■ CHILDREN'S ORTHOPAEDICS

The outcome and prognostic factors in children with bilateral Perthes' disease

A PROSPECTIVE STUDY OF 40 CHILDREN WITH FOLLOW-UP OVER FIVE YEARS

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Aims

The aims of this study were to describe the course of non-operatively managed, bilateral Perthes' disease, and to determine specific prognostic factors for the radiographic and clinical outcome.

Patients and Methods

We identified 40 children with a mean age of 5.9 years (1.8 to 13.5), who were managed non-operatively for bilateral Perthes' disease from our prospective, multicentre study of this condition, which included all children in Norway who were diagnosed with Perthes' disease in the five-year period between 1996 and 2000. All children were followed up for five years.

The hips were classified according to the Catterall classification. A modified three-group Stulberg classification was used as an outcome measure, with a spherical femoral head being defined as a good outcome, an oval head as fair, and a flat femoral head as a poor outcome.

Results

Concurrent, simultaneous bilateral Perthes' disease was seen in 23 children and 17 had the sequential onset of bilateral disease. The mean delay in onset for the second hip in the latter group was 1.9 years (0.3 to 5.5).

The five-year radiographic outcome was good in 30 (39%), fair in 25 (33%) and poor in 21 (28%) of the hips. The strongest predictors of poor outcome were > 50% necrosis of the femoral head, with odds ratio (OR) 19.6, and age at diagnosis > 6 years (OR 3.3). Other risk factors for poor outcome were the timing of the onset of disease, where children with the sequential onset of bilateral disease had a higher risk than those with the concurrent onset of bilateral disease (p = 0.021, chi-squared test).

Following a diagnosis of Perthes' disease in one hip, there was a 5% chance of developing it in the contralateral hip.

Conclusion

These results imply that we need to distinguish between children with concurrent onset and those with sequential onset of bilateral Perthes' disease, as the outcomes may be different. This has not been previously described. Children with concurrent onset of bilateral disease had a similar outcome to our previous series of those with unilateral disease, whereas children with sequential onset of bilateral disease had a worse prognosis. The increased risk of developing Perthes' disease in the contralateral hip in those with unilateral disease is important information for the child and parents.

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Perthes' disease of the hip is a condition of childhood that can lead to disabling symptoms. Great variability (5 to 12 per 100 000 individuals per year)[1] has been reported regarding the incidence and affects both hips in 8% to 24% of children.[2] The diagnosis, prognosis and outcome is known to be different for children with bilateral disease, however, the evidence is confused. One study reported an inferior outcome in children with bilateral involvement,[3] whilst a larger retrospective study[2] showed a tendency for bilateral disease to be milder. Others have suggested that children diagnosed with concurrent bilateral disease aged < 6 years do not in fact have Perthes' disease, but have a yet to be described disorder of the femoral head.[4] Some authors imply that the treatment of one hip might affect the outcome for the contralateral hip, whereas others have suggested that the development of

Perthes' disease and the outcome is independent for each hip.[2,5]

The aims of this study were to describe the course of non-operatively managed, bilateral Perthes' disease, and to determine specific prognostic factors for the radiographic and clinical outcome. To the best of our knowledge, this is the only prospective study focusing solely on children with bilateral Perthes' disease.

Patients and Methods

Over a five-year period from January 1996 to December 2000, all new cases of Perthes' disease were reported to the Norwegian study on Perthes' disease. This was a prospective multicentre study involving all 28 hospitals with a paediatric orthopaedic service in Norway.[1] The study was approved by the Norwegian Data Inspectorate and Directorate of Health and Social Affairs and recruitment required informed consent.

The responsible orthopaedic surgeon established the diagnosis of Perthes' disease on the basis of clinical examination and radiographic changes of the hip. In order to exclude other conditions, radiographs of the spine and lower extremities were obtained when indicated. Demographic and clinical data were recorded at the time of diagnosis for submission to the study group.

The original study included 425 children with uni or bilateral disease.[1] This study investigated the epidemiology and aetiological features of Perthes disease in Norway. For the purpose of the present study we identified a subgroup of 55 children with bilateral disease (13%). We excluded five children who had been diagnosed with unilateral disease in the contralateral hip prior to the study period. We also excluded eight children who underwent surgery; seven who had a unilateral femoral osteotomy and one who had bilateral femoral osteotomies. We also excluded two children with inadequate radiographs. The remaining 40 children (35 boys and 5 girls) had a mean age of 5.9 years (1.8 to 13.5). They were treated with either physiotherapy (72 hips) or a Scottish Rite abduction orthosis (eight hips), which was applied according to the choice of the local orthopaedic surgeons. Physiotherapy consisted of range of movement exercises, with emphasis on abduction, internal rotation and extension, in addition to muscle strengthening. In order to use the Scottish Rite orthosis, abduction of the hip had to exceed 35º. It held both hips in slight flexion, and abduction to about 40º. The orthosis was worn for a minimum of 23 hours a day and was only removed for bathing and swimming. The orthosis was discontinued when there were signs of new bone formation on both anteroposterior and frog-leg lateral (Lauenstein) view.

All patients had clinical and radiological follow-up at one, three, and five years after diagnosis for the first hip. Additional radiographs were obtained at five-year follow-up for the second hip in patients with sequential onset disease. At the five-year follow-up, the parents and child were questioned regarding the child's walking distance and participation in sporting activities. This was recorded as normal if the distance was > 5 km. Participation in sporting activity was classified as: normal function; participation in all activities with a somewhat reduced function; unable to participate in all activities or unable to participate in sports activities at all.

Radiographic assessment. The radiographs were all assessed by a single author (SS). Based on anteroposterior and frog-leg lateral projections, the hips were grouped according to a modification of the classification of Catterall.[6,7] We combined Catterall groups 1 and 2 (< 50% necrosis of the femoral head), and Catterall groups 3 and 4 (> 50% necrosis).[6] The Catterall grouping was based on both the initial radiographs and those at the one-year follow-up. If involvement was more severe after one year, the highest Catterall group was used.

We also assessed the radiological "phase" of disease at the time of diagnosis according to Waldenstrøm.[8] The initial phase was characterised by a difference in epiphyseal height, metaphyseal width and the structure of the bone compared with the normal hip. The fragmentation phase included hips with partial or total resorption of the necrotic bone. Hips with obvious signs of re-ossification were classified as being in the re-ossification phase, and if the entire epiphysis was ossified the hip was classified as healed.

At the five year follow-up, the hips were classified into three groups according to a modified Stulberg classification.[9] Group A were hips with a good radiographic result and a spherical femoral head (Stulberg class I and II). Group B hips had a fair radiographic result and an oval femoral head (Stulberg class III). Group C hips had a poor radiographic result with a flat femoral head (Stulberg class IV and V).[10]

The percentage cover of the femoral head was measured radiographically throughout the five-year follow-up period by SS according to Heyman and Herndon.[11]

We have previously assessed the reliability of the radiographic evaluation and found satisfactory inter-observer agreement of the modified two group Catterall classification and measurement of the femoral head cover[6] and the three group Stulberg classification.[10]

Statistical analysis. This was performed using SPSS version 16.0 (Statistical Package of Social Sciences Inc., Chicago, Illinois). Differences between the groups on baseline characteristics with continuous data were tested with an analysis of variance (ANOVA) and the chi-squared test was used for categorical data. Differences were considered significant if the p-value was < 0.05. The outcome at five years was assessed using the three, ordinal Stulberg categories. In order to account for dependencies within each patient, because both hips were affected, ordinal regression was performed using Generalised Estimating Equations (GEE) with an exchangeable working correlation matrix. The results from the ordinal regression are presented as cumulative odds ratios with 95% confidence intervals and p-values.

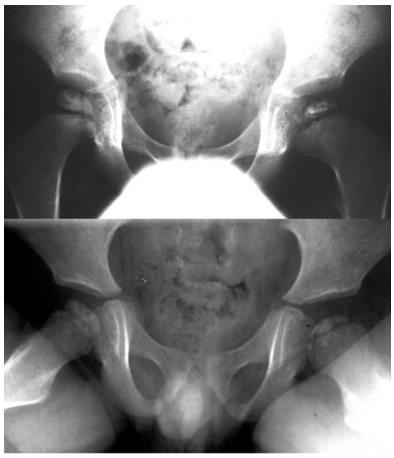

Fig. 1a

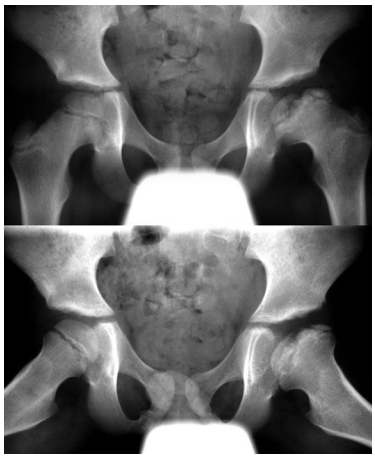

Fig. 1b

Anteroposterior and Lauenstein radiograph projections of the hips of a 3.5 year old boy with the concurrent onset of bilateral Perthes' disease, at the time of diagnosis (a). The right hip was classified as Catterall I, the left as Catterall IV. And (b); five years after diagnosis. The right hip was classified as spherical (Stulberg 1) and the left hip as oval (Stulberg 3)

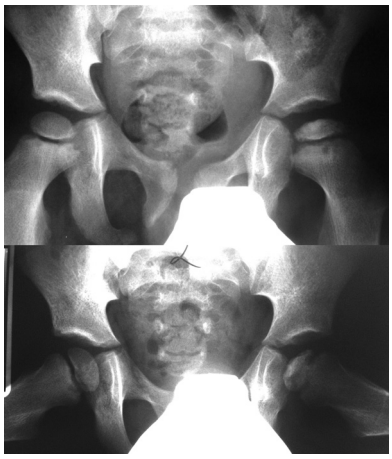

Fig. 2a

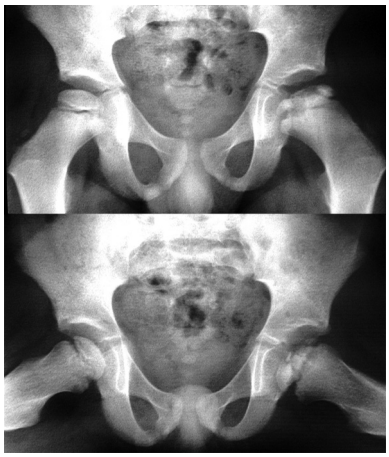

Fig. 2b

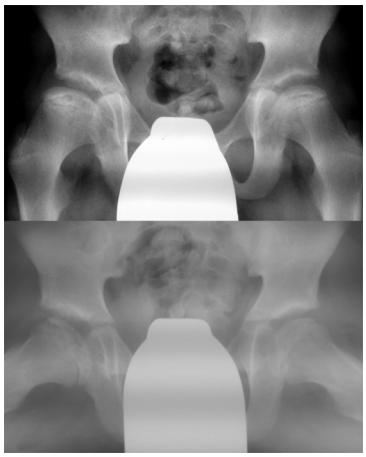

Fig. 2c

Anteroposterior and Lauenstein radiograph projections of the hips of a 4.5 years old boy with the sequential onset of bilateral Perthes' disease, at the time of diagnosis (a) The left hip was classified as Catterall group III. And (b); six months later. The right hip is now also affected, in the initial phase of the disease and classified as Catterall IV when in the fragmentation phase. And (c); When aged ten years with both hips classified as oval (Stulberg 3).

Results

We identified two groups: those who presented with bilateral concurrent disease (23 children) (Fig. 1) and those who presented with sequential lbilateral disease (17 children) (Fig. 2).

The concurrent onset of bilateral disease (23 children). There were 21 boys and two girls in this group. The mean age at diagnosis was 5.4 years (Table I). The mean duration of symptoms prior to diagnosis was 4.4 months (1 to 8). At the time of diagnosis, 11 hips were in the initial phase and 31 were in the fragmentation phase. We were not able to determine the phase in four hips (two patients) due to poor quality radiographs. The same radiographic phase was seen bilaterally in ten children, whilst 11 were in different phases. A total of 12 hips were Catterall group 1 or 2, and 34 were Catterall group 3 or 4. A similar proportion of femoral head necrosis was seen between the two sides in 17 children (74%) (either < 50% or > 50% necrosis).

No child was lost to follow-up. At five years, most had no pain (16 children) whereas seven had slight pain in the hip. Five children had a limping gait. A total of 17 (74%) had a normal level of function and could participate in all sporting activities, whereas six had a reduction in their ability to participate in sports. Only one child was not able to walk 5 km.

The sequential onset of bilateral disease (17 children). There were 14 boys and three girls in this group. The mean age at diagnosis in the first hip was 5.5 years (1.8 to 13.1) and 7.4 years (3.8 to 13.5) in the second hip. The mean period of time

Table I. Age at diagnosis, extent of necrosis and femoral head shape five years after diagnosis for children with a diagnosis of concurrent bilateral Perthes and those with a sequential, bilateral diagnosis

Types of Perthes' disease	Mean age at diagnosis (range)	Extent of femoral head necrosis		Femoral head shape		
		< 50%	> 50%	Spherical	Oval	Flat
		n (%)	n (%)	n (%)	n (%)	n (%)
Concurrent bilateral	5.4 (3.1 to 8.2)	12 (*26*)	34 (*74*)	23 (*50*)	15 (*33*)	8 (*17*)
Sequential bilateral	6.4 (1.8 to 13.5)	7 (*21*)	27 (*79*)	7 (*23*)	10 (*33*)	13 (*44*)
First hip	5.5	3	14	4	6	7
Second hip	7.4	4	13	3	4	6

Table II. Multivariable ordinal regression analysis of prognostic factors in 40 children with bilateral Perthes' disease

Prognostic factor	Odds ratio	95% Confidence intervals	p-value
Extent of necrosis	19.6	3.9 to 97.3	< 0.001
Manner of onset	3.7	0.9 to 15.4	0.071
Age at diagnosis	3.3	1.1 to 10.0	0.034
Gender	1.1	0.3 to 4.2	0.876

Extent of necrosis is more or less than 50% femoral head necrosis; manner of onset is concurrent or sequential onset bilateral disease; age is children > 6.0 years compared with younger children

between diagnosis of the first and second sides was 1.9 years (0.3 to 5.5). The mean duration of symptoms prior to diagnosis of the first hip was 4.5 months (1 to 15). At the time of diagnosis, six hips were in the initial phase, 17 in the fragmentation phase, eight in the re-ossification phase, and one hip was healed. We were not able to determine the phase in two hips. Only five children had hips that were classified as being in the same Waldenström radiographic phase when the second hip was diagnosed.

According to the modified Catterall classification, seven hips were in Catterall groups 1 or 2 and 27 hips were in groups 3 or 4. No hip with < 50% femoral head necrosis in the first hip developed > 50% necrosis in the second hip, whilst all but one first hip with > 50% necrosis developed > 50% necrosis in the second hip. There was no significant difference in the extent of femoral head necrosis between the concurrent and sequential onset groups ($p = 0.21$; ANOVA).

No child was lost to clinical follow-up. At the five-year follow-up (for the first hip), ten of the 17 children had slight to considerable pain or discomfort, and six had a limping gait. Only six children (35%) had a normal level of function and could participate in all kinds of sports, whereas ten felt their function was impaired when participating in sports. One child could only manage to swim. Eight children had reduced walking capacity.

Radiographic outcome at five years. Radiographs of all 40 children (76 hips) were available at five-year follow-up. Four patients in the sequential onset group had five-year radiographic follow-up of the first hip only. Follow-up of the second hip was too short in these patients as additional radiographs to extend the follow-up had not been taken after the five-year follow-up of the first hip.

The mean follow-up time was 5.6 years (4.5 to 8.1) in the concurrent onset group, 6.0 years (4.1 to 10.7) in the first hip of the sequential onset group, and 5.5 years (3.8 to 7.1) in the second hip. The radiographic outcome was good in 30 (39%) of the hips, fair in 25 (33%) and poor in 21 (28%). In children in the concurrent bilateral onset group, the radiographic outcome was good in 23 hips (50%) and poor in eight hips (17%) (Table I). In the sequential onset group, the outcome was good in seven hips (23%) and poor in 13 hips (44%). The outcome was significantly worse in the sequential onset group ($p = 0.021$, chi-squared test). Ordinal regression analysis showed that the strongest predictor of radiographic outcome (femoral head shape) at five years after diagnosis was the extent of femoral head necrosis. Those children with > 50% necrosis had increased odds for developing a flat femoral head (Table II). The age at diagnosis was the second strongest predictor. Children older than six years had a higher risk of developing a flat femoral head. The manner of onset of the disease was a highly probable predictor, with $p = 0.07$. Children with sequential onset bilateral disease had the highest risk of having a flat femoral head at five years.

Over the five-year period, the cover of the femoral head decreased (Table III). This decrease was similar for concurrent onset and the first hip of those with sequential onset bilateral disease. For the second hip, only measurements at the time of diagnosis of the first hip and at the five-year follow-up were included, since exact measurements at one year and three years were not available.

Discussion

This study suggests that the natural history of concurrent onset bilateral Perthes' disease is more benign than

Table III. Femoral head cover at time of diagnosis and at one, three and five-year follow-up in patients with concurrent bilateral onset and sequential bilateral onset of Perthes' disease

Type of Perthes	Femoral head cover (%)			
	Diagnosis Mean (range)	1 yr Mean (range)	3 yrs Mean (range)	5 yrs Mean (range)
Concurrent bilateral	95.5 (80 to 117)	89.6 (66 to 119)	85.4 (66 to 106)	82.6 (49 to 100)
Sequential bilateral:				
- First hip	90.7 (64 to 127)	85.8 (61 to 113)	79.1 (62 to 100)	78.4 (59 to 100)
- Second hip	98.5 (70 to 130)			78.9 (55 to 97)

Table IV. Radiographic outcome in children with bilateral Perthes' disease in different studies according to the manner of onset

				Radiographic outcome						
					Group A		Group B		Group C	
Author	**Manner of onset**	**Age (yrs)**	**Catterall 3/4 (%)**	**n**	**n**	**%**	**n**	**%**	**n**	**%**
Bogaert[3]	Concurrent	5.1 to 5.5	57	14	6	43	1	7	7	50
Guille gr I[2]	Concurrent	6.2	57	46	34	74	6	13	6	13
Wiig (current study)	Concurrent	5.4	74	46	23	50	15	33	8	17
Total	**Concurrent**			**106**	**63**	*59*	**22**	*21*	**21**	20
Bogaert[3]	Sequential	6.0-6.5	89	36	9	25	10	28	17	47
Guille gr III[2]	Sequential	6.2	83	16	5	31	9	56	2	13
Wiig (current study)	Sequential	6.4	79	30	7	23	10	33	13	44
Total	**Sequential**			**82**	**21**	*26*	**29**	*35*	**32**	*39*

Concurrent is disease in both hips at the time of diagnosis; Sequential is unilateral disease in a child at the time of diagnosis that later developed Perthes' in the opposite hip; Age is mean age at time of diagnosis; Group A is spherical femoral head shape, Group B is oval femoral head shape, Group C is flat femoral head shape

sequential onset disease. Other risk factors for a poor outcome in bilateral disease were necrosis of > 50% of the femoral head and age of > six years at first diagnosis.

The reported prevalence of bilateral Perthes' disease ranges from 8% to 24%.[2] This range probably reflects the heterogeneity of the populations studied. In our study, which comprised all children with Perthes' disease in Norway, we found that both hips were affected in 13% (55 of 425 children), which is similar to that found by Guille et al.[2] If the disease initially presented unilaterally, the risk of developing Perthes' disease in the contralateral hip was 5%, which is higher than the prevalence in the general population.[1] This is in accordance with a previous study which found that 4% presented with concurrent bilateral disease and a further 6% went on to develop changes in the contralateral hip.[5] Therefore, if a child presents with unilateral disease, the child and his/her parents should be informed about the increased risk of developing Perthes' disease in the contralateral hip.

In a retrospective study of 25 children with bilateral disease,[3] seven had the concurrent onset of bilateral disease and 18 had sequential onset. The mean age at diagnosis of the first hip was 5.1 years, which is similar to our group of concurrent bilateral onset and the first hip in those with sequential onset, whereas Guille et al[2] found that the mean age of onset in those with concurrent onset was 6.2 years.

In children with the sequential onset of bilateral disease, the second hip was diagnosed a mean of 1.9 years after the first, which is in accordance with a previous study which also found a mean delay of 1.9 years.[3] A somewhat shorter mean delay of 1.3 years was found by Futami and Suzuki,[5] whereas a longer mean delay of 3.0 years was reported by Guille et al.[2] In a study of 25 children, van den Boegaert et al[3] found a high percentage with extensive femoral head necrosis (80% Catterall groups 3 and 4) and concluded that bilateral disease was more severe than in a series of unilateral cases reported by Ippolito et al.[12] Similarly, 76% of our 40 children had > 50% necrosis of the femoral head. There was no significant difference in the extent of necrosis between those with concurrent and those with sequential onset, and no hip with < 50% necrosis in the first hip developed > 50% necrosis in the second hip. Our previous cohort of unilateral cases[13] had a similar frequency of severe femoral head necrosis (83% Catterall groups 3 and 4).

There is no consensus in the literature as to whether the prognosis in bilateral Perthes' disease is more or less severe than in unilateral disease. Van den Bogaert et al[3] reported an inferior radiographic outcome in children with bilateral involvement (48% Stulberg class IV/V). In a study of 83 children, Guille et al[2] found that the disease was milder and reported a poor outcome in only 12% of the hips. We believe that it is necessary to study the children

prospectively in order to answer this question and to distinguish between the three groups of patients: those with unilateral disease and those with the concurrent onset and sequential onset of bilateral disease. Our multinominal regression analysis showed that the extent of femoral head necrosis and age at diagnosis were significant prognostic factors, which is similar to that in children with unilateral disease.[13-15] In addition, concurrent or sequential onset bilateral disease had a significant bearing on the prognosis, regardless of the age at diagnosis and the extent of femoral head necrosis.

Our overall results showed that 28% of the hips had a flat femoral head after five years. The outcome was significantly worse in those with the sequential onset than in those with the concurrent onset of bilateral disease. The outcome for patients with concurrent onset was similar to the outcome in our series of 212 children with unilateral disease who were also treated with physiotherapy alone.[13]

In order to further evaluate the difference between concurrent and sequential onset disease, we compared our results with those of the patients in the studies of Van den Bogaert et al[3] and Guille et al.[2] This analysis included 186 hips (Table IV) and showed that sequential onset disease has approximately half as many good radiographic results and twice as many poor results compared with concurrent onset disease. This supports our findings of an improved outcome in concurrent onset disease, which has not been previously reported.

In children who were aged < 6 years when diagnosed with concurrent onset bilateral disease, the radiographic outcome was good in 55% of the hips, fair in 32%, and poor in 13%. In a corresponding group of 12 children, Rosenfeld et al[4] demonstrated a markedly better prognosis: a good radiographic outcome (Stulberg class I/II) in 87% of the hips and fair outcome in 13%. They suggested that patients with concurrent onset bilateral disease diagnosed before the age of six years were atypical and might have an as yet undescribed disorder of the femoral head. Our results do not confirm this theory of a separate, more benign form of disease in this age group.

The cover of the femoral head decreased throughout the course of the disease in children with bilateral disease in a similar way as we have previously found in unilateral Perthes' disease.[13] The second hip had a somewhat greater reduction in femoral head cover during the follow-up period, which might have contributed to the rather poor results in this group, since low femoral head cover (< 80%) was identified as a risk factor for a poor radiographic outcome in unilateral Perthes' disease.[13]

Children with sequential onset disease tended to have more pain or discomfort and a reduced level of function and walking capacity at the five-year follow-up as compared with either those with concurrent onset of disease or our series of children with unilateral disease.[15] This is expected, as they have a worse radiographic outcome and a more prolonged clinical course.

The main strength of the study was that it was prospective, although a larger cohort of bilateral cases would have made the statistics more reliable. There are several other limitations to this study. First, the distinction between bilateral Perthes' and generalised skeletal dysplasias can be difficult.[16] We addressed this by obtaining radiographs of the spine and lower extremities when in doubt. However, we recognise that other joints are not always affected in multiple epiphyseal dysplasia and that the distinction between these two conditions is particularly difficult.

A significant proportion of our children were skeletally immature at the five-year follow-up, which may make both the clinical and radiological results worse than they may be in a skeletally mature population. However, all hips were healed and we believe, as did Cooperman and Stulberg,[17] that we could reliably apply the Stulberg classification.

Patient recorded outcome measures (PROMs) would add value to our study, to understand the clinical outcome of bilateral Perthes' disease better. However, validated PROMs were not widely used at the time this study was performed. We also acknowledge that a proportion of our children were treated with an abduction splint rather than physiotherapy. However, prospective studies [14,15] have shown no significant effect on the sphericity of the femoral head in children treated in this way. Thus we do not believe this will have significantly affected the outcomes.

Author contributions:
O. Wiig: designed the study and wrote the manuscript.
S. Huhnstock: contributed to the design of the study and to preparation of the manuscript.
T. Terjesen: designed the study and contributed to preparation of the manuscript.
A. H. Pripp: performed the statistical analyses.
S. Svenningsen: contributed to the design of the study and measured and assessed the radiographs.

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