICATIONS

Morphological variants to predict outcome of avascular necrosis in Developmental Dysplasia of the Hip. **V. Pollet**, J. Bonsel, B. Ganzeboom, R. Sakkers, J. Waarsing. Bone Joint J. 2020; *revised - accepted.*

"Abduction treatment in stable hip dysplasia does not alter the acetabular growth: results of a randomized clinical trial". **V. Pollet**, R.M.Castelein, M. van de Sande, M. Witbreuk, A.K. Mostert, A. Besselaar, C. van den Bergen, E. Beek , C.S.P.M. Uiterwaal, R.J.B. Sakkers. Sci Rep. 2020; 10,9647.

The natural history of abnormal ultrasound findings in hips of infants under six months of age". Sakkers R, **Pollet V**. J Child Orthop. 2018;12(4):302-307

"Long term outcomes following the medial approach for open reduction of the hip in children with developmental dysplasia." **V. Pollet**, L. van Dijk, M. Reijman, R. Sakkers, R. Castelein. Bone Joint J. 2018 ; 100 - B(6): 822-827.

"Long term follow-up and development of foot complaints in a surgically treated mirror foot – a case report and review of the literature". S. Lalé, E. Burger, J. Bessems, **V. Pollet**, C. van Nieuwenhoven. Foot Ankle Surg. 2017; 23 (4).

"A long term follow-up study of the development of hip disease in Mucopolysaccharidosis type VI." Oussoren E, Bessems JHJM, **Pollet V**, van der Meijden JC, van der Giessen LJ, Plug I, Devos AS, Ruijter GJG, van der Ploeg AT, Langeveld M. Mol Genet Metab. 2017; S1096-7192(17)30176-2.

"The Dutch version of the Oxford Ankle and Foot Questionnaire for Children: Useful for evaluation of pediatric foot problems in groups." Burger E, Selles R, van Nieuwkasteele S, Bessems G, **Pollet V**, Hovius S, van Nieuwenhoven C.Foot Ankle Surg. 2019; 25(2):204-210

"Relative Risk And Incidence For Developmental Dysplasia of the Hip." **Pollet V**, Percy V, Prior H. - J Pediatr 2017; 181:202-207.

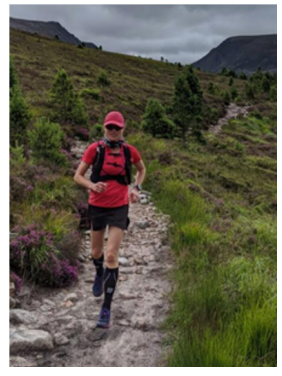
"Results of Pavlik harness treatment in children with dislocated hips between 6 and 24 months." **Pollet V,** Pruijs H, Sakkers R, Castelein R. J pediatr Orthop, 2010; 30(5):437-42

“Os trigonum Syndrome”, Wybenga JM, Biemans JM, **Pollet V**.
JBR-BTR 2008, May-Jun; 91(3):128-129.

“The role of the Rolimeter in quantifying knee instability compared to the functional outcome of ACL reconstructed and conservatively treated knees”, **Pollet V**, Barrat D, Meirhaeghe E, Vaes P, Handelberg F. Knee Surg Sports Traumatol Arthrosc. 2005 Jan;13(1):12-8.

“Stress fracture at the acetabular roof: case report and value of MRI.” **Pollet V**, Bellemans M, Damry N, Lamoureux J.Acta Orthopaedica Belgica, vol 65 – 4, 1999, 518 – 520.

CURRICULUM VITAE



Ms Virginie Pollet is born on the 9th of February 1972 in Waregem, Belgium. She studied Latin-Science at the Onze Lieve Vrouw Hemelvaart institute in Waregem followed by graduating in Medicine (Cum Laude) at the Free University in Brussels (VUB) in 1997.

Her love for Paediatric Orthopaedic Surgery started during her first year of surgical rotation in Managua, Nicaragua, where she also worked as a volunteer at the Velez País Children’s hospital in Managua.

Upon her return to Belgium, she continued her training in Orthopaedic surgery and traumatology. During this time, she also obtained a post-graduate degree in Sports medicine (Magna Cum Laude), was awarded the ABA (Belgian Arthroscopy Society) travel fellowship for best clinical paper and obtained a post-graduate certificate in disaster medicine as she volunteered on the VUB medical team at large events around Brussels. She also worked for the Flemish anti-doping agency on weekends at major national and international sports events.

Upon graduation as an Orthopaedic surgeon in 2003, she accepted a position as consultant at the Twenteborg hospital in the Netherlands in 2003, where her son Julian was born in 2005.

In 2007, two months of observership at the Scottish Rite Children’s Hospital (Prof. Herring) in Dallas, USA, triggered to pursue a Clinical fellowship at the Wilhemina Children’s Hospital of the University Medical Center in Utrecht, The Netherlands (Prof dr. Castelein), followed by a two-year fellowship program at Robert-Debré Children’s hospital in Paris, France (Prof. Penneçot).

During this time, she was awarded with the Travel Fellowship of EPOS in 2009 traveling in the North-East of the USA, visiting major Paediatric orthopaedic centers in Iowa, Chicago, St Louis and Boston and became an alumni of the EPOS Marie Curie instructional courses held in Vienna, Helsinki, Marseille and Tel Aviv.

In 2010, she accepted a position as assistant professor at the University of Manitoba in Winnipeg, Canada, but due to illness of her father, she returned to Europe in 2014 and worked as a consultant at the Sophia Children’s Hospital of the Erasmus Medical Center in

Rotterdam, the Netherlands (Prof Dr. Verhaar).

In 2018, she moved to the UK and is now working as a consultant at the Royal Manchester Children's Hospital.

She is currently also a board member of the executive committee of the European Paediatric Orthopaedic Society.

In her free time, she enjoys the outdoors and the freedom of running on scenic trails.

ACKNOWLEDGEMENTS/DANKWOORD

This dissertation did not just come about. It is the result of many years of effort, persistence, many evening & weekend hours, in addition to a busy job as a pediatric orthopedic surgeon and having worked in 4 different countries. I couldn't have done this without the help of many. So I want to thank everyone for your help and for continuing to believe in me that I could do this one day!

An extra word of thanks to:

My co-supervisor Dr. Ralph Sakkers. Dear Ralph, thank you for your continued support during all these years and the many hours (what's app and in vivo during the EPOS conferences) discussing and brainstorming on how we are actually going to tackle hip dysplasia? I think our conversations are not alone fun but also inspiring and we have come already a long way! Our collaboration has led to international recognition, whereby we dare to go against the "standard of care" and to question current beliefs about DDH that are not always received without resistance. However, this is science that leads to progress and innovation. Without a critical eye, we will not be one step further in the coming 50 years... I hope that our collaboration does not end here and that we continue to better understand and shape DDH, because in the end it is all about the shape of the hip!

Next, a word of thanks to my supervisor prof. Dr. Castelein. Dear René, you rightly pointed out to me that it would be best to stay in one place ("for the time being" that is Manchester) until I have completed this thesis. I finally succeeded! Thank you for your patience and the freedom you have given me to shape this work. Your research experience and clinical outlook has brought this thesis to a higher level.

Dear Vanessa and Heather, thank you so much for your help and input identifying the risk factors in the province of Manitoba. I enjoyed our collaboration and learnt a lot about regional and cultural differences. My plan was to create a screening programme for the region based on our results, but due to unforeseen circumstances, I had to move back to Europe. I hope this will be in place soon!

Melinda, Michiel, Ad, Arnold, Christiaan, Cuno, Erik, Ralph, René, plaster room in the Sophia children's hospital, parents and patients, and everyone involved in the RCT abduction treatment! What an interesting and unique experience to be able to coordinate this type of study as a principal investigator. A bit of persistence was needed but we succeeded! Hopefully this will remain a good reference work for many years to come and will trigger a change in policy.

Lisa, Britt and Joshua, I really enjoyed guiding you during your master project and it was great to see that this resulted in two publications. Good luck with your further career. Erwin and Max, thank you for your help and insight as well as great research meetings in the Sophia Children's Hospital.

Dear Esmée, thank you for your support and friendship. We are clearly on the same wavelength! You were just one step ahead of me with your dissertation but you have further encouraged me to finish mine! I am not only looking forward to scientific collaboration on metabolic hip abnormalities, but also just socializing over a bite and a drink. Hopefully soon!

Last but not least, I would like to thank my family and friends for all the support, especially listening ear when I was a bit down, but also for sharing my enthusiasm when a new chapter was successfully completed! Roger and Julian, you had to miss me a lot while I spent the weekends and evenings doing research and work on this dissertation, as well as the many hours I spent running in nature to gather my thoughts and get inspiration! I can't thank you enough!!! My mom and my sister, always there for me! Love you!

Writing a dissertation is just like running a trail ultramarathon...you start, with passion and motivation, you encounter the necessary obstacles, hills become mountains, sun gives way to heavy rain showers, but you have to continue, because you can't go back...In good spirits you plod along, wondering why you are actually doing this, but you know that you are not alone, the support of family and friends will pull you through. Eventually, the finish is in sight, just hang on...Finishing this thesis gives me the same feeling of satisfaction. However, just like an ultra, it does not stop here...the next project is already lining up!

- I'd rather be a comma than a full stop -
Coldplay