Heterotopic Ossification Following Hip Osteotomies in Cerebral Palsy: Incidence and Risk Factors

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Abstract: The aims of this study are, first, to determine the incidence of heterotopic ossification (HO) in patients with cerebral palsy (CP) who have undergone pelvic and/or proximal femoral osteotomies and, second, to identify any risk factors that may contribute to its development in this patient population. The radiographs of 219 consecutive patients with CP who underwent proximal femoral osteotomies with or without pelvic osteotomies were reviewed. Risk factors including gender, age, and degree of involvement, ambulatory status, previous hip operations, bilateral hip surgery, capsular release, concomitant pelvic osteotomy, infection, and history of exuberant callus were evaluated. Thirty-five (16%) patients were diagnosed with HO and the 5 factors that cause HO were identified, which are degree of involvement (quadriplegic), ambulatory status, capsular release, infection, and previous hip operations. Based on logistic regression analysis, if a patient had quadriplegic type of CP, then they have 17.5 times more risk for HO than a patient with hemiplegic type, and capsular release increases the risk 237 times. Although HO occurred in 16% of patients treated with bony procedures in the hip, in a small group (2%) of children it had a clinically significant limitation requiring surgical resection. In this study, clear risk factors were presented for the development of HO; however, none of these risk factors can be altered in ways that will reduce the risk for HO. These risk factors might be used to define a high-risk group in whom attempts at prophylactic treatment for prevention of HO could be initiated.

Key Words: heterotopic ossification, cerebral palsy, hip osteotomy

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Heterotopic ossification (HO) is the abnormal formation of bone outside the normal skeletal tissue. The mechanism to its formation, however, still remains unknown. It usually occurs following trauma, burns, injuries to the brain or spinal cord, and total joint arthroplasty;[1–5] however, occasionally it develops in patients who have cerebral palsy (CP) or anoxic brain injury.[1] Krum and Miller[6] showed that its incidence was significant after soft tissue release around the hip and the severity of HO formation might be aggravated by performing a concomitant spine surgery.[7] This, however, rarely caused any limitation of motion around the hip.

The incidence of HO after bony procedures around the hip such as femoral and pelvic osteotomies is still unknown. Aside, from spine surgery, no additional risk factors that may contribute to the formation of HO in this patient population were identified. The aims of this study are, first, to determine the incidence of HO in patients with CP who have undergone pelvic and/or proximal femoral osteotomies and, second, to identify any risk factors that may contribute to its development in this patient population.

METHODS

After the institutional review board approval was obtained, the medical charts and radiographs of 219 consecutive patients with CP who underwent proximal femoral osteotomies with or without pelvic osteotomies between 1991 and 2003 were reviewed. HO was identified in 35 patients (16%). Anteroposterior radiographs of these hips were reviewed preoperatively and a minimum of 12 months after surgical procedures.

The data recorded from the charts included (1) gender, (2) age, (3) involvement, (4) ambulatory status, (5) previous hip operations, (6) bilateral hip surgery, (7) capsular release, (8) concomitant pelvic osteotomy, (9) infection, and (10) history of exuberant callus. Involvement was divided into 3 subgroups: hemiplegic, diplegic, and quadriplegic. Ambulatory status was classified according to functional capacity whether they were independent ambulators, community ambulators with assistive device, household ambulators, or nonambulators. Associated soft tissue release consisted of adductor, iliopsoas, or hamstring release. Pelvic osteotomy and spine surgery was recorded if it was performed at the same time with femoral osteotomy. Surgical wound infection was defined as superficial or deep.

Radiographically, HO was classified according to anatomic area: iliopsoas type, pericapsular type, and periarticular type. Iliopsoas type was determined if HO begins from lesser trochanter and extension to iliopsoas muscles (Fig. 1) and clinically similar or minimal (0–20 degrees of flexion and 0–10 degrees of abduction) loss of the hip motion if compared with preoperative hip motion. Pericapsular type was identified if there is HO around the hip capsule

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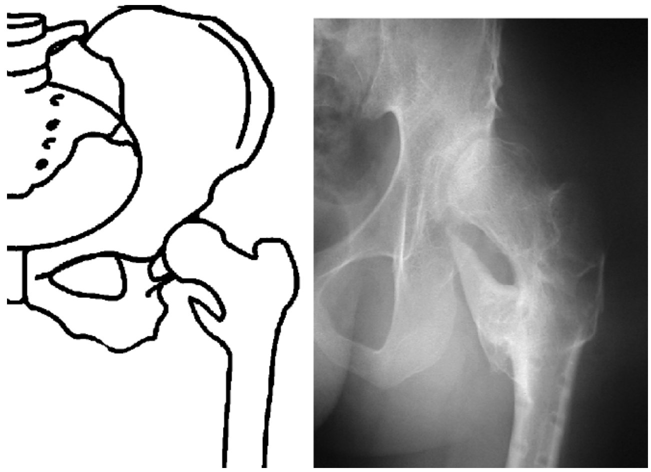

FIGURE 1. Iliopsoas type of HO begins from the lesser trochanter and extends to the iliopsoas muscles.

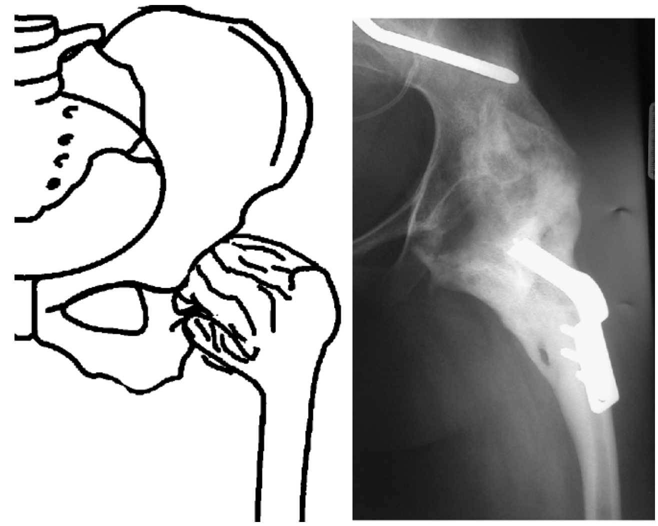

FIGURE 3. Periarticular type is described if HO develops from the proximal femur to the acetabulum.

without any connection with the proximal femur or pelvis (Fig. 2) and clinically similar or moderate (0–40 degrees of flexion and 0–10 degrees abduction) loss of the hip motion when compared with preoperative hip motion. Periarticular type was described if HO develops from proximal femur to acetabulum (Fig. 3), and clinically severe loss of hip motion was defined as no hip motion or very limited motion.

Data Analysis

Outcomes were analyzed using both univariate and multivariate methodologies. Univariate analyses were completed using gender, age, involvement, ambulatory status, previous hip operations, capsular release, pelvic osteotomy, infection, and history of exuberant callus. A direct-entry multivariate, logistic regression analysis was preformed with HO serving as the outcome. Before the analysis, the variables were examined to determine whether they met the following assumptions for logistic analysis: (1) absence of multivariate collinearity, (2) absence of suppressor variables, (3) linearity of the logit (ie, the homoscedasticity of regression assumption), (4) absence of multivariate outliers, and (5) adequacy of expected frequencies and power. No multivariate collinearity was evident. In addition, given the number of available subjects and the number of predictors, we followed the logistic regression methodology employed.[8] Thereby, the number of predictors was reduced to the 5 variables that showed statistically significant bivariate correlations with the HO criterion (involvement, ambulatory status, infections,

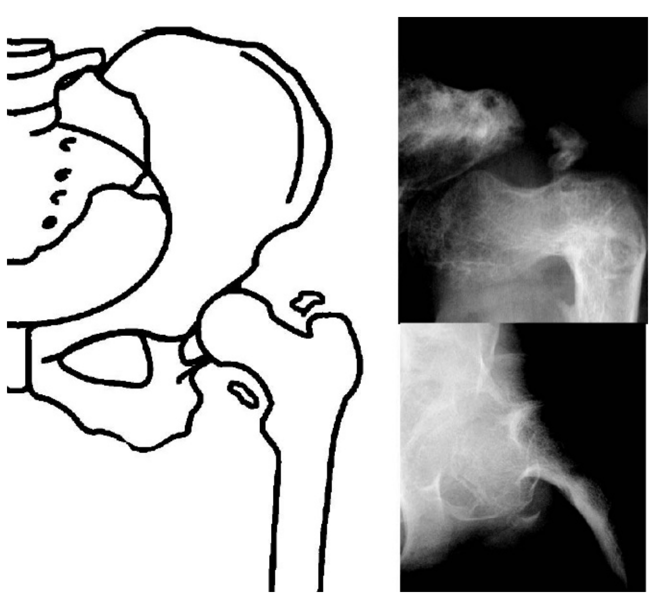

FIGURE 2. Pericapsular type is identified if there is HO around the hip capsule without any connection to the proximal femur or pelvis.

TABLE 1. Demographic Data of the Patients

Risk Factors		Heterotopic Ossification Yes	Heterotopic Ossification No
Gender	Male	19	101
	Female	16	83
Race	White	22	128
	African American	13	56
Neurologic involvement	Hemiplegic	0	17
	Diplegic	8	139
	Quadriplegic	27	28
Ambulatory status	Ambulatory	4	148
	Household	5	16
	Nonambulatory	26	20
VDRO	Unilateral	3	42
	Bilateral	27	147
VDRO + peri-ileal osteotomy	Unilateral	16	108
	Bilateral	11	37
Infections		21	198
Extuberant callus		8	21
Capsular release		26	70
Previous hip surgery		19	52

TABLE 2. Classification Results Between Predicted Versus Observed Result Outcomes

Observed Outcome	Predicted Outcome With HO	Predicted Outcome Without HO	Percentage Correct
With HO	61	2	96.8
Without HO	9	26	74.3

capsular release, and previous hip operations). Statistical significance was set as $P < 0.050$.

RESULTS

Two hundred nineteen patients were reviewed in which 120 were male and 99 were female. Demographic data are showed in detail on Table 1. HO was diagnosed in 35 patients (16%). Of these, 19 were male and 16 were female. The incidence of HO according to gender was 15.8% for the male patients (19 of 120) and 16% for the female patients (16 of 99). Of the 35 patients diagnosed with HO, 26 patients were classified as having the iliopsoas type, 7 had the pericapsular type, and 2 patients had the periacetabular type of HO. The average age of all patients at the time of surgery was 10.1 years (range, 4–20 years), 12.4 years (range, 6–20 years) in the HO group, and 10.2 years in the group without HO. According to race, HO occurred in 22 (14%) of 150 white patients and 13 (19%) of 69 African American patients.

According to the degree of neurologic involvement, 17 patients (7.7%) were hemiplegic, 147 patients were diplegic (67%), and 55 patients (25%) had quadriplegic type of CP. In the 35 patients identified with HO, 49% were quadriplegic (27 patients), 5.4% were diplegic (8 patients), and no hemiplegics. According to ambulatory status, 152 patients were independent ambulators or ambulated with assistance. Four of these 152 patients (2.6%) had HO. Twenty-one patients were household ambulators and 5 (24%) of the 21 patients had HO. Forty-six patients were nonambulatory and 26 (56%) of these had HO.

In the HO group, 19 patients had no previous hip surgery, 11 patients had 1, 4 patients had 2, and 1 patient had 3. Failed soft tissue procedures consisted of adductor release, hamstring release, iliopsoas release, or combination of these. Failed bony procedures included varus derotation osteotomy in the proximal femur (VDRO) with pelvic osteotomy in 2 patients (3 hips) and without pelvic osteotomy in 4 patients.

Bilateral VDRO was performed in 174 of 219 patients and 30 patients (17.2 %) had HO. The remaining 45 patients were treated with unilateral VDRO and HO developed in 5 of them (11%). A concomitant peri-ileal pelvic osteotomy was performed in 114 patients unilaterally and in 48 patients bilaterally. HO developed in 16 (14%) of 114 patients treated with unilateral peri-ileal osteotomy and 11 (23%) of 48 patients treated with bilateral peri-ileal pelvic osteotomy.

There was exuberant callus formation in 8 of 35 patients (23%), including 6 iliopsoas type, 1 pericapsular type, and 1 periacetabular type of HO. Inferior capsular release was performed in 96 patients. HO developed in 26 patients (27%). Nineteen patients had iliopsoas type, 5 patients had pericapsular type, and 2 patients had periacetabular type of HO.

Infection developed in 16 of 219 patients and HO occurred in 7 patients after infection (superficial in 2 patients and deep in 5 patients). Periacetabular HO developed in 2 patients after deep infection. The first case had bilateral VDRO combined with bilateral peri-ileal pelvic osteotomy. Bilateral postoperative deep wound infection developed, and local debridement with irrigation was performed in the operation room. *Staphylococcus aureus* was grown in the culture and intravenous antibiotics were begun. Hardware was removed 3 months postoperative and subsequent bilateral autofusion of the hip occurred. To restore hip motion, a total hip arthroplasty was performed. The second case, bilateral periarticular type of HO, was observed after bilateral VDRO and peri-ileal osteotomy. This case was treated with debridement, irrigation, and intravenous antibiotics. Later, resection of heterotopic bone with radiation therapy and intra-articular steroid injection was performed to prevent recurrence. There was no recurrence and this patient had moderate hip motion at follow-up.

Resection of HO and radiotherapy was performed to improve hip motion at 6 and 12 months after the initial procedure in 2 additional patients (4 hips) who had pericapsular-type HO secondary to deep infection. At follow-up, no recurrence of HO was observed. One patient had normal hip motion and the second patient had limited hip motion.

Data Analysis

A test of the full logistic model was statistically significant with all 10 predictors against a constant-only

TABLE 3. Logistic Regression Analysis of results as a Function of HO Variable

Variable	Beta Coefficient	Wald Test (z ratio)	P	Odds Ratio	95% Confidence Interval for Odds Ratio: Lower	95% Confidence Interval for Odds Ratio: Upper
Involvement	2.87	4.621	0.032	17.5	1.287	239.240
Ambulatory status	−0.181	0.031	0.861	0.835	0.110	6.312
Infections	−1.028	1.375	0.241	0.358	0.064	1.995
Capsular release	5.616	21.097	0.001	274.7	25.013	3017.167
Previous operations	1.404	2.578	0.108	4.072	0.734	22.559

P indicates statistical significance level.

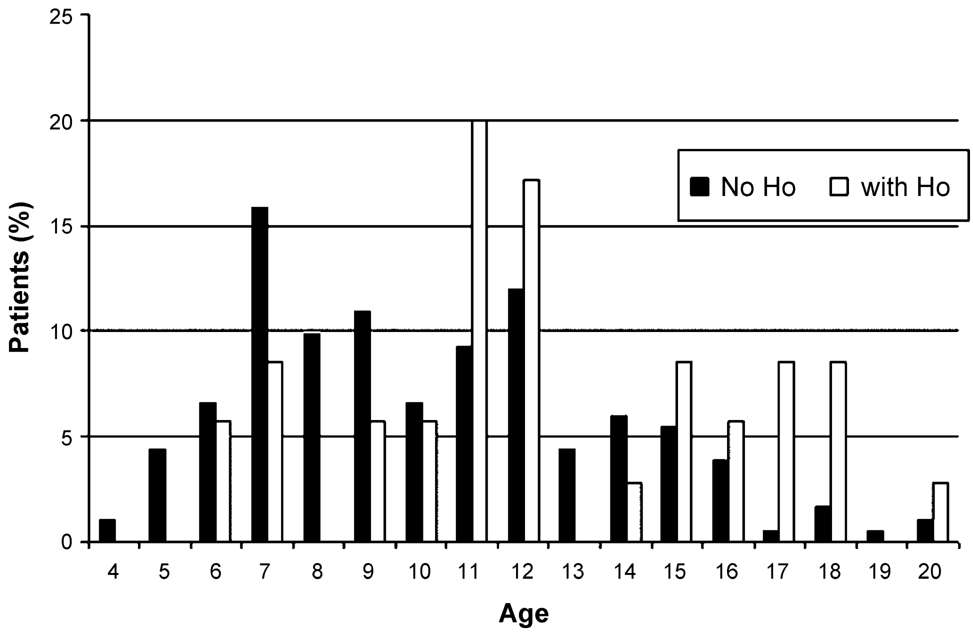

FIGURE 4. The percentage of patients with HO according to age.

model, χ^2 (df = 5) = 74.784, $P < 0.05$. This finding revealed that, as a set, the 5 of 10 predictors, which are degree of involvement (quadriplegic), ambulatory status, capsular release, infection, and previous hip operations, were able to reliably distinguish between subjects who had HO outcomes versus those with no HO outcomes. Table 2 provides classification results using the overall equation. Results show an overall diagnostic sensitivity of 0.871, specificity of 0.929, and an odds ratio of 88.1. Likewise, the amount of criterion variance that could be accounted for was substantial (Nagelkerke R^2 statistic = 0.733).

Regression coefficients, Wald statistics, significance levels, odds ratios, and 95% confidence intervals for odds ratios for each of the 5 predictors were preformed (Table 3). According to the Wald statistic, 2 variables made statistically significant contributions to the prediction of the HO outcome: involvement and capsular release. Odds ratios were interpreted for the 2 significant variables. Results show that when subjects have an involvement status "quadriplegic type," they are 17.5 times more likely to have an HO outcome than subjects with an involvement status "hemiplegic type." More importantly, subjects who had a capsular release are 274 times more likely to have HO outcome than subjects without a capsular release.

DISCUSSION

Dislocation or subluxation of the hip in older patients with CP causes pain and functional disabilities. It has been commonly treated surgically with soft tissue procedures, femoral osteotomies, pelvic osteotomies, or any combination of these.[9–11] Bouchard et al[12] and Krum et al[6] found that the incidence of HO after soft tissue procedures around the hip was 16% and 17.3%, respectively. If a spine surgery is performed concomitantly, the incidence of HO increases to 40%. In our study, the incidence of HO in patients treated with bony procedures around the hip was found to be 16%, and the most important risk factors identified were the degree of involvement (quadriplegic type) and whether a capsular release was done. Five of 10 factors including gender, age, bilateral hip surgery, concomitant pelvic osteotomy, and history of exuberant callus did not significantly increase the risk of HO.

The relationship between age and HO is still in question. Some authors reported that older age might be a risk factor in patients with spinal cord injuries, brain injury, or total hip arthroplasty.[13,14] Some studies, on the other hand, reported that age is not an important factor.[15,16] The limitation in these studies was that their patient population was older than 20 years and might not be comparable to the pediatric population. Garland and Orwin[17] investigated HO after spinal cord injury in the pediatric population; however, their study did not give any detail with regard to age. In our study, the average age of patients in the HO group was older than the group without HO and the incidence of HO was higher in children older than 11 years (Fig. 4).

Based on the literature, males have a higher incidence of developing HO than females after total hip arthroplasty and spinal cord injury.[18,19] Whether this fact applies to the CP population remains in question. Lee et al[7] reported only 3 cases with CP developing HO after hip surgery; 2 of which were female. Our study showed that females had a higher risk for developing HO as compared with males (84% and 67%, respectively). This is not in agreement with the current literature and is probably due to the difference in patient population.

Based on current study, the incidence of HO also seemed to be higher in the white population as compared with the African American population. This has not been discussed in detail in the literature and the only reports that pertain to this showed no statistical differences between races.[14]

According to our study, severity of involvement was important because our study showed that quadriplegics were 17.5 times more likely to develop HO than hemiplegics. The similar observation was reported for the patients who had spinal cord injuries.[20,21] A parallel observation was seen when functional status was evaluated in that nonambulatory patients seemed to have a greater risk of developing HO as compared with the independent or assisted ambulators.

Repeated surgery also has a higher risk than primary surgery, which was supported by the current study. Broker et al[2] reported that repeated hip surgery and history of HO were risk factors following total hip arthroplasty.

Surgical trauma, stripping the capsule off of the acetabulum, and pelvic osteotomies were significant risk factors in increasing the rate of HO.[22] These combined procedures produce trauma to the muscles and may cause the release of some osteogenic factors. These factors may also be released from osteotomized pelvic bone and raise the risk of HO. This fact was supported in our study in that HO occurred more in patients who had bilateral hip surgery as compared with those with unilateral procedures. The site that had a pelvic osteotomy performed also had a higher risk compared with the contralateral site.

The anatomic area of HO involvement have been described as lateral in the abductor muscles after total hip arthroplasty, from the anterior superior iliac spine toward the lesser trochanter after spinal cord injury, and from the anterior superior iliac spine toward the greater trochanter after traumatic brain injury.[2,23,15] The diffuse periarticular form can be seen after direct trauma or burn injuries.[23] In our study, the most common site of HO was the iliopsoas muscle, and it generally formed within a plane from the lesser trochanter toward the acetabulum in the anteroposterior view and anteriorly in the lateral view. Although we could not support this statistically, we believe the iliopsoas-type HO is commonly formed after division or separation of the tendon–periosteum complex from lesser trochanter or lack of total excision of the apophysis of the iliopsoas muscle was attached to the lesser trochanter.

McHale[24] reported a case of a 7-year-old girl with quadriplegic type of CP developing bilateral spontaneous arthrodesis of the hip joint after combined VDRO and shelf acetabular augmentation. She explained this arthrodesis as a complication of shelf procedure. Krum et al[6] reported spontaneous arthrodesis after soft tissue release and concomitant spinal fusion and they did not suggest that this was a result of the procedure. We believe that infection is an important risk factor for the development of periacetabular HO, which we found in 4 hips secondary to a deep surgical site infection.

Although HO is seen up to 50% after surgical procedure, resection of HO may rarely require restoring joint motion.[17,25–27] However, optimal timing of surgical resection of HO is still uncertain. Gardland and Keenan[26] advocated that HO should not be resected before 6 months after the onset because recurrence of bone formation is the most common complication.[28] In our series, periacetabular HO causing limitation, 2 hips were treated with resection of HO through lateral incision and radiation therapy 1 year following the primary procedure and there was no recurrence of HO in all 5 hips.

The most common sign of HO is pain associated with decreased hip motion. However, discrimination of pain can be difficult after surgical procedure especially in patients with mental retardation. We observed that the iliopsoas type of HO did not cause hip limitation and pain. However, patients with pericapsular type of HO had severe pain despite normal or mild hip limitation. We could not draw any conclusions for the periacetabular type of HO because this type was commonly seen after infection and the factors that cause pain were not clear.

In this study, 5 factors were identified that cause HO, which are degree of involvement (quadriplegic), ambulatory capacity, capsular release, infection, and previous hip operations. Based on logistic regression analysis, if a patient had quadriplegic type of CP, then they have 17.5 times more risk for HO than a patient with hemiplegic type, and capsular release increases the risk 237 times, most commonly iliopsoas type of HO. Although HO occurred in 16% of patients treated with bony procedures in the hip, only 5 of them caused clinically significant limited hip motion, and HO caused severe hip limitation in 2 patients with postoperative deep infection.

In conclusion, we found HO occurring in 16% of hip in children having hip osteotomies. Most of these cause little clinical significance; however, in a small group (2%) of children, clinically significant limitation occurred that required surgical resection. Resection of the HO with radiation therapy provided an acceptable clinical outcome. Clear risk factors were present for the development of HO; however, none of the risk factors can be altered in ways that will reduce the risk for HO. These risk factors might be used to define a high-risk group in whom attempts at prophylactic treatment for prevention of HO could be initiated.

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