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Heterotopic ossification in rehabilitation patients who have had internal fixation of an acetabular fracture

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Abstract—High-energy trauma patients often have multiple injuries and are frequently seen by a physiatrist following their acute care. Acetabular fractures are common in this patient population. Following surgical treatment of acetabular fractures, a very high incidence of heterotopic ossification can occur. We describe 94 patients who underwent posterior surgical fixation of an acetabular fracture. Of these, 87 received heterotopic ossification prophylaxis in the form of irradiation or indomethacin; 5 did not receive prophylaxis. Seven of the 45 patients who were initially started on indomethacin had their medication discontinued for various reasons. Of the 12 patients who did not receive adequate prophylaxis, 5 developed disabling heterotopic ossification. We present our experience with this patient population, and we discuss the importance of adequate prophylaxis for heterotopic ossification.

Key words: *acetabular, fracture, heterotopic, ossification.*

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INTRODUCTION

Heterotopic ossification (HO) is a common and disabling problem in patients who require rehabilitation. It can severely limit motion in affected joints and can be a source of pain. Rehabilitation of a patient with HO can be difficult.

HO may be caused by either neurogenic or traumatic processes, and often both processes may occur simultaneously. Neurogenic heterotopic ossification has been well described in patients with spinal cord injuries (1–3) and in patients with traumatic brain injuries (4–7).

In these patient groups, the joints most commonly affected are the elbow, hip, shoulder, and knee. Traumatic HO is seen following fractures, dislocations, burns, or after certain operative procedures such as total hip arthroplasty (8–10), open treatment of elbow fractures (11), and after intramedullary fixation of femoral shaft fractures (12).

A significant incidence of postoperative HO about the hip is encountered in patients who have undergone operative fixation of an acetabular fracture (13–21). Without prophylaxis, the rate of formation of HO has been reported to be as high as 90 percent in certain at risk populations (13). Two methods of prophylaxis have been described:

local treatment with radiation therapy in varying doses (13,20,21), and systemic treatment with indomethacin for varying periods (14,17,26,33). Although the problem of HO after acetabular fracture has been investigated in the orthopedic literature, the rehabilitation implications have not been described in the physical medicine and rehabilitation literature to our knowledge.

Because the prophylaxis of local postoperative HO is somewhat different than that of the generalized neurogenic HO, we are reporting our experience with the formation of HO about the hip after acetabular fracture fixation.

METHODS

We retrospectively reviewed the charts and radiographs of 94 patients at our institution who underwent open reduction and internal fixation of an acetabular fracture through a posterior or extensile approach between 1992 and 1997. Some of these patients were part of a randomized, prospective study comparing indomethacin versus radiation therapy for prophylaxis against HO in acetabular fractures; 12 did not receive adequate prophylaxis due to reasons to be discussed, and of the remaining patients, 44 had low-dose irradiation for prophylaxis, and 38 had a course of indomethacin.

The first five patients did not receive any HO prophylaxis, and an additional seven were started on indomethacin, but the medication was discontinued during the postoperative period for various reasons. Several had their indomethacin discontinued by other physicians who were unaware of the reason for its use. Of the five untreated patients, follow-up radiographs were available for four; radiographs were available for all of the seven who discontinued their indomethacin. Of the 82 who completed their prophylaxis regimen, follow-up radiographs available for 80. Most patients had clinical information regarding range of motion (ROM) and function available, and this was reviewed as well. The follow-up period averaged 16 mo, with a range of 1.5 to 56 mo.

Plain radiographs of the pelvis were reviewed and scored by two independent observers for HO about the hip joint according to the classification of Brooker, et al (22), reviewed in **Figure 1.** When the observers recorded different grades of HO, the higher score was used.

The hip ROM was considered acceptable if within 20° of normal, as judged by the contralateral hip, in all planes. Alkaline phosphatase was not routinely measured, as it was not felt to be useful in treatment decisions. Statistical evaluation was performed using Systat software (Systat Inc., Evanston, IL). Group comparisons were made using Chi square analysis or Analysis of Variance with a Tukey correction for multiple pairwise comparisons.

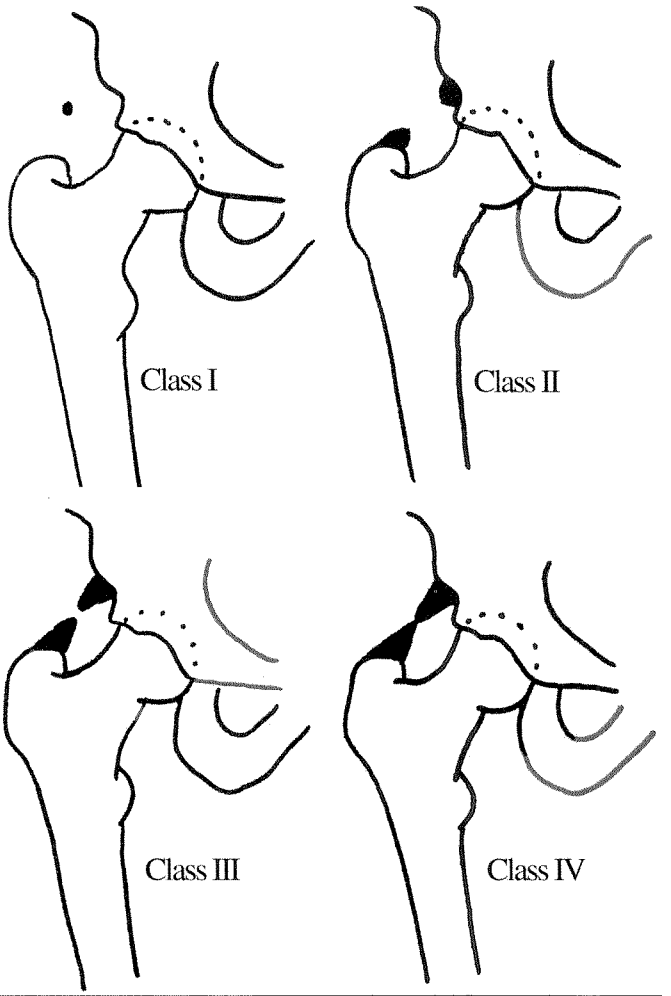

Figure 1.
The Brooker Classification of Heterotopic Ossification around the hip joint. **Class I** has islands of bone within the soft tissues. **Class II** has bone spurs from the pelvis or proximal end of the femur, leaving at least 1 cm between opposing surfaces. **Class III** has bone spurs from the pelvis and/or proximal end of the femur, reducing the space between opposing bone surfaces to less than 1 cm. **Class IV** shows apparent bone ankylosis of the hip.

RESULTS

The distribution of HO in the untreated, insufficiently treated, and treated groups can be seen in **Table 1.** All of the four available patients who did not receive pro-

Table 1.
Treatment group versus Brooker Class heterotopic ossification: distribution of the HO grades between the treatment groups.

		Brooker Class					
Treatment	**No.**	**Unk**	**0**	**1**	**2**	**3**	**4**
No prophylaxis	5	1	0	0	1	2	1
Indocin, imcomplete course	7	0	2	0	3	0	2
Indocin, 6 weeks	38	1	20	8	3	4	2
Radiation	44	1	24	13	3	3	0

No.=number of patients; Unk=unknown Brooker Class; the difference between treatment and no/incomplete treatment is statistically significant at $p<0.001$; the differences between the two treatment groups is not statistically significant ($p=0.8$).

Table 2.
Relationships of Heterotopic ossification to range-of-motion group: the number of each range-of-motion outcome group sorted by Brooker Class of heterotopic ossification. The difference between the groups is statistically significant at $p<0.0001$.

Brooker Class	Unknown	Acceptable	Unacceptable
Unknown	3	0	0
0	1	35	12
1	2	11	7
2	2	4	2
3	2	1	7
4	0	0	5

phylaxis developed HO: one grade II, and the rest grade III or IV ossification. Of the seven patients who were inadequately treated with indomethacin, five developed HO: three grade II, and two grade IV ossification. The difference between those receiving adequate prophylaxis and those who did not was statistically significant, $p<0.001$. These results are displayed in **Table 1.**

Thirty-two patients were adequately treated with indomethacin; 18 of these had no HO, 10 grade I or II, and 4 had grade III or IV HO. Thirty-six patients were treated with radiation therapy; of these, 23 had no HO, 11 grade I or II, and 2 grade III or IV HO. There was not a statistically significant difference between the two treatment method groups, $p=0.8$.

Fifty patients achieved a ROM defined as acceptable (<20° restriction in any plane). Of those, 35 had grade 0 HO, 11 grade I, 4 hgrade II, and 1 grade III. Forty-four had 20° or more of restriction in at least one plane: 12 had grade 0 HO, 7 grade I, 2 grade II, 7 grade III, and 5 grade IV. Of the 28 patients with grade 0–III HO and unacceptable range, 6 had avascular necrosis, 11 had posttraumatic arthritis, 1 had metastatic carcinoma, and 10 had otherwise good or excellent function. In 10 patients, the final ROM was unclear. The relationship between grade of HO and ROM classification (acceptable or unacceptable) was statistically significant, $p<0.0001$. This is shown in **Table 2.**

DISCUSSION

While the rehabilitation literature is replete with reports of neurogenic HO, there appears to be little information regarding HO resulting from trauma or surgery. More specifically, there is really no information regarding this problem in patients who have undergone surgical fixation of an acetabular fracture.

When soft tissue mesenchymal cells undergo metaplasia to form bone precursors, HO develops. The triggering event in this cascade remains unclear; however, certain patient populations have been noted to be at particular risk, and specific risk factors identified. Three basic forms of HO exist: neurogenic, traumatic, and *myositis ossificans progressiva*. Neurogenic HO has been described following closed head injuries, spinal cord trauma, central nervous system infections, strokes, and tumors. It always occurs below the level of the neurologic lesion and may be partially mediated by a humoral factor (23). Neurogenic HO can be severe and may lead to ankylosis in 5–16 percent of cases (24). *Myositis ossificans progressiva* is a rare, autosomal dominant disease that starts in early infancy and leads to complete immobility early in life. Traumatic HO is seen after burns, fractures, dislocations, and after various surgeries, including total hip arthroplasty and open reduction and internal fixation of acetabular fractures.

HO can affect a patient's functional outcome. Limitations in ROM can compromise sitting, dressing, transfers, and even ambulation. Although mild (Brooker Class I or II) HO is generally well tolerated, patients become very limited as they approach ankylosis due to HO. We are aware of only a few studies regarding the effects of HO on functional outcome. Ritter et al. (25) reviewed 507 total hip arthroplasties of which 149 developed HO: 114 class I, 27 class II, and 8 class III. While the ROM of the hips with HO was less than the hips without, the long-term function of the patients were similar in both groups. No patients developed grade IV, which causes much more limitation due to ankylosis.

In our study population, five patients developed class IV HO. This was severely disabling in terms of function to these patients: all five patients required surgical excision of the ossification. For those with less severe HO, the outcome was more dependent upon other factors, such as avascular necrosis and/or posttraumatic degenerative joint disease.

The best treatment of HO is prevention. Various prophylactic regimens have been described. Nonsteroidal anti-inflammatory medications are thought to limit HO by inhibiting cyclooxygenase and preventing prostaglandin synthesis. This may result in the inhibition of mesenchymal cell proliferation (26) and differentiation of mesenchymal cells into osteogenic cells (27). Various nonsteroidal anti-inflammatory medications have been shown to decrease HO in the postoperative period (28). Oral naproxen (28) and intravenous ketorolac (29) have demonstrated effectiveness after total hip replacement. Indomethacin is the most extensively studied nonsteroidal anti-inflammatory medication for use in preventing HO. It has been successful in limiting the condition in patients undergoing total hip arthroplasty (30–32) and in those undergoing open reduction and internal fixation of acetabular fractures (16,17,33). The duration of prophylactic treatment using indomethacin has generally been 6 weeks, although some reports suggest 3 weeks of therapy may be effective (27). Sodium didronate has been used to prevent HO, but since it does not prevent formation of osteoid, but only the mineralization of it, it must be continued indefinitely.

HO following operative treatment of acetabular fractures is quite common. Routt and Swiontkowski (34) reported an incidence of 100 percent in their surgically treated group. Daum et al. (16) noted functionally significant HO in 23 percent of their patients. The incidence of HO is highly dependent upon the surgical approach for the fracture fixation. Posterior approaches and extensile approaches carry a high risk of it, while anterior approaches are uncommonly associated with it. Many authors have documented the success of radiation and/or indomethacin in the prevention of HO following surgery for acetabular fractures. Bosse et al. (13) reported on the results of 17 patients who each received 5 postoperative doses of radiation therapy. The incidence of HO in the irradiated limbs was much lower than in a control group of 29 who who did not receive prophylaxis. Moed and Letournel (20) treated 53 patients with both radiation and indomethacin following acetabular fracture fixation. They had 44 fractures exhibit no HO, and 10 fractures that developed Brooker class I HO. We (21) also found a significant reduction in the incidence of HO in patients treated with a single dose of radiation following a posterior or extensile approach for the fixation of acetabular fractures. McClaren (14) reported on 44 such patients: 18 received 6 weeks of indomethacin, and 26 received no prophylaxis. Grade II or more severe HO occurred in 50 percent of the latter group and in only 5.5 percent of the former. Others (16,17) have also reported a significant reduction in HO in patients treated with indomethacin. The results we have reported here are in agreement with other authors. Patients treated with either single-dose irradiation or a 6-week course of indomethacin had less risk of developing severe HO following operative fixation of acetabular fractures.

ROM was used as a possible measure of functional outcome in this study. Acceptable range of hip motion was defined as restriction less than 20° in any plane. This is an arbitrary level, but it has been used in the literature previously. Nonetheless, 8 of the 44 patients whose hip motion was deemed unacceptable otherwise functioned well, with no significant limitations. While we found that the occurrence of unacceptable motion restrictions was statistically associated with development of higher grade HO, and that the development of higher grade HO was statistically related to treatment group, there was no significant relationship of unacceptably restricted motion to treatment group (**Table 3.**). Restriction of motion was multifactorial and was related to the occurrence of other complications (avascular necrosis and posttraumatic arthritis) as well as HO.

In conclusion, we have reviewed the risks of traumatic HO in postoperative patients following acetabular fracture fixation. Despite good functional results with lesser degrees of HO, it remains important to prevent severe HO from forming in this patient population. The

Table 3.
Treatment group and range of motion: comparison of range-of-motion category distribution between treatment groups. Acceptable motion is defined as loss of <20° of motion in any plane. There was no statistically significant difference between the treatment groups.

	Unknown	Acceptable	Unacceptable
No/Incomplete treatment	3	4	5
Radiation	5	23	16
Indomethacin	2	24	12

present standard remains prevention. The two methods of prophylaxis with proven efficacy are radiation therapy and indomethacin therapy.

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