Neonatal Ultrasound and Radiographic Markers of Hip Dysplasia in Young Adults

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abstract

OBJECTIVES: To examine radiologic outcomes at skeletal maturity of sonographically normal, immature, mildly, and severely dysplastic newborn hips.

METHODS: During 1988 to 1990, 11 925 newborns were enrolled in a randomized controlled trial examining screening strategies for developmental hip dysplasia. In total, 4469 were invited to clinical and radiologic follow-up 18 years later, of which 1735 had received neonatal ultrasound. Radiographic markers for dysplasia in left adult hips included the center-edge (CE) angle.

RESULTS: At follow-up, 984 of 1735 (56.7%) with newborn ultrasound met, of which 966 (614 females) had valid radiographs and were thus included. For females, 34 (10.2%) and 1 (0.3%) of the 332 sonographically normal left neonatal hips were judged borderline ($20^\circ \leq$ CE $< 25^\circ$) or dysplastic (CE $< 20^\circ$) at skeletal maturity respectively. Corresponding numbers were 36 (19.7%) and 3 (1.6%) of the 183 immature, 12 (15.6%) and 2 (2.6%) of the 77 mildly dysplastic, and 3 (13.6%) and 3 (13.6%) of the 22 severely dysplastic neonatal left hips ($P \leq .001$). In males, no associations were found. In females, adult joint hypermobility was associated with sonographic neonatal hip instability ($P = .046$), as well as with adult acetabular dysplasia ($P = .024$).

CONCLUSIONS: Significant associations between neonatal hip phenotypes and adult dysplasia were revealed in females. This indicates the possibility of different mechanisms affecting the course of developmental dysplasia of the hip for females and males, prompting consideration of prolonged clinical and radiologic follow-up for females with dysplastic neonatal hips. Results in males are limited by low numbers of dysplastic hips. The significance of joint hypermobility warrants further investigation.

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This study is registered on March 21, 2013, at ClinicalTrials.gov, #NCT01818934, https://clinicaltrials.gov/ct2/show/NCT01818934. Deidentified individual participant data will be made available upon publication to researchers who provide a methodologically sound proposal for use in achieving the goals of the approved proposal. Proposals should be submitted to karen.rosendahl@unn.no.

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WHAT'S KNOWN ON THIS SUBJECT: Despite early detection and treatment, developmental hip dysplasia can persist until early adulthood, increasing the risk of early osteoarthritis. Associations between neonatal hip ultrasound and radiographic acetabular dysplasia at 18 to 19 years are incompletely understood.

WHAT THIS STUDY ADDS: In females, neonatal phenotypes including sonographically normal, immature, mildly, and severely dysplastic hips were significantly associated with adult acetabular dysplasia. Further, adult joint hypermobility was associated with sonographic neonatal hip instability, as well as with adult acetabular dysplasia in females.

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Developmental dysplasia of the hip (DDH) is a congenital disorder, characterized by a shallow, or dysplastic, hip socket, with potential risks of developing osteoarthritis from young adulthood and serious functional disability.[1,2] When detected in the newborn period, DDH is typically treated with an abduction device for around 3 months. Management of late-detected DDH[3] is more challenging, and severe cases may require major, invasive surgery. The reported rate of late cases varies significantly.[4] Despite early detection and treatment, however, dysplasia can persist until early adulthood (residual dysplasia), increasing the risk of early osteoarthritis. According to the Norwegian Arthroplasty Register, osteoarthritis of the hip affects 1 in 10 >65 years of age, and during 2019, led to nearly 8000 hip replacements in Norway. In 8% of these patients, DDH was the underlying cause, increasing to nearly one-third in those <40 years of age.[5]

Over the last 3 decades, we have established a unique, longitudinal, population-based hip "phenobank," which includes standardized ultrasound (US) examinations of the newborn hip, as well as radiographs at skeletal maturity. We have previously shown that early life factors significantly predicting radiographic acetabular dysplasia at age 18 to 19 years included female gender, breech, low acetabular inclination (α) angle and sonographic hip instability, and abduction treatment, as well as the velocity of growth during childhood. A positive family history of DDH was not associated with acetabular dysplasia at skeletal maturity.[6] Previous studies have shown that, on the basis of US, around 84% of all newborns have normal hips, whereas 13% have at least 1 immature and 3.4% have at least 1 dysplastic hip.[7] Most of the immature and around half of the mildly dysplastic hips normalize spontaneously within 3 to 6 months, without treatment. The radiologic outcome at skeletal maturity has, however, not yet been examined. We hypothesized that radiographic acetabular morphology at skeletal maturity is associated with sonographic acetabular morphology in neonates. Here, we report on the radiologic outcome at skeletal maturity of 4 neonatal hip types: Sonographically normal, immature, mildly, and severely dysplastic hips.

METHODS

Data Collected in the Neonatal Period, During the Original Randomized Controlled Trial, 1988 to 1990: Ultrasound Assessment of Hip Morphology and Stability

During 1988 to 1990, 11 925 newborns were enrolled in a clinical trial designed to evaluate the effectiveness of 3 different screening strategies for DDH: Universal US; selective US based on anamnestic risk factors (breech presentation at delivery, a positive family history, foot deformities) or clinical hip instability; and no US. All 3 groups had a clinical hip examination performed within the first 3 days of life by 1 of 8 pediatricians with >2 years of experience in doing the Barlow/Ortolani tests.[8]

In total, 4229 of the 11 925 newborns had a hip US performed within the first 3 days of life. The acetabular morphology and inclination were assessed by measuring the α angle (Fig 1), followed by a stability test (normal, pathologically unstable [significant movement but not dislocatable], dislocatable, or dislocated).[9] Subtle instability, or elastic feathering, was considered normal. Several other parameters were also assessed on neonatal hip US. The femoral head coverage was graded into <50%, 50%, or >50% by using a vector line as advised by Zieger et al.[10] Moreover, we measured the β angle (acetabular roof angle; the angle formed between the baseline [iliac line] and the cartilage roof line), and noted whether the epiphysis was ossified at birth. Finally, we described the acetabular corner at age 4 weeks as sharp, slightly rounded, or rounded, and noted whether an acetabular notch had been formed.

Indications for immediate abduction treatment were persistent dislocatable or dislocated hips on a repeated, single-examiner clinical examination, or severe sonographic dysplasia (α <43°) irrespective of clinical and sonographic instability. Hips with a mildly dysplastic morphology (43°≤

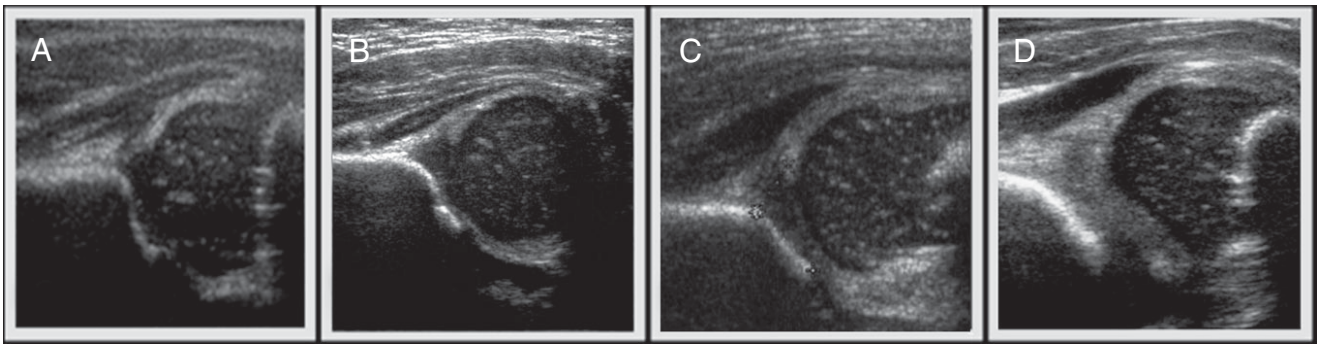

FIGURE 1

Neonatal hip US performed by a single observer in a standardized manner on the basis of Graf's method, classifying the hips into normal (A, α angle ≥60°), immature (B, 50°≤ α angle <60°), mildly dysplastic (C, 43°≤ α angle <50°), or severely dysplastic (D, α angle <43°)[26].

α <50°) were treated if they were also clinically or sonographically dislocatable/dislocated. Sonographically immature (50°≤ α <60°) or mildly (43°≤ α <50°) dysplastic but clinically stable hips had sonographic and clinical surveillance every fourth week until normalization, or until treatment was instigated because of lack of improvement.[8]

Routines for abduction treatment included a Frejka's pillow from birth until around 3 to 4 months of age. If further abduction treatment was required, an age-adapted stiffer orthosis was used until satisfactory acetabular shape and femoral head position were reached radiographically. Late-detected cases of DDH were defined as cases occurring after 1 month of age.[11,12]

Attendance and Dropout at Follow-Up

We invited 4469 of the initial 11925 randomized controlled trial (RCT) participants (all those born in 1989 [n = 3968], as well as all participants with a pathologic neonatal hip US born in 1988 and 1990 [n = 501]), for a clinical and radiologic follow-up 18 to 19 years later, in 2007 to 2009, of which 2370 (53%) met. Of the 4469 invited, 1735 (945 females, 790 males) also had a neonatal hip US, and of the 2370 young adults who met at follow-up, 984 (622 females, 362 males) also had a neonatal hip US (Supplemental Fig 5). For the 1735 (945 females, 790 males) with neonatal US who were invited to follow-up, the 984 (622 [63.2%] females, 362 males) who attended have been compared with the 751 (323 [43.0%] females, 428 males) who dropped out and did not attend, for females and males separately (Supplemental Tables 9 and 10). Follow-up attendance rate was 65.8% (622 of 945) and 45.8% (362 of 790) for females and males, respectively. This comparison of neonatal characteristics showed that birth weight, randomization group at initial RCT, breech, and reported family history of DDH did not differ between the males who attended and those who did not. For females, breech (P = .032) and reported family history of DDH (P = .002) differed between attendees and dropouts, whereas birth weight and randomization group did not. We have recently shown in an extended version of this cohort that family history of DDH does not predict acetabular dysplasia at skeletal maturity, and the difference should therefore not affect the results in this article.[6]

Data Collected at Skeletal Maturity (18–19 Years): Radiographic Protocol, Evaluation of Images, and Radiographic Measurements for Acetabular Dysplasia

The follow-up included radiologic assessment, clinical examination, questionnaires, collection of anthropometric data (height and length) from birth to puberty, and collection of saliva from a subsample of 1800 subjects.

The radiologic assessment included a weight-bearing, anteroposterior view and a frog-leg view, according to a standardized protocol.[13] All radiographs were obtained by 1 specifically trained radiographer, using a low-dose digital radiography technique (DigitalDiagnost system, version 1.5, Philips Medical Systems, Best, Netherlands). The film/focus distance was 1.2 m and centered 2 cm proximal to the symphysis. The radiographs were measured in the digital measurement program "Adult DDH" (University of Iowa Hospitals and Clinics, Iowa City, Iowa, United States), by 3 trained examiners. Detailed descriptions of the digital measurement program, of its accuracy and of the measurements included, have been reported previously.[13] Because there is no clear consensus on the definition of acetabular dysplasia at skeletal maturity, the 4 most common radiographic measurements associated with acetabular dysplasia were assessed (Fig 2): The center-edge (CE) angle of Wiberg, the femoral head extrusion index (FHEI), the acetabular depth-width ratio (ADR), and Sharp's angle. For FHEI, ADR, and Sharp's angle, the measured values were dichotomized into normal (≤2 SD) or pathologic (>2 SD) on the basis of published reference values.[14] For the most commonly used measurement, the CE angle, we subgrouped into normal (≥25°), borderline (≥20°–25°), or dysplastic (<20°). All hips were also assessed subjectively by the senior author, who revealed no cases of an undergone avascular necrosis as a complication of treatment.

The clinical examination included the Beighton score for joint laxity/hypermobility. This score consists of 5 elements, of which 1 (the spine) accounts for 1 point, and the remaining 4 (knee, elbow, thumb, and fifth finger) are scored for right and left side separately. Maximum score is therefore 9 points, with a score of 4 points and above indicative of pathologic joint hypermobility.[15,16]

Ethics

The research protocol, including analyses of the nonresponders, was approved by the Regional Ethical Committee for Medical and Health Research (Regional etisk komite [in Norwegian] 20594). The protocol was registered at ClinicalTrials.gov (NCT01818934, March 21, 2013). All participants of the follow-up study gave written informed consent according to the 1964 Declaration of Helsinki.

Statistical Analysis

Continuous data are presented as means and SDs, and dichotomous data as proportions. All analyses are performed for females and males separately. Differences according to sex and side were examined using t tests or Fisher's exact/χ^2 tests as appropriate, whereas differences in outcome measures across sonographic hip types were examined using Fisher's exact/χ^2 tests or 1-way between groups analysis of variance with post-hoc tests and measurement of effect size (η^2; 0.01 = small effect, 0.06 = medium, and 0.14 is a large effect), as appropriate.[17] All statistical analyses were performed using IBM SPSS version 29 (IBM, Chicago, Illinois). The level of statistical significance was set at 5% (P < .05).

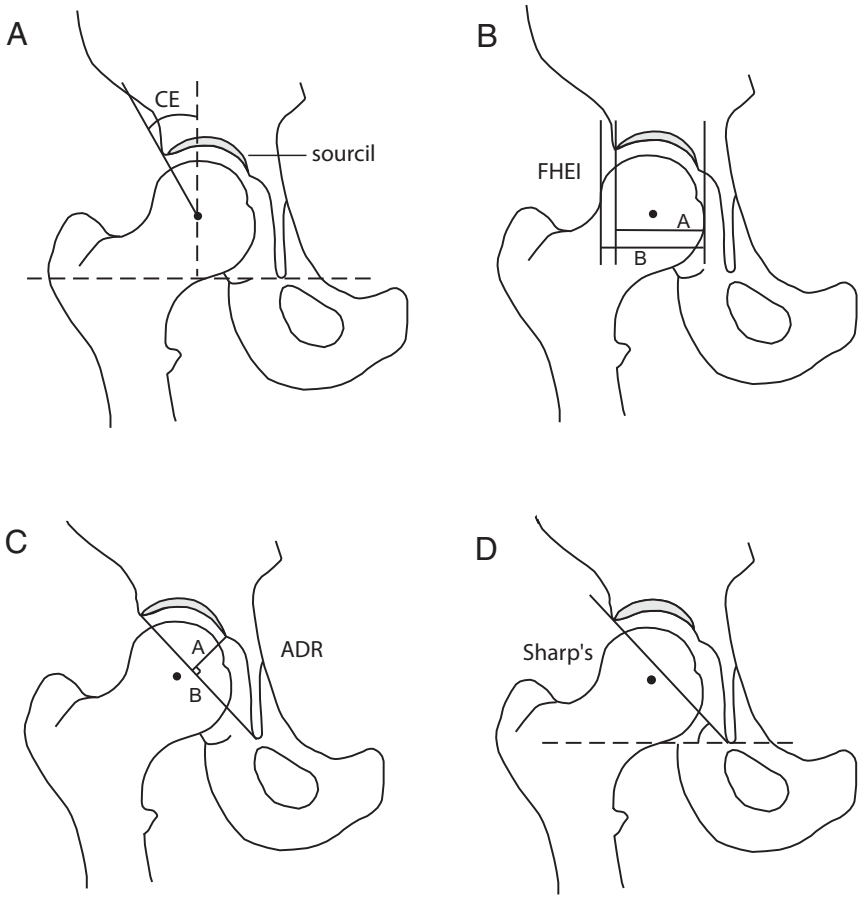

FIGURE 2
The 4 most common radiographic measurements associated with acetabular dysplasia at skeletal maturity. Measurements describing the position of the femoral head relative to the acetabular cavity: CE angle of Wiberg (A), and FHEI (B). Measurements describing the acetabular anatomy: ADR (A/B) x 1000) (C), and Sharp's angle (D)[26].

RESULTS

At follow-up, 966 (614 females) of the 2340 18- to 19-year-olds attending had received a newborn hip US and also had a technically adequate anteroposterior hip radiograph at age 18 to 19 years, and were thus included in this study. Preliminary analysis showed that the results differed significantly by sex but not by side. The results are therefore reported for left hips only, and for males and females separately.

Neonatal Sonographic Hip Phenotypes

Of 614 female left neonatal hips, 332 were morphologically normal on US in the newborn period, whereas 183 were immature, 77 were mildly dysplastic, and 22 were severely dysplastic. Of 352 male left neonatal hips, 277 were morphologically normal on US in the newborn period, whereas 61 were immature, 12 were mildly dysplastic, and 2 were severely dysplastic. Neonatal hip instability on US

TABLE 1 Neonatal Characteristics for 614 Females With Normal, Immature, or Dysplastic Left Hips

		US Morphology at Birth				
	Normal, $n = 332$	Immature, $n = 183$	Mild Dysplasia, $n = 77$	Severe Dysplasia, $n = 22$	Total, $n = 614$	*P*
Known risk factors for neonatal DDH						
Positive family history	58	29	21	6	114	.067
Breech	30	19	12	6	67	.029
Neonatal hip instability on US[a]	4	22	73	21	120	<.001
Early abduction treatment	15	22	77	20	134	N/A
Late abduction treatment	6[b]	1	0	0	7	N/A

N/A, not applicable.
[a] Included significant movement of hip without the hip being dislocatable, hip being dislocatable, or hip being dislocated.
[b] Additional treatment: 1 female had a cast for 12 months.

TABLE 2 Neonatal Characteristics for 352 Newborn Males With Normal, Immature, or Dysplastic Left Hips

	US Morphology at Birth				
	Normal, $n = 277$	Immature, $n = 61$	Dysplasia (Mild + Severe), $n = 12 + 2$	Total, $n = 352$	*P*
Known risk factors for neonatal DDH					
Positive family history	58	11	2 + 1	99	.710
Breech	16	3	0	19	.824
Neonatal hip-instability on US[a]	1	5	11 + 2	19	<.001
Early abduction treatment	5	5	12 + 2	24	N/A
Late abduction treatment	0	0	0	0	N/A

N/A, not applicable.
[a] Included significant movement of hip without the hip being dislocatable, hip being dislocatable, or hip being dislocated.

was significantly associated with an immature or dysplastic acetabulum for both sexes, whereas breech position was significantly associated for females only. A positive family history was not associated with immature or dysplastic acetabulum in neither males nor females. Neonatal characteristics are given in Tables 1 and 2 for females and males separately. No females or males received cast treatment after early abduction treatment. One female with a late-detected dysplasia at 6 months of age had a cast for 12 months. No females or males underwent hip surgery.

Mean Radiologic Hip Measurements at Skeletal Maturity by Sex and by Neonatal Sonographic Hip Phenotypes

At time of follow-up, females ($n = 614$) had significantly higher mean Sharp's angle and lower mean CE angle as compared with males ($n = 352$) ($P < .001$). No sex differences were seen for ADR ($P = .499$) or FHEI ($P = .817$). Mean values for the Sharp's angle, CE angle, ADR, and FHEI, for each of the neonatal sonographic hip phenotypes, are reported for females and males separately (Table 3 and 4). For females, the mean values for Sharp's, CE angle, and FHEI at skeletal maturity differed significantly between neonatal phenotype groups. No significant difference was found for ADR (Table 3). For males, no differences in mean radiologic measurements were found across the neonatal sonographic hip phenotypes.

Radiologic Classification into Normal, Borderline, or Dysplastic at Skeletal Maturity by Sex and Neonatal Sonographic Hip Phenotypes

For females, 34 (10.2%) and 1 (0.3%) of the 332 sonographically normal left neonatal hips were judged borderline or dysplastic at skeletal maturity, respectively, when based on the CE angle. Corresponding numbers were 36 (19.7%) and 3 (1.6%) of the 183 immature, 12 (15.6%) and 2 (2.6%) of the 77 mildly dysplastic, and 3 (13.6%) and 3 (13.6%) of the 22 severely dysplastic neonatal left hips ($P \leq .001$) (Table 5). Significant associations between neonatal hip phenotypes and acetabular dysplasia at skeletal maturity based on the Sharp's angle ($P < .044$) and on the FHEI ($P > .001$) were also revealed. In males, no such associations were found (Table 6). For males, 28 (10.1%) and 5 (1.8%) of the 277 sonographically normal left neonatal hips were judged borderline or dysplastic, respectively, when based on the CE angle. This was true for 7 (11.5%) and 1 (1.6%) of 61 immature and 1 (8.3%) and 1 (8.3%) of 14 dysplastic neonatal hips ($P = .700$).

Depending on the radiologic measurement and corresponding cutoff value used, between 0.6% and 10.5% of female hips judged to be sonographically normal at birth showed signs of dysplasia (including borderline for the CE angle) at skeletal maturity (Table 5). Corresponding figures were 2.7% to 21.3% of the immature, 2.6% to 18.2% of the mildly dysplastic, and 9.1% to 27.2% of the severely dysplastic hips (Fig 3). For males, the corresponding figures were 1.1% to 11.9% for normal neonatal hips, 1.6% to 13.1% for immature hips, and 0% to 14.2% for dysplastic (mildly or severely) hips, respectively (Table 6, Fig 4).

Neonatal Ultrasound Features or Measurements of Significance for the CE Angle as Radiologic Outcome of Hip Dysplasia at Skeletal Maturity

In females, acetabular morphology on US in the newborn period was significantly associated with a borderline/dysplastic

TABLE 3 Mean Values, Radiologic Measurements at Skeletal Maturity by Ultrasound Morphology at Birth, for 614 Females, Left Hips

Radiologic Measurement at Skeletal Maturity	US Morphology at Birth					
	Normal, $n = 332$	Immature, $n = 183$	Mild Dysplasia, $n = 77$	Severe Dysplasia, $n = 22$	Total, $n = 614$	P[a]
Sharp's° (SD°)	40.7 (3.3)	41.5 (3.7)	41.7 (2.9)	42.7 (3.0)	41.1 (3.4)	.006
CE Wiberg° (SD)	31.5 (5.6)	30.2 (5.9)	30.9 (5.9)	27.5 (6.6)	30.9 (5.8)	.003
ADR, $^{0}/_{00}$ (SD)	301.6 (34.6)	294.0 (34.6)	300.9 (36.6)	289.7 (48.3)	299.0 (35.5)	.066
FHEI, % (SD)	87.1 (6.3)	85.4 (6.4)	85.9 (6.1)	82.5 (7.7)	86.3 (6.4)	<.001

[a] *P* value refers to a 1-way analysis of variance.

TABLE 4 Mean Values, Radiologic Measurements at Skeletal Maturity by Ultrasound Morphology at Birth, for 352 Males, Left Hips						
Radiologic Measurement at Skeletal Maturity	US Morphology at Birth					
	Normal, $n = 277$	Immature, $n = 61$	Mild Dysplasia, $n = 12$	Severe Dysplasia, $n = 2$	Total, $n = 352$	P[a]
Sharp's° (SD°)	39.0 (3.3)	38.8 (3.8)	38.3 (3.7)	38.4 (1.7)	39.0 (3.4)	.852
CE Wiberg° (SD)	32.4 (5.8)	32.5 (6.2)	31.4 (5.7)	36.8 (6.8)	32.4 (5.9)	.695
ADR, $^{0}/_{00}$ (SD)	299.0 (34.9)	294.7 (34.2)	274.7 (20.2)	300.0 (17.4)	297.2 (34.5)	.111
FHEI, % (SD)	86.4 (6.0)	86.6 (6.3)	85.0 (6.1)	87.4 (4.4)	86.4 (6.0)	.839

[a] P value refers to a 1-way analysis of variance.

left hip at skeletal maturity. No associations were detected for sonographic instability, the β angle, an ossified epiphysis or femoral head coverage at birth, nor for the shape of the acetabular corner at 4 weeks follow-up (Table 7). In males, none of the above factors were associated with a borderline/dysplastic hip at skeletal maturity (Table 8).

A Beighton score of 4 or more, indicative of joint hypermobility, was seen in 136 of 520 (26.2%) of females with a normal CE angle at skeletal maturity, versus 35 of 94 (37.2%) of those with a borderline or dysplastic left hip ($P = .033$). For males, the corresponding figures were 24 of 309 (7.8%) vs 1 of 43 (2.3%) ($P = .338$). Similar, there was a positive association between a positive Beighton score and hip instability as assessed by US in the newborn period for females (Fisher's exact test $P = .031$) but not for males ($P = .636$).

DISCUSSION

We have shown that, in females, immature or dysplastic hips in the neonatal period are associated with a poorer acetabular shape at skeletal maturity, as assessed radiographically by the CE angle, Sharp's angle, and the FHEI, but not by the ADR. No such associations were seen for males. Femoral head coverage as measured sonographically at birth was not associated with acetabular immaturity or dysplasia at skeletal maturity in either sex. Moreover, in females, joint hypermobility at 18 to 19 years of age was associated with both neonatal hip instability and with later borderline/dysplasia.

One of the main challenges of dysplasia at skeletal maturity is the lack of a strict definition and precise measurements upon which a diagnosis can be based. In the current study, we included the 4 most widely used measurements, namely the CE angle and the FHEI as measures of femoral head coverage, Sharp's angle as a measure of acetabular inclination, and the ADR, for which we previously have published reference values in 18- to 19-year-olds.[14] In the current study, we used 2 SDs as a cutoff to define normal versus pathologic hips, except for the CE angle, where the commonly used definitions, normal, borderline, or dysplastic, were applied.

Despite early abduction treatment according to a predefined protocol, between 9.1% and 27.2% of sonographically dysplastic left newborn female hips showed residual borderline/dysplasia when radiographed 18 years later, depending on the radiographic measurement used. In comparison, 0.6% to 10.5% of sonographically normal, nontreated hips showed radiographic borderline/dysplasia at age 18 to 19 years. This contrasts the results found for males, who had less dysplasia at skeletal maturity for all neonatal US hip types.

TABLE 5 Classification of Left Hips at Skeletal Maturity Into Normal, Borderline, or Dysplastic Based on the CE Angle of Wiberg, and Normal/Dysplastic Based on Sharp's Angle, ADH, and FHEI, in 614 Females, Left Hips						
Classification Based on Radiologic Measurements at Skeletal Maturity	US Morphology at Birth, Female					
	Normal, $n = 332$	Immature, $n = 183$	Mild Dysplasia, $n = 77$	Severe Dysplasia, $n = 22$	Total, $n = 614$	P
CE angle of Wiberg						<.001
Normal	297 (89.5%)	144 (78.7%)	63 (81.8%)	16 (72.7%)	520 (84.7%)	
Borderline	34 (10.2%)	36 (19.7%)	12 (15.6%)	3 (13.6%)	85 (13.8%)	
Dysplastic	1 (0.3%)	3 (1.6%)	2 (2.6%)	3 (13.6%)	9 (1.5%)	
Sharp's angle						.044
Normal	316	163	72	19	570	
Dysplastic (>46)	16 (4.8%)	20 (10.9%)	5 (6.3%)	3 (13.6%)	44 (7.2%)	
ADR						.499
Normal	322	177	74	20	593	
Dysplastic (<235)	10 (3.0%)	6 (3.3%)	3 (3.9%)	2 (9.1%)	21 (3.4%)	
FHEI						<.001
Normal	330	178	75	19	602	
Dysplastic	2 (0.6%)	5 (2.7%)	2 (2.6%)	3 (13.6%)	12 (2.0%)	

TABLE 6 Classification of Left Hips at Skeletal Maturity, Into Normal, Borderline or Dysplastic Based on the CE Angle of Wiberg, and Normal/Dysplastic Based on Sharp's Angle, ADH, and FHEI in 352 Males

Classification Based on Radiologic Measurements at Skeletal Maturity	US Morphology at Birth, Male				
	Normal, $n = 277$	Immature, $n = 61$	Mild and Severe Dysplasia, $n = 14$	Total, $n = 352$	*P*
CE angle of Wiberg					.700
Normal	244 (88.1%)	53 (86.9%)	12 (85.7%)	309 (87.8)	
Borderline	28 (10.1%)	7 (11.5%)	1 (7.1%)	36 (10.2%)	
Dysplasia	5 (1.8%)	1 (1.6%)	1 (7.1%)	7 (2.0%)	
Sharp's angle					.832
Normal	271	60	14	345	
Dysplastic	6 (2.2%)	1 (1.6%)	0 (0.0%)	7	
ADR					.381
Normal	274	59	14	347	
Dysplastic	3 (1.1%)	2 (3.3%)	0 (0.0%)	5 (1.4%)	
FHEI					.858
Normal	274	60	14	348	
Dysplastic (<74)	3 (1.1%)	1 (1.6%)	0 (0%)	4 (1.1%)	

At follow-up at 18 to 19 years of age, females had a significantly higher acetabular inclination angle (Sharp's angle), a poorer femoral head coverage (CE angle), and a higher proportion of dysplasia across neonatal US hip phenotypes, as compared with males. Moreover, for females, but not for males, there was a clear association between sonographic dysplasia at birth and later hip dysplasia as assessed by 3 of the 4 radiologic markers applied in the study. This indicates the possibility of different mechanisms affecting the natural course of DDH for females and males through childhood and adolescence. Although, outside the scope of this article, obesity or the velocity of growth during childhood might impact the course of DDH from neonatal dysplasia to later acetabular dysplasia. Because immature and dysplastic hips in the neonatal period are associated with a poorer acetabular shape at skeletal maturity, a prolonged clinical and radiologic follow-up for girls with dysplastic neonatal hips until normalization might have beneficial value.

The association between general joint hypermobility and dysplasia at skeletal maturity may in part explain

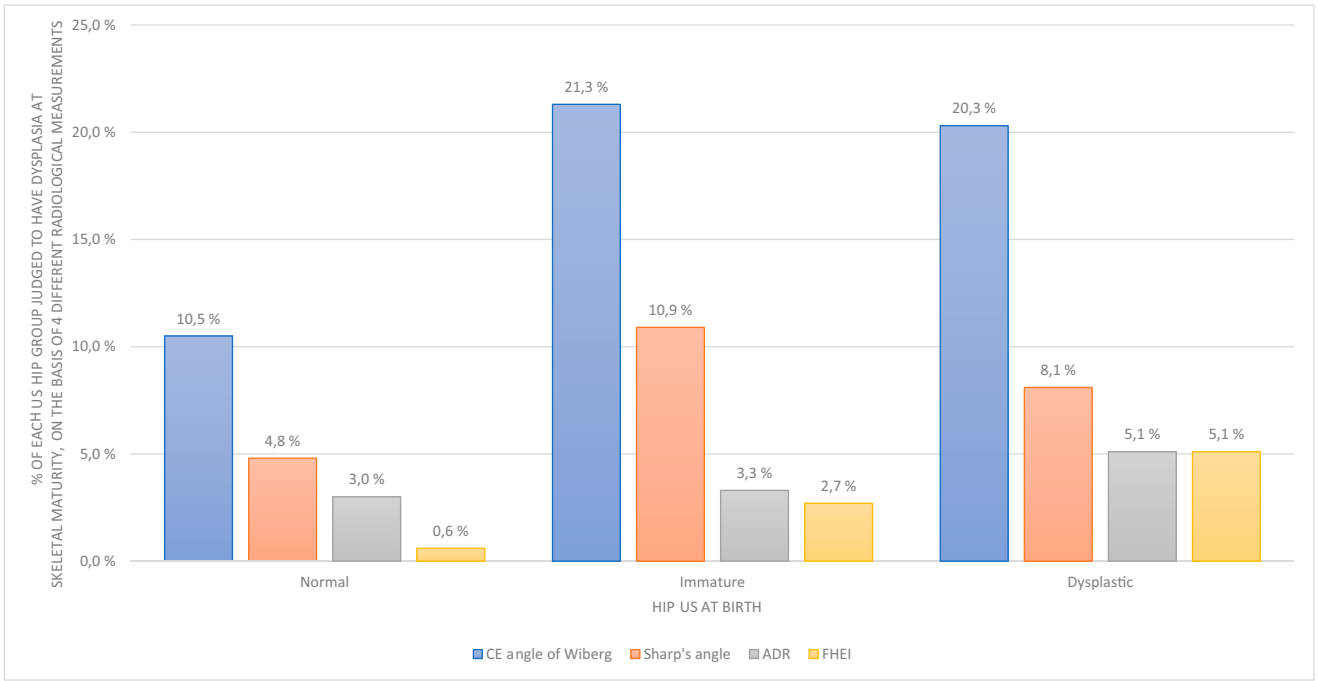

FIGURE 3
Percentage of sonographically normal ($n = 332$), immature ($n = 183$), or dysplastic hips ($n = 77 + 22$) at birth, judged to have borderline/dysplasia on the basis of the CE angle of Wiberg, and dysplasia on the basis of Sharp's angle, ADH, and FHEI at skeletal maturity. Six-hundred and fourteen females, left hips.

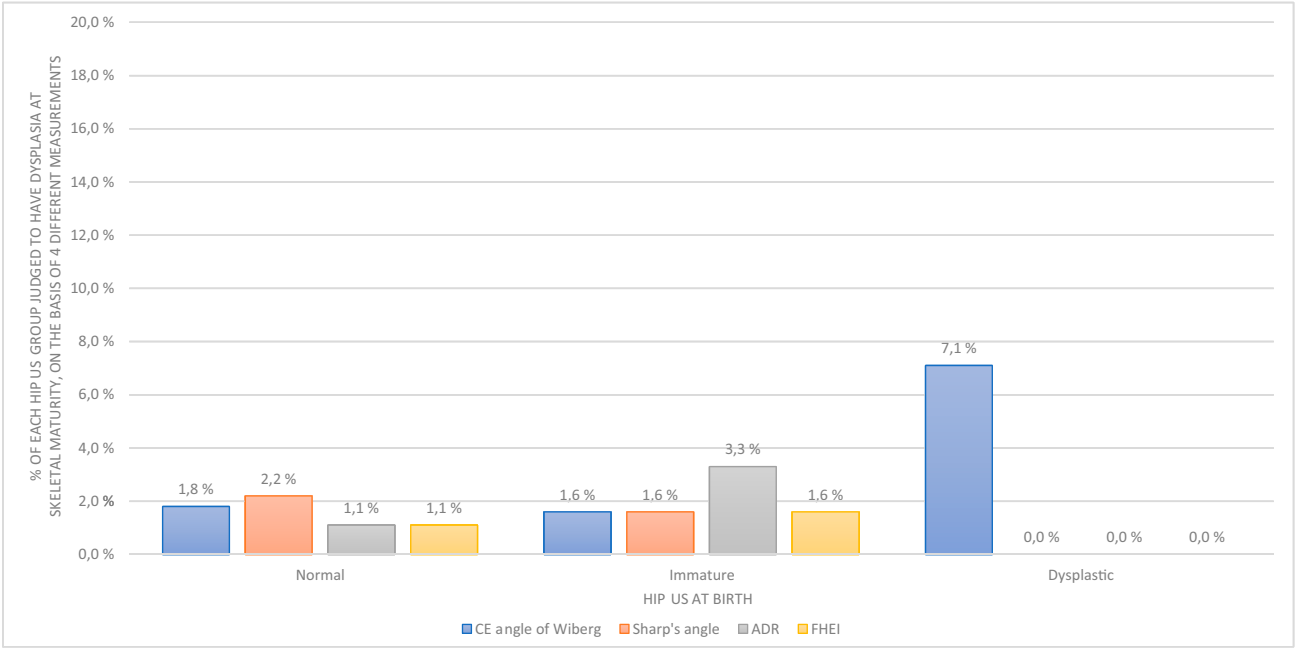

FIGURE 4

Percentage of sonographically normal ($n = 277$), immature ($n = 61$), or dysplastic hips ($n = 14$ [12 + 2]) at birth, judged to have borderline/dysplasia on the basis of the CE angle of Wiberg, and dysplasia on the basis of Sharp's angle, ADH, and FHEI at skeletal maturity. Three-hundred and fifty-two males, left hips.

the difference between males and females, and this interesting finding warrants further investigation. A related finding was recently reported in a study of 1004 adult patients presenting with hip pain, of whom one-third were diagnosed with DDH. The prevalence of generalized joint hypermobility was significantly higher in patients with DDH, as compared with those without, and was higher in females, as well as in the younger age group.[18]

TABLE 7 Neonatal Ultrasound (US) Features/Measures for Those Having Normal Hips as Assessed by the CE Angle of Wiberg at Skeletal Maturity Versus Those Having Borderline/Dysplastic Hips ($n = 614$ Female Left Hips)

	Normal CE Angle ($n = 520$)	Borderline/Dysplastic ($n = 94$)	*P*
At birth ($n = 614$)			
US morphology at birth, *n* (%)			.002
Normal	297 (57.1)	35 (37.2)	
Immature	144 (27.7)	39 (41.5)	
Dysplastic	79 (15.2)	20 (21.3)	
Additional US measures/features			
US instability, *n* (%)[a]	97 (18.8)	23 (24.7)	.202
Ossified epiphysis, *n* (%)	6 (1.2)	0 (0.0)	.368
β angle, mean°, (SD°)[b]	63.4 (7.2)	65.0 (7.3)	.050
Femoral head coverage ($n = 558$), *n* (%)			
>50%	388 (82.9)	70 (77.8)	.488
50%	66 (14.1)	17 (18.9)	
<50%	14 (3.0)	3 (3.3)	
At 4 wk ($n = 153$)			
Acetabular corner, *n* (%)			
Sharp	69 (54.8)	10 (37.0)	.383
Slightly rounded	32 (25.4)	10 (37.0)	
Rounded	12 (9.5)	4 (14.8)	
Acetabular notch	13 (10.3%)	3 (11.1%)	

[a] Included significant movement of hip without the hip being dislocatable, hip being dislocatable, or hip being dislocated.
[b] Independent samples *t* test.

TABLE 8 Neonatal Ultrasound Features/Measures for Those Having Normal Hips as Assessed by the CE Angle of Wiberg at Skeletal Maturity Versus Those Having Borderline/Dysplastic Hips (n = 352 Male Left Hips)

	Normal CE Angle of Wiberg (n = 315)	Borderline/Dysplastic (n = 42)	*P*
US at birth (%)			.939
Normal	244 (79.0)	33 (76.7)	
Immature	53 (17.2)	8 (18.6)	
Dysplastic	12 (3.9)	2 (4.7)	
US instability (%)[a]	17	2	0.814
Ossified epiphysis	2 (0.7)	0 (0)	.753
Additional US measures/features			
At birth			
β angle, mean°, (SD°)[b]	61.1 (6.7)	59.9 (6.7)	.271
Femoral head coverage, (n = 286), n (%)			.739
>50%	229 (90.9)	31 (91.2)	
50%	19 (7.5)	3 (8.8)	
<50%	4 (1.6)	0 (0.0)	
At 4 wk (n = 61)			
Acetabular corner, n (%)			
Sharp	27 (54.0)	8 (72.7)	.465
Slightly rounded	18 (36.0)	2 (18.2)	
Rounded	3 (6.0)	0 (0.0)	
Acetabular notch	2 (4.0)	1 (9.1)	

[a] Included significant movement of hip without the hip being dislocatable, hip being dislocatable, or hip being dislocated.
[b] Independent samples t test.

Because the current study showed that joint hypermobility was associated with both neonatal hip instability, and with dysplasia at 18 year of age in females, we suggest that the neonatal instability be assessed both clinically and sonographically.

Interestingly, we found that, in females, between 0.6% and 10.5% of hips judged to be sonographically normal at birth showed borderline or dysplastic hips, depending on the radiologic measurement used, at skeletal maturity. Corresponding figures were 2.7% to 21.3% of the immature and 5.1% to 20.3% of the dysplastic hips. When excluding the borderline dysplastic and only looking at classic dysplastic adult hips, the figures dropped to 0.3% to 4.8% for sonographically normal hips, 1.6% to 10.9% for immature hips, and 5.1% to 8.1% for dysplastic hips. Thus, despite immediate abduction treatment of all sonographically dysplastic hips from birth, except for those being mildly dysplastic and stable, a relatively high proportion showed borderline or dysplasia at skeletal maturity. Our results are in line with a recent systematic review and meta-analysis, demonstrating a prevalence of borderline dysplasia of 19.8% to 23.3% in the asymptomatic general population based on measurements of the CE angle.[19] One might speculate why hips, judged to be sonographically normal and stable at birth, can end up as borderline or dysplastic at 18 to 19 years of age. However, several studies have shown discordant findings between US and radiography, reflecting that the 2 methods measure different anatomic features. In a study of 90 dysplastic neonatal hips, treated until sonographically normal using Graf's technique, a hip radiograph at 15 months of age revealed that 60% had residual dysplasia.[20] Another study, applying a dynamic US technique, showed similar findings, with 29% being dysplastic at 5 months of age.[21] Using Rosendahl's approach, we found that 8% of initially mildly dysplastic hips, judged to be sonographically normal after 3 to 4 months of abduction treatment, showed residual dysplasia radiographically at 1 year of age.[22] Indeed, although a hip radiograph represents a sum of overlapping acetabular contours, the standard US plane provides 1 image plane through the mid-acetabulum. We suggest including an additional plane through the anterior and most-affected part of the acetabulum to help monitoring acetabular development until normalization. Another option might be three-dimensional US; however, the method needs further validation.[23]

Our study did not show any associations between femoral head coverage as assessed sonographically at birth and later dysplasia, questioning the value of this US marker. A previous study has shown that the femoral head coverage as measured on the standard coronal view is highly influenced by hip instability, with the risk of overcalling hip dysplasia.[24] This might also be true for the β angle as introduced by Graf, and later widely used as part of the static Graf technique.[25] On the basis of our findings, the measurement of the α angle appears more accurate and reliable than the femoral head coverage to assess the acetabular morphology in newborns.

We acknowledge some limitations to our study. First, although no significant associations were found between neonatal hip phenotype in males, these results and conclusions are limited by the low number of dysplastic hips in this subgroup. Second, the lack of a strictly standardized definition and precise measurements for hip dysplasia at skeletal maturity remains a challenge, which may lead to variability in assessments and diagnoses. Third, the study's findings may be specific to the Norwegian population and geographic region studied, therefore limiting the generalizability to other populations with potentially different risk factors and outcomes. Fourth, this study assesses associations between neonatal and adult acetabular morphologies, with limited ability to draw firm conclusions about causality. We have previously examined the predictive effect of early life factors on radiographic measurements of hip dysplasia in an extended version of this cohort, also including neonates without neonatal hip US.[6] Findings showed that female gender, breech, low acetabular inclination, clinical hip instability, having undergone abduction treatment, and velocity of growth during childhood were all factors that predicted adult hip dysplasia, whereas reported family history, interestingly, had no predictive effect. Strengths of our study include a strict RCT protocol, high quality of the collected data, few and experienced pediatricians performing the newborn clinical hip examinations, and a single, highly experienced examiner performing the newborn hip US throughout the whole study period. The prospectively collected data in this cohort belongs to an extensive data set originating from a well-reported RCT with follow-up exams, spanning >3 decades, and its quality and accuracy, along with the study design, have been thoroughly described in previous publications.[8,14,26] The hip radiographs at follow-up were performed by 1 radiographer, using a detailed protocol and with the subject properly positioned, whereas all measurements were performed using a validated, digital program by only 3 examiners.[13]

CONCLUSIONS

In females, significant associations between neonatal hip phenotypes and dysplasia at skeletal maturity were revealed. In females, one-tenth of sonographically normal hips show borderline/dysplasia at skeletal maturity, whereas this is the case for around one-fifth of sonographically immature, mildly, or severely dysplastic hips. Males had less dysplasia at skeletal maturity for all neonatal US hip types, but these results might be limited because of low numbers of dysplastic male hips. Our findings suggest the possibility of different mechanisms in males and females affecting the acetabular development during childhood and adolescence, eliciting the consideration of prolonged clinical and radiologic follow-up for girls with dysplastic neonatal hips. Because the current study showed that joint hypermobility was associated with both neonatal hip instability and with dysplasia at 18 year of age in females, we suggest that hip instability be assessed both clinically and sonographically in neonates. The role of joint hypermobility warrants further investigation.

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ABBREVIATIONS

ADR: acetabular depth-width ratio
CE: center-edge
DDH: developmental dysplasia of the hip
FHEI: femoral head extrusion index
RCT: randomized controlled trial
US: ultrasound

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Dr Laborie collected the data material at follow-up, was responsible for the linkage of data from the initial trial and from the follow-up study, performed the radiographic digital measurements together with 2 other qualified researchers, drafted the initial manuscript and was co-responsible for the statistical analyses, and revised the manuscript; Drs Rasmussen and Jacobsen were co-responsible for drafting and reviewing the manuscript, and interpreting the statistical analyses, and revised the manuscript; Dr Gundersen collected the data material at follow-up and designed the follow-up study, was responsible

for the linkage of data from the initial trial and from the follow-up study, performed the radiographic digital measurements together with 2 other qualified researchers, drafted the initial manuscript, and revised the manuscript; Dr Rosendahl conceptualized and designed the initial randomized controlled trial and also the follow-up study, collected all data and performed all ultrasounds for the initial trial, interpreted all radiographs at skeletal maturity by gross vision, contributed to the statistical analyses, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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