Incidence and Clinical Characteristics of Slipped Capital Femoral Epiphysis in Patients with Endocrinopathy

A Population-Based Cohort Study

Sunghyun Hwang, MD, Yun Jeong Lee, MD, Mi Hyun Song, MD, Tae-Joon Cho, MD, In Ho Choi, MD, and Chang Ho Shin, MD

Investigation performed at the Seoul National University Children's Hospital, Seoul, Republic of Korea

Background: Endocrinopathy is a risk factor for slipped capital femoral epiphysis (SCFE). We aimed to determine (1) the incidence of endocrinopathy-associated SCFE compared with that of non-endocrinopathy-associated SCFE, (2) whether the incidence of SCFE increases with the number of deficient hormones, and (3) the clinical characteristics of endocrinopathy-associated SCFE.

Methods: We conducted a population-based cohort study using a nationwide database in South Korea. All new diagnoses of endocrinopathy or SCFE between 2002 and 2019 in children born between 2002 and 2005 were identified. The incidence of SCFE was calculated for each type of endocrinopathy. The trend of the incidence of SCFE relative to the number of deficient hormones was analyzed. The male:female ratio was compared between endocrinopathy-associated SCFE and non-endocrinopathy-associated SCFE. For endocrinopathy-associated SCFE, the time between the diagnoses of SCFE and endocrinopathy was evaluated.

Results: The incidence of SCFE was higher in children with endocrinopathy than in those without endocrinopathy (37.1/100,000 versus 9.0/100,000 children) (relative risk, 4.1 [95% confidence interval, 2.8-6.1]). Among various endocrinopathies, growth hormone deficiency showed the highest incidence of SCFE (583.8/100,000 children). The Cochran-Armitage test showed a linear trend, with an increased number of deficient hormones being associated with a higher incidence of SCFE ($p < 0.001$). Male sex was dominant in the non-endocrinopathy-associated SCFE group (73%; 117 of 161), whereas female sex was dominant in the endocrinopathy-associated SCFE group (53%; 16 of 30) ($p = 0.009$). Twenty-two of the 30 cases of endocrinopathy-associated SCFE were diagnosed after the diagnosis of endocrinopathy, with a median time of 3.6 years between the diagnoses. Six (27%) of these 22 children developed SCFE >5 years after the diagnosis of endocrinopathy.

Conclusions: The incidence of SCFE was approximately 4 times higher in children with endocrinopathy than in those without endocrinopathy. The risk of SCFE increased with an increased number of deficient hormones. Long-term monitoring of SCFE occurrence in children with endocrinopathies is strongly recommended.

Level of Evidence: Diagnostic Level III. See Instructions for Authors for a complete description of levels of evidence.

Slipped capital femoral epiphysis (SCFE) is a disorder, occurring mainly in prepubescence and early adolescence, in which the proximal femoral metaphysis is displaced relative to the epiphysis[1]. The slip is a consequence of either a higher-than-usual load across a normal physis, a physiological load across a physis that is weaker than normal, or a combination of the two[2,3]. Obesity may cause an abnormally high load across the physis[4]. Small epiphyseal tubercles, down-regulation of type-II collagen and aggrecan expression in the physis, radiation therapy, and diseases associated with SCFE, such as renal failure osteodystrophy and endocrinopathy, may weaken the physis[5-11]. When SCFE occurs with an associated disease or a history of radiation therapy, it is classified as atypical[8,12]. Endocrinopathy is the most common cause of atypical SCFE[12].

The incidence of SCFE in the general population has been explored in many studies, with a relatively recently reported

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incidence of approximately 10 per 100,000 children in the United States[1,13-17]. However, to our knowledge, the exact incidence of endocrinopathy-associated SCFE has not been investigated. The overall incidence of SCFE among patients with endocrinopathy was estimated in only 1 study on the basis of many assumptions[18], whereas the incidence among patients with specific endocrinopathies was reported in 5 studies, including 4 on growth hormone deficiency (GHD) and 1 on central precocious puberty (CPP)[19-23]. Because the incidence of SCFE is affected by age, sex, race, season, region, and study period[1], it must be compared between patients with endocrinopathy and a relevant control group. However, the 5 studies that investigated the incidence of SCFE in patients with specific endocrinopathies did not include control groups and compared the incidence with that in historical reports[19-23]. Therefore, whether the incidence of SCFE is higher in patients with endocrinopathy than in those without endocrinopathy, and the extent to which the incidence of SCFE increases with endocrinopathy, are unknown. Even among patients with endocrinopathy, the incidence of SCFE could vary depending on the type of endocrinopathy and the number of deficient hormones, which has not been investigated.

We aimed to determine (1) the incidence of SCFE in children with endocrinopathy overall, as well as in children with specific endocrinopathies, compared with that in children without endocrinopathy, (2) whether the incidence of SCFE increases with the number of deficient hormones, and (3) the clinical characteristics of endocrinopathy-associated SCFE.

Materials and Methods

Data Source

We utilized the database of the National Health Insurance Service (NHIS), a mandatory single-payer organization that covers >99% of the population in South Korea[24]. Since 2002, the NHIS has accumulated information regarding the demographic characteristics, diagnoses, and medical treatments whenever patients visit a clinic or hospital. This allows for a comprehensive longitudinal follow-up of interactions between patients and health-care providers. The database uses the diagnostic codes of the International Classification of Diseases, 10th Revision (ICD-10); Drug Identification Numbers of South Korea, 147th edition; and procedure codes of the South Korea Health Insurance Review and Assessment Service. The NHIS approved the use of its database and provided data after excluding patient identification information (NHIS-2021-1-182). Our institutional review board waived the need for the approval of this study.

Study Population

We performed a population-based cohort study using data that were collected between January 1, 2002, and December 31, 2019. We included children who had been born between January 1, 2002, and December 31, 2005; the study population was limited to 2002 to 2005 birth-year cohorts to ensure a minimum follow-up period of 14 years from their birth. We identified all children having ≥1 diagnostic code for endocrinopathies in which SCFE has been reported to occur: (1) hypothyroidism[11,25,26], (2) central precocious puberty (CPP)[21], (3) hypopituitarism[18,27], (4) hypergonadotropic hypogonadism[18], (5) GHD[20,23,28], (6) hyperparathyroidism[29], (7) congenital adrenogenital disorders[30], (8) gigantism[31], or (9) pseudohypoparathyroidism[32] (see Appendix Table I). GHD was defined as the presence of both a diagnostic code for GHD and drug identification numbers for growth hormone (see Appendix Table II). Children with a diagnostic code for CPP but without drug identification numbers for gonadotropin-releasing hormone (GnRH) agonists were excluded because all instances of CPP-associated SCFE in previous reports occurred in children receiving GnRH agonist therapy and not in children with CPP only[21,33,34] (see Appendix Table II). Patients who died or emigrated before 2019 were excluded from this study.

All patients with the diagnostic code for SCFE (ICD-10 code M930) were also identified. To increase the validity of SCFE diagnosis, we only included patients in the study if they had an SCFE-relevant operating code. Patients with diagnostic codes for congenital deformities or developmental dysplasia of the hip (Q65), juvenile osteonecrosis of the femoral head (M911), traumatic femoral fracture or hip dislocation (S72 and S73), infectious arthritis of the hip (M0005, M0015, M0025, M0085, and M0095), or osteomyelitis of the femur (M8605 and M8615) were excluded.

Incidence and Clinical Characteristics of Endocrinopathy-Associated SCFE

The incidence of SCFE was compared between children with and without endocrinopathy in the overall population, in boys, and in girls. The incidence of SCFE was also compared between boys and girls in the overall population and in children with and without endocrinopathy. In children with endocrinopathy, the incidence of SCFE was calculated for each endocrinopathy type.

To identify the trend of the incidence of SCFE relative to the number of deficient hormones, we defined the group with 1 hormone deficiency as patients who had only 1 diagnostic code for hypothyroidism (thyroid hormone), hypergonadotropic hypogonadism (sex hormone), or GHD (growth hormone). Groups with 2 or 3 deficient hormones were defined as patients with 2 or all 3 diagnostic codes, respectively.

The male:female ratio and the age at the time of diagnosis were compared between the endocrinopathy-associated SCFE and non-endocrinopathy-associated SCFE groups. In the endocrinopathy-associated SCFE group, the time between the diagnosis of SCFE and the diagnosis of endocrinopathy was evaluated.

Statistical Analysis

Given that the data were from a nationwide population, no adjustment procedure was required to determine the incidence[35,36]. Continuous variables were compared with use of the Student t test after the Shapiro-Wilk test demonstrated normality. Categorical variables were compared between the groups with use of the chi-square test or the Fisher exact test. We evaluated the trend of the incidence of SCFE relative to the number of deficient hormones with use of the Cochran-Armitage test. The relative risk (RR) of SCFE and its 95% confidence interval (CI)

were calculated on the basis of the presence of endocrinopathy, sex, and the number of deficient hormones. The level of significance was set at $p < 0.05$. All statistical analyses were performed with use of SAS 9.4 (SAS Institute).

Results

Of the 1,876,592 children, 80,769 were diagnosed with endocrinopathy and 191 were diagnosed with SCFE (Fig. 1). The mean age was 16.0 ± 1.1 years (range, 14.0 to 17.9 years) in the overall population. The demographic characteristics of the study population are presented in Table I. Among the 80,769 children with endocrinopathy, 30 had SCFE. Among the 191 patients with SCFE, 30 (16%) had endocrinopathy and 161 (84%) did not (Fig. 1). The overall mean duration of follow-up (and standard deviation) after the diagnosis of SCFE was 3.9 ± 1.9 years.

Incidence of Endocrinopathy-Associated SCFE

The overall incidence of SCFE in the study cohort was 10.2/100,000 children. The incidence of SCFE was higher in children with endocrinopathy than in those without endocrinopathy (37.1/100,000 versus 9.0/100,000 children; $p < 0.001$) (RR, 4.1 [95% CI, 2.8-6.1]) (Table I). In subgroup analyses by sex, the incidence of SCFE was higher in boys with endocrinopathy than in those without endocrinopathy (57.7/100,000 versus 12.3/100,000 children; $p < 0.001$) (RR, 4.7 [95% CI, 2.7-8.2]) and was higher in girls with endocrinopathy than in those without endocrinopathy (28.3/100,000 versus 5.2/100,000 children; $p < 0.001$) (RR, 5.4 [95% CI, 3.1-9.6]).

The incidence of SCFE was higher in boys than in girls in both the endocrinopathy group (57.7/100,000 versus 28.3/100,000 children; $p = 0.047$) (RR, 2.0 [95% CI, 1.0-4.2]) and the non-endocrinopathy group (12.3/100,000 versus 5.2/100,000; $p < 0.001$) (RR, 2.4 [95% CI, 1.7-3.3]) (Table I).

Among the various endocrinopathies, GHD showed the highest incidence of SCFE (583.8/100,000 children) (Table II). All children with GHD and SCFE had multiple hormone deficiencies (Table III).

The number of children according to the number and type of deficient hormones is shown in Figure 2. The Cochran-Armitage test showed a linear trend, with an increased number of deficient hormones associated with a higher incidence of SCFE (chi-square = 170.85; $p < 0.001$) (Table III).

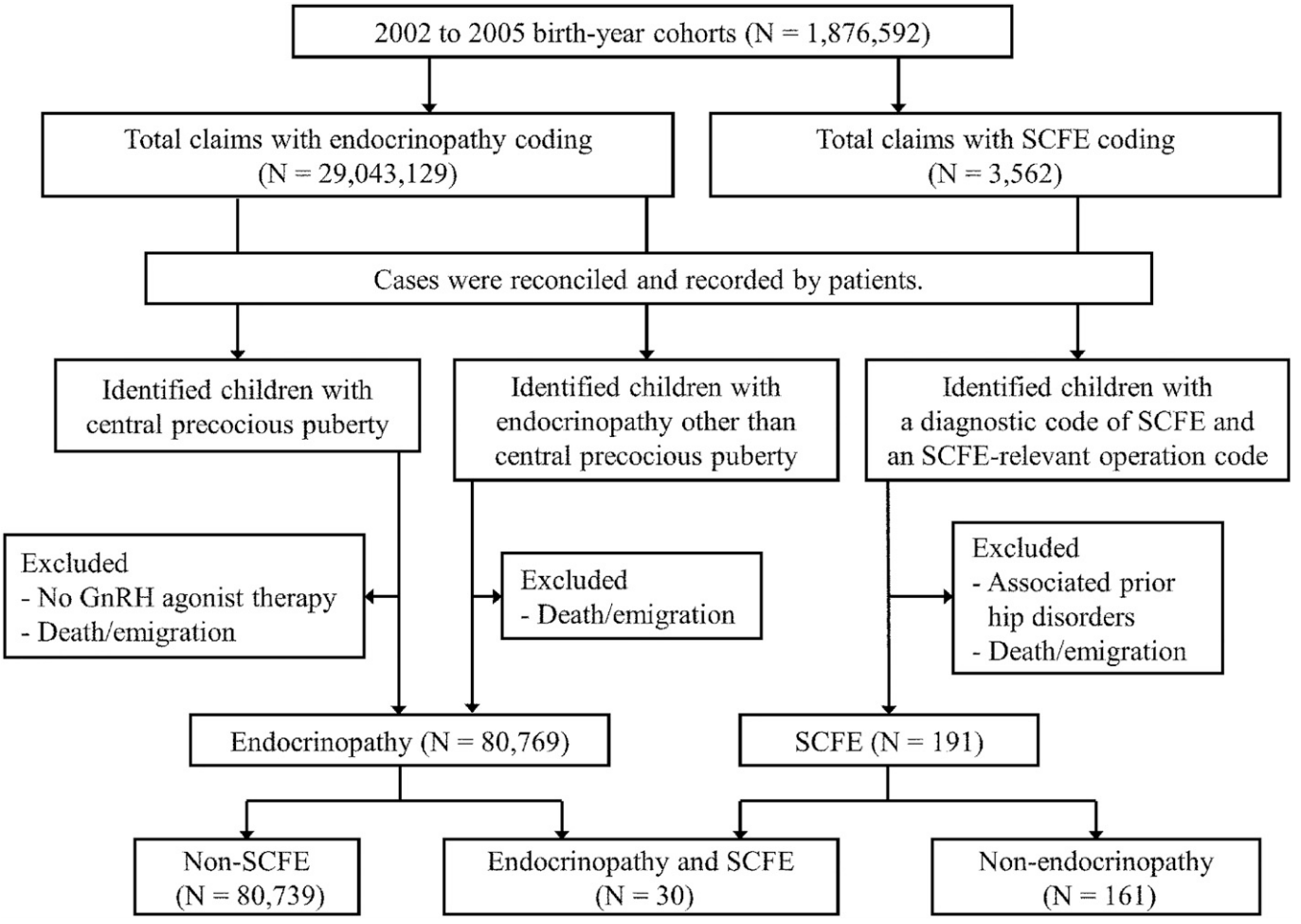

Fig. 1

Flowchart of the study population. SCFE = slipped capital femoral epiphysis and GnRH = gonadotropin-releasing hormone.

TABLE I Demographic Characteristics of the Study Population and Incidence of SCFE According to Presence of Endocrinopathy

Characteristic	Overall (N = 1,876,592)	Non-Endocrinopathy Group (N = 1,795,823)	Endocrinopathy Group (N = 80,769)	RR (95% CI)*	P Value
Sex†					
Male	976,927 (52%)	952,667 (53%)	24,260 (30%)		<0.001‡
Female	899,665 (48%)	843,156 (47%)	56,509 (70%)		
SCFE†					
Total	191	161	30		
Male	131 (69%)	117 (73%)	14 (47%)		0.009‡
Female	60 (31%)	44 (27%)	16 (53%)		
Age at diagnosis of SCFE§ *(yr)*					
Total	11.6 ± 1.7 (5 to 16)	11.6 ± 1.5 (7 to 15)	11 ± 2.1 (5 to 16)		0.212#
Male	11.9 ± 1.7 (5 to 16)	11.9 ± 1.5 (7 to 15)	11 ± 2.6 (5 to 16)		0.520#
Female	10.9 ± 1.4 (8 to 14)	10.8 ± 1.3 (8 to 14)	10 ± 1.6 (8 to 14)		0.805#
SCFE incidence**					
Total	10.2	9.0	37.1	4.1 (2.8-6.1)	<0.001‡
Male	13.4	12.3	57.7	4.7 (2.7-8.2)	<0.001‡
Female	6.7	5.2	28.3	5.4 (3.1-9.6)	<0.001‡
RR†† (95% CI)	2.0 (1.5-2.7)	2.4 (1.7-3.3)	2.0 (1.0-4.2)		
P value‡	<0.001	<0.001	0.047		

*Relative risk (RR) >1 indicates increased risk of slipped capital femoral epiphysis in the endocrinopathy group compared with that in the non-endocrinopathy group. †The values are presented as the number of children, with the percentage in parentheses. ‡Chi-square test. §The values are presented as the mean and the standard deviation, with the range in parentheses. #Student t test. **Per 100,000 children. ††Relative risk (RR) >1 indicates increased risk of slipped capital femoral epiphysis in boys compared with that in girls.

Clinical Characteristics of Endocrinopathy-Associated SCFE

Among the 191 patients with SCFE, male sex was dominant in the non-endocrinopathy SCFE group (73%; 117 of 161), whereas female sex was dominant in endocrinopathy-associated SCFE group (53%; 16 of 30) (p = 0.009) (Table I). The mean age at the time of diagnosis of SCFE did not differ between the patients with and without endocrinopathy (Table I). The mean age at the time of diagnosis of endocrinopathy in children with

TABLE II Incidence of SCFE in Children with Specific Endocrinopathies*

Variable	Hypothyroidism	CPP	Hypopituitarism	HH	GHD	Hyperparathyroidism	CAD	Gigantism	PHP
SCFE†									
Total	20	10	13	6	10	2	1	0	0
Male	11	4	6	1	4	1	0	0	0
Female	9	6	7	5	6	1	1	0	0
Endocrinopathy†									
Total	50,093	28,582	6,340	2,764	1,713	1,510	601	441	84
Male	19,667	1,343	3,050	1,999	1,015	794	335	103	37
Female	30,426	27,239	3,290	765	698	716	266	338	47
SCFE incidence‡									
Total	39.9	35.0	205.0	217.1	583.8	132.5	166.4	0	0
Male	55.9	297.8	196.7	50.0	394.1	125.9	0	0	0
Female	29.6	22.0	212.8	653.6	859.6	139.7	375.9	0	0
RR (95% CI)§	4.5 (2.8-7.1)	3.9 (2.1-7.4)	22.9 (13.0-40.2)	24.2 (10.7-54.7)	65.1 (34.4-123.1)	14.8 (3.7-59.5)	18.6 (2.6-132.3)		
P value	<0.001#	<0.001#	<0.001#	<0.001#	<0.001#	<0.001**	<0.001**		

*CPP = central precocious puberty, HH = hypergonadotropic hypogonadism, GHD = growth hormone deficiency, CAD = congenital adrenogenital disorders, PHP = pseudohypoparathyroidism. †The values are presented as the number of children. Children with multiple endocrinopathies were counted in each individual endocrinopathy. ‡Per 100,000 children. §Relative risk (RR) >1 indicates increased risk of slipped capital femoral epiphysis in children with each endocrinopathy compared with that in children without endocrinopathy. #Chi-square test. **Fisher exact test.

TABLE III Incidence of SCFE According to Number of Deficient Hormones*

Variable	No Deficiency	Total	1 Hormone			2 Hormones	3 Hormones
			Hypothyroidism	Hypergonadotropic Hypogonadism	GHD		
SCFE†							
Total	161	13	11	2	0	7	3
Male	117	8	7	1	0	4	0
Female	44	5	4	1	0	3	3
Endocrinopathy†							
Total	1,795,823	52,679	49,237	2,275	1,167	878	45
Male	952,667	21,701	19,210	1,769	722	475	10
Female	843,156	30,978	30,027	506	445	403	35
SCFE incidence†							
Total	9.0	24.7	22.3	87.9	0	797.3	6,666.7
Male	12.3	36.9	36.4	56.5	0	842.1	0
Female	5.2	16.1	13.3	197.6	0	744.4	8,571.4
RR (95% CI)§	Ref.	2.8 (1.6-4.8)	2.5 (1.4-4.6)	9.8 (2.4-39.5)	—	88.9 (41.8-189.0)	743.6 (246.5-2243.1)
P value	—	<0.001#	0.002#	0.004**	—	<0.001#	<0.001**

*GHD = growth hormone deficiency. †The values are presented as the number of children. ‡Per 100,000 children. §Relative risk (RR) >1 indicates increased risk of slipped capital femoral epiphysis in children with hormonal deficiency compared with that in children without hormonal deficiency. #Chi-square test. **Fisher exact test.

endocrinopathy-associated SCFE was 8.1 ± 3.7 years (range, 0.4 to 16.0 years).

Of the 30 patients with endocrinopathy-associated SCFE, 22 (73%) were diagnosed with SCFE after endocrinopathy, whereas 8 (27%) were diagnosed with endocrinopathy after SCFE. In the group of 22 children in whom SCFE was diagnosed after endocrinopathy, the median time between the diagnosis of endocrinopathy and the diagnosis of SCFE was 3.6 years (interquartile range [IQR], 2.9 to 5.1 years), with 6 patients (27%) being diagnosed with SCFE >5 years after the diagnosis of endocrinopathy. In the group of 8 children who were diagnosed with endocrinopathy after SCFE, the median time between the diagnosis of SCFE and the diagnosis of endocrinopathy was 41 days (IQR, 8 to 272 days); in that group, 5 patients (63%) had hypothyroidism, 1 (13%) had hypergonadotropic hypogonadism, 1 (13%) had hypothyroidism and GHD, and 1 (13%) had hypergonadotropic hypogonadism and GHD.

Discussion

SCFE is a relatively uncommon disease[37]; therefore, previous studies on endocrinopathy-associated SCFE were based on a small number of patients and could not present the exact incidence[8,11,12,18,38]. Using a nationwide database, we demonstrated not only the overall incidence of SCFE in patients with an endocrinopathy but also the incidences in patients with various specific endocrinopathies. To our knowledge, this is the first study to provide clear evidence of a higher incidence of SCFE in children with endocrinopathy than in those without. We also found that the incidence of SCFE increased as the number of deficient hormones increased.

Although the incidence of SCFE varies depending on ethnicity, the study period, and other factors, the overall incidence of SCFE in the present study was comparable with those in previous studies[4,14,15]. As the exact incidence of endocrinopathy-associated SCFE has not been reported, we could not directly compare our results with those of previous studies. Wells et al. estimated that 9 (1.15%) of 784 patients with ≥1 endocrinopathy exhibited SCFE, whereas 122 (0.18%) of 69,474 children without endocrinopathy exhibited SCFE ($p < 0.001$)[18]. The incidences of SCFE in that study were higher than those in both the endocrinopathy and non-endocrinopathy groups in the present study. However, their estimation was based on several assumptions, including the number of patients newly diagnosed with endocrinopathy.

Loder et al. reported that 33% of typical SCFEs and 70% of atypical SCFEs occurred in girls ($p = 0.034$)[12]. Similarly, in the present study, 27% of non-endocrinopathy SCFEs and 53% of endocrinopathy-associated SCFEs occurred in girls (Table I). However, female sex was dominant in the group with endocrinopathy-associated SCFE because endocrinopathies occurred more often in girls (70%) than in boys (30%). The incidence of SCFE was higher in boys than in girls in both the endocrinopathy and non-endocrinopathy groups (Table I).

In the endocrinopathy-associated SCFE group, hypothyroidism was the most common endocrinopathy (Table II), presumably resulting from the high frequency of hypothyroidism in

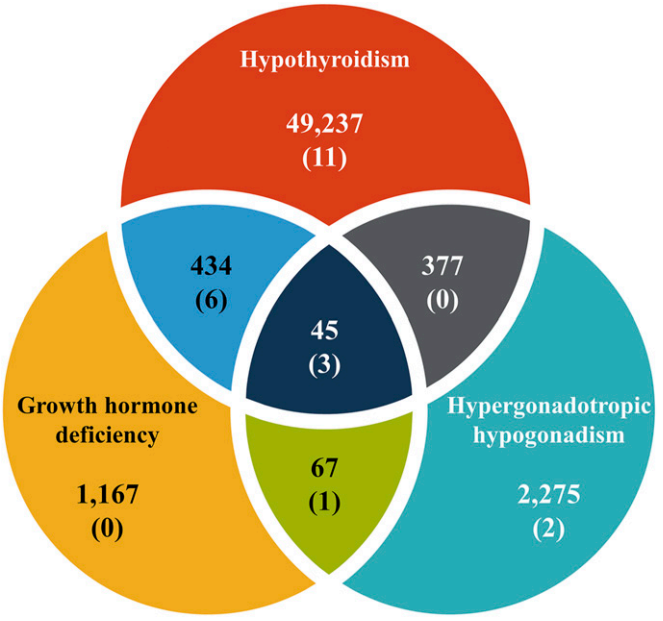

Fig. 2

Diagram showing the number of children according to the number and type of deficient hormones. The 2-hormone deficiency group consisted of 434 children (255 boys and 179 girls) with hypothyroidism and growth hormone deficiencies, 377 children (192 boys and 185 girls) with hypothyroidism and hypergonadotropic hypogonadism, and 67 children (28 boys and 39 girls) with hypergonadotropic hypogonadism and growth hormone deficiencies. The 3-hormone deficiency group consisted of 45 children (10 boys and 35 girls). The numbers in parentheses indicate the number of children with SCFE. The size of the circles does not correlate with the number of children.

our population, which concurs with previous results[11,18,38]. Conversely, among the patients with various endocrinopathies examined in this study, those with GHD had the highest incidence of SCFE, with 65 times the incidence of SCFE compared with that in the control group of children without endocrinopathy. In the National Cooperative Growth Study, SCFE occurred in 11 of 6,686 patients with idiopathic GHD who were receiving growth hormone therapy (incidence, 164.5/100,000 children) and in 8 of 2,020 patients with non-idiopathic GHD who were receiving growth hormone therapy (incidence, 396.0/100,000 children)[20]. The incidence of SCFE in patients with GHD was higher in our study, which might be because 546 (32%) of 1,713 patients with GHD had multiple hormone deficiencies (Fig. 2).

In the present study, the greater the number of deficient hormones, the higher the incidence of SCFE. Thyroid hormones stimulate the proliferation and differentiation of physeal chondrocytes and promote physeal closure during puberty[2,39]. Sex hormones regulate growth plate maturation, ultimately leading to physeal closure[2,40]. Growth hormone therapy induces an increase in the number of proliferative and hypertrophic chondrocytes in the growth plate[39-41], reducing the force required to displace the epiphysis[42]. A combination of hormone deficiencies and growth hormone therapy may exert a synergistic effect on physeal strength, resulting in a much higher incidence of SCFE in children with more "endocrinological burdens."

The age at the time of diagnosis of SCFE did not differ between the children with and without endocrinopathy (Table I). Chung et al. also did not find a difference in age at the time of diagnosis between patients with atypical SCFE (10.4 years) and those with typical SCFE (11.2 years)[8]. However, Burrow et al. reported that the mean age at the time of diagnosis of SCFE was greater in children with endocrinopathy (13.8 years) than in children without endocrinopathy (12.6 years) ($p < 0.005$)[38]. In the study by Loder et al., the chronological age at the time of diagnosis of SCFE was not different between patients with atypical (13.1 years) and typical SCFE (12.0 years)[12]. However, the Oxford bone age was greater in patients with typical SCFE (13.1 years) than in those with atypical SCFE (11.6 years) ($p = 0.003$). These mixed results may be attributed to differences in the study populations and follow-up periods. We could not compare bone age between the endocrinopathy and non-endocrinopathy groups because of the unavailability of hip radiographs in the nationwide database.

In the current study, 22 (73%) of 30 children with endocrinopathy-associated SCFE were diagnosed with SCFE after endocrinopathy. In a previous study by Loder and colleagues, 44 (54%) of 81 children with endocrinopathy-associated SCFE were diagnosed with SCFE after endocrinopathy[11]. The time between the diagnosis of endocrinopathy and SCFE in our study (median, 3.6 years) is longer than that in the previous study (mean, 2.2 years), which could be partially attributed to a younger age at the time of diagnosis of endocrinopathy in our study than in the previous study (mean, 8.1 versus 13.2 years)[11]. The difference between the 2 studies in terms of age at the time of diagnosis of endocrinopathy may be attributable to the difference in access to health care between countries, the distribution of endocrinopathy types between the study populations, and advances in diagnostic modalities to detect endocrinopathy. In the present study, SCFE was diagnosed >5 years after endocrinopathy in more than a quarter of the 22 children in whom SCFE was diagnosed after endocrinopathy. Although the risk of SCFE may vary depending on the type of endocrinopathy or treatment status, this finding indicates the need for long-term monitoring for SCFE in children with endocrinopathy.

The present study had some limitations. First, our follow-up period was relatively short, considering that endocrinopathy-associated SCFE can occur even in patients >20 years of age[43-46], which may have resulted in the underestimation of the incidence of endocrinopathy-associated SCFE. Further studies should be conducted when nationwide data are accumulated over longer periods. Second, the diagnosis of endocrinopathy or SCFE in some patients may not be consistent with the actual diagnosis because of the nature of NHIS claims data. Although we retrieved drug identification numbers for growth hormone and GnRH agonists, as well as SCFE-relevant operation codes together with ICD-10 codes, more information on the medication histories of our patients and access to their radiographs could decrease misclassification errors. Third, children in the same endocrinopathy

group may have a heterogeneous hormonal status. However, we could not include data on hormonal levels or the detailed treatment status of each patient. Similarly, we could not include data on SCFE severity. Fourth, our study did not account for potential confounding factors such as age and race. South Korea is racially homogeneous (96% in 2015)[47]. Because of racial variability in SCFE[14,16], the incidence of endocrinopathy-associated SCFE in our study may differ from that in studies from other countries. However, mono-ethnicity allowed for the comparison of the incidence of SCFE between children with and without endocrinopathy, minimizing the confounding effect of race. Last, despite the ability to track the entire country, the number of SCFE cases in patients with certain endocrinopathies was small.

In conclusion, the incidence of SCFE was approximately 4 times higher in children with endocrinopathy than in those without it and was approximately 2 times higher in boys than in girls among children with and without endocrinopathy. The risk of SCFE increased with an increasing number of deficient hormones. Long-term monitoring for SCFE in children with endocrinopathies is strongly recommended.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJS/H789). ■

Sunghyun Hwang, MD[1]
Yun Jeong Lee, MD[2]
Mi Hyun Song, MD[1,3]
Tae-Joon Cho, MD[1,3]
In Ho Choi, MD[3]
Chang Ho Shin, MD[1,3]

[1]Division of Pediatric Orthopaedics, Seoul National University Children's Hospital, Seoul, Republic of Korea

[2]Department of Pediatrics, Seoul National University Children's Hospital, Seoul, Republic of Korea

[3]Department of Orthopaedics, Seoul National University College of Medicine, Seoul, Republic of Korea

Email for corresponding author: drshinch@gmail.com

References

1. Loder RT, Skopelja EN. The epidemiology and demographics of slipped capital femoral epiphysis. ISRN Orthop. 2011 Sep 21;2011:486512.
2. Witbreuk M, van Kemenade FJ, van der Sluijs JA, Jansma EP, Rotteveel J, van Royen BJ. Slipped capital femoral epiphysis and its association with endocrine, metabolic and chronic diseases: a systematic review of the literature. J Child Orthop. 2013 Jun;7(3):213-23.
3. Shaw KA, Shiver AL, Oakes T, Fletcher ND. Slipped capital femoral epiphysis associated with endocrinopathy: a narrative review. JBJS Rev. 2022 Feb 7;10(2):1-7.
4. Murray AW, Wilson NI. Changing incidence of slipped capital femoral epiphysis: a relationship with obesity? J Bone Joint Surg Br. 2008 Jan;90(1):92-4.
5. Scharschmidt T, Jacquet R, Weiner D, Lowder E, Schrickel T, Landis WJ. Gene expression in slipped capital femoral epiphysis. Evaluation with laser capture microdissection and quantitative reverse transcription-polymerase chain reaction. J Bone Joint Surg Am. 2009 Feb;91(2):366-77.
6. Novais EN, Maranho DA, Vairagade A, Kim YJ, Kiapour A. Smaller Epiphyseal Tubercle and Larger Peripheral Cupping in Slipped Capital Femoral Epiphysis Compared with Healthy Hips: A 3-Dimensional Computed Tomography Study. J Bone Joint Surg Am. 2020 Jan 2;102(1):29-36.
7. Liu RW, Armstrong DG, Levine AD, Gilmore A, Thompson GH, Cooperman DR. An anatomic study of the epiphyseal tubercle and its importance in the pathogenesis of slipped capital femoral epiphysis. J Bone Joint Surg Am. 2013 Mar 20;95(6):e341-8.
8. Chung CH, Ko KR, Kim JH, Shim JS. Clinical and radiographic characteristics of atypical slipped capital femoral epiphysis. J Pediatr Orthop. 2019 Nov/Dec;39(10):e742-9.
9. Loder RT, Hensinger RN, Alburger PD, Aronsson DD, Beaty JH, Roy DR, Stanton RP, Turker R. Slipped capital femoral epiphysis associated with radiation therapy. J Pediatr Orthop. 1998 Sep-Oct;18(5):630-6.
10. Loder RT, Hensinger RN. Slipped capital femoral epiphysis associated with renal failure osteodystrophy. J Pediatr Orthop. 1997 Mar-Apr;17(2):205-11.
11. Loder RT, Wittenberg B, DeSilva G. Slipped capital femoral epiphysis associated with endocrine disorders. J Pediatr Orthop. 1995 May-Jun;15(3):349-56.
12. Loder RT, Starnes T, Dikos G. Atypical and typical (idiopathic) slipped capital femoral epiphysis. Reconfirmation of the age-weight test and description of the height and age-height tests. J Bone Joint Surg Am. 2006 Jul;88(7):1574-81.
13. Larson AN, Yu EM, Melton LJ 3rd, Peterson HA, Stans AA. Incidence of slipped capital femoral epiphysis: a population-based study. J Pediatr Orthop B. 2010 Jan;19(1):9-12.
14. Lehmann CL, Arons RR, Loder RT, Vitale MG. The epidemiology of slipped capital femoral epiphysis: an update. J Pediatr Orthop. 2006 May-Jun;26(3):286-90.
15. Benson EC, Miller M, Bosch P, Szalay EA. A new look at the incidence of slipped capital femoral epiphysis in New Mexico. J Pediatr Orthop. 2008 Jul-Aug;28(5):529-33.
16. Kelsey JL, Keggi KJ, Southwick WO. The incidence and distribution of slipped capital femoral epiphysis in Connecticut and Southwestern United States. J Bone Joint Surg Am. 1970 Sep;52(6):1203-16.
17. Bertrand T, Urbaniak JR, Lark RK. Vascularized fibular grafts for avascular necrosis after slipped capital femoral epiphysis: is hip preservation possible? Clin Orthop Relat Res. 2013 Jul;471(7):2206-11.
18. Wells D, King JD, Roe TF, Kaufman FR. Review of slipped capital femoral epiphysis associated with endocrine disease. J Pediatr Orthop. 1993 Sep-Oct;13(5):610-4.
19. Wilton P, Bagewitz A. Incidence of slipped capital femoral epiphysis in GH treated children experience from KIGS. Presented as a poster exhibit at the 35th Annual Meeting of the ESPE; 1996 Sep 15-18; Montpellier, France. Poster no. 209.
20. Blethen SL, Rundle AC. Slipped capital femoral epiphysis in children treated with growth hormone. A summary of the National Cooperative Growth Study experience. Horm Res. 1996;46(3):113-6.
21. Inman M, Hursh BE, Mokashi A, Pinto T, Metzger DL, Cummings EA. Occurrence of slipped capital femoral epiphysis in children undergoing gonadotropin-releasing hormone agonist therapy for the treatment of central precocious puberty. Horm Res Paediatr. 2013;80(1):64-8.
22. Maneatis T, Baptista J, Connelly K, Blethen S. Growth hormone safety update from the National Cooperative Growth Study. J Pediatr Endocrinol Metab. 2000 Sep;13(Suppl 2):1035-44.
23. Rappaport EB, Fife D. Slipped capital femoral epiphysis in growth hormone-deficient patients. Am J Dis Child. 1985 Apr;139(4):396-9.
24. Song SO, Jung CH, Song YD, Park CY, Kwon HS, Cha BS, Park JY, Lee KU, Ko KS, Lee BW. Background and data configuration process of a nationwide population-based study using the Korean national health insurance system. Diabetes Metab J. 2014 Oct;38(5):395-403.
25. Heyerman W, Weiner D. Slipped epiphysis associated with hypothyroidism. J Pediatr Orthop. 1984 Sep;4(5):569-73.
26. Zubrow AB, Lane JM, Parks JS. Slipped capital femoral epiphysis occurring during treatment for hypothyroidism. J Bone Joint Surg Am. 1978 Mar;60(2):256-8.
27. Heatley FW, Greenwood RH, Boase DL. Slipping of the upper femoral epiphyses in patients with intracranial tumours causing hypopituitarism and chiasmal compression. J Bone Joint Surg Br. 1976 May;58(2):169-75.
28. Fidler MW, Brook CG. Slipped upper femoral epiphysis following treatment with human growth hormone. J Bone Joint Surg Am. 1974 Dec;56(8):1719-22.
29. Bone LB, Roach JW, Ward WT, Worthen HG. Slipped capital femoral epiphysis associated with hyperparathyroidism. J Pediatr Orthop. 1985 Sep-Oct;5(5):589-92.
30. Yang F, Zhao Y, Lv J, Sheng X, Wang L. A new compound heterozygous mutation in a female with 17α-hydroxylase/17,20-lyase deficiency, slipped capital femoral epiphysis, and adrenal myelolipoma. Gynecol Endocrinol. 2019 May;35(5):385-9.

31. Reeves GD, Gibbs M, Paulshock BZ, Rosenblum H. Gigantism with slipped capital femoral epiphysis. Am J Dis Child. 1978 May;132(5):529-30.
32. Somasundaram KR, Sankararaman S, Siddiqui A, Zadeh H. Pseudohypoparathyroidism as a rare cause of bilateral slipped capital femoral epiphysis. Indian J Orthop. 2012 Nov;46(6):705-9.
33. Kempers MJ, Noordam C, Rouwé CW, Otten BJ. Can GnRH-agonist treatment cause slipped capital femoral epiphysis? J Pediatr Endocrinol Metab. 2001 Jun;14(6):729-34.
34. van Puijenbroek E, Verhoef E, de Graaf L. Slipped capital femoral epiphyses associated with the withdrawal of a gonadotrophin releasing hormone. BMJ. 2004 Jun 5;328(7452):1353.
35. Chan A, Cundy PJ, Foster BK, Keane RJ, Byron-Scott R. Late diagnosis of congenital dislocation of the hip and presence of a screening programme: South Australian population-based study. Lancet. 1999 Oct 30;354(9189):1514-7.
36. Chang CH, Wang SM, Kuo KN. The Ponseti method decreased the surgical incidence in children with congenital clubfoot: a population-based, 8 birth-year cohort study. J Bone Joint Surg Am. 2019 Nov 6;101(21):1955-60.
37. Noguchi Y, Sakamaki T; Multicenter Sutdy Commitee of the Japanese Pediatric Orthopaedic Association. Epidemiology and demographics of slipped capital femoral epiphysis in Japan: a multicenter study by the Japanese Paediatric Orthopaedic Association. J Orthop Sci. 2002;7(6):610-7.
38. Burrow SR, Alman B, Wright JG. Short stature as a screening test for endocrinopathy in slipped capital femoral epiphysis. J Bone Joint Surg Br. 2001 Mar;83(2):263-8.
39. van der Eerden BC, Karperien M, Wit JM. Systemic and local regulation of the growth plate. Endocr Rev. 2003 Dec;24(6):782-801.
40. Phillip M, Lazar L. The regulatory effect of hormones and growth factors on the pubertal growth spurt. Endocrinologist. 2003;13(6):465-9.
41. Clayton PE, Cowell CT. Safety issues in children and adolescents during growth hormone therapy—a review. Growth Horm IGF Res. 2000 Dec;10(6):306-17.
42. Harris WR. The endocrine basis for slipping of the upper femoral epiphysis. J Bone Joint Surg Br. 1950;32(1):5-11.
43. McAfee PC, Cady RB. Endocrinologic and metabolic factors in atypical presentations of slipped capital femoral epiphysis. Report of four cases and review of the literature. Clin Orthop Relat Res. 1983 Nov;(180):188-97.
44. Nourbakhsh A, Ahmed HA, McAuliffe TB, Garges KJ. Case report: bilateral slipped capital femoral epiphyses and hormone replacement. Clin Orthop Relat Res. 2008 Mar;466(3):743-8.
45. Hennessy MJ, Jones KL. Slipped capital femoral epiphysis in a hypothyroid adult male. Clin Orthop Relat Res. 1982 May;(165):204-8.
46. Epps CH, Martin ED. Slipped capital femoral epiphysis in a sexually mature myxedematous female. JAMA. 1963;183(4):287-9.
47. Choi HS. Integration policy study of the Korean society according to the increase of multicultural family -application possibility of reciprocity principle of Singapore and China to the Korean society. J Koreanology. 2009;35:343-75.