Risk Factors for the Development of Heterotopic Ossification After Acetabular Fracture Fixation

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Abstract

Background Heterotopic ossification (HO) is a common complication of the operative treatment of acetabular fractures. Although the surgical approach has been shown to correlate with the development of ectopic bone, specific risk factors have not been elucidated.

Questions/purposes The purposes of this study were to determine specific risk factors associated with the development of severe HO and the frequency with which patients

develop severe HO after acetabular fracture fixation through an isolated Kocher-Langenbeck approach.

Methods Using an institutional orthopaedic trauma database at a regional Level I trauma center, patients undergoing open treatment of acetabular fractures during the study period (January 2000 to January 2010) were identified. A review of medical records and imaging studies was performed on 508 patients who were treated by the senior author (MR) through an isolated Kocher-Langenbeck approach. During the study period, the senior author used indomethacin for HO prophylaxis in patients who had ipsilateral femur fracture treated with antegrade reamed medullary nailing or severe local soft tissue injury; 49 (10%) of the patients he treated with the Kocher-Langenbeck approach received prophylaxis, and they were excluded from this study, leaving a total of 459 patients who met inclusion criteria. Of those, 147 (29%) were lost to followup or did not have radiographs both before and at a minimum of 6 weeks (median, 1 week; range, 0–3 weeks), leaving 312 (61% of the patients treated with the Kocher-Langenbeck approach during this time) available for this analysis. Demographic data as well as information related to cause of injury, associated periacetabular findings, other system injuries, and treatment were gathered. Final followup radiographs were assessed for the presence of ectopic bone by two of the authors (TJO, AS) using the modified Brooker classification. Logistic regression was performed to identify possible predictors of development of severe ectopic bone. **Results** The only predictor we identified for the development of severe HO was the need for prolonged mechanical ventilation (odds ratio, 7.1; 95% confidence interval, 2.9–17.3; $p = 0.001$). Injury Severity Score, sex, presence of comminution, femoral head impaction, dislocation, degloving injury, debris in the joint, number of other fractures, and head and chest Abbreviated Injury

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

This work was performed at Harborview Medical Center, Seattle, WA, USA.

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Score > 2 did not correlate with severe HO. Severe HO (Brooker Class III or IV) developed in 38 of 312 patients (12%).

Conclusions Patients with prolonged mechanical ventilation might benefit from HO prophylaxis given the increased risk of developing severe HO in this patient population. However, future prospective studies need to be performed to verify this finding given the fact that a considerable number of patients were prophylactically treated in this study.

Level of Evidence Level IV, prognostic study. See Guidelines for Authors for a complete description of levels of evidence.

Introduction

Heterotopic ossification (HO) is a common complication of the operative treatment of acetabular fractures with an incidence of 7% to 100% [1, 2, 5–8, 10–16, 18, 21, 24, 25, 27, 29, 31, 33]; with a range that wide, it is important to try to identify patients at particular risk for this complication. The choice of surgical approach has been shown to affect the likelihood of development of ectopic bone. The Kocher-Langenbeck approach is associated with intermediate risk, in contrast to the low-risk ilioinguinal and high-risk extended iliofemoral approaches [12]. Complex exposures, double exposures, and concurrent trochanteric osteotomy are associated with increased risk [1, 2, 10, 21, 27, 29]. In addition to surgical approach, other factors have been previously identified as potential risk factors for the development of ectopic bone, including male sex, concurrent craniocerebral trauma or thoracoabdominal trauma, T-type acetabular fracture-associated findings such as sciatic nerve injury, femoral head injury, intraarticular debris, and delay to surgery [5, 7, 19, 33]. Ipsilateral femur fracture may also be associated with increased risk [4]. Injury Severity Score (ISS) has also been demonstrated as a risk factor for ectopic bone around the hip after femoral nailing as well as around the knee after knee dislocation [17, 20]. Need for prolonged mechanical ventilation has been demonstrated as a risk factor for the development of ectopic bone in uninjured joints of polytraumatized patients as well as around the hip after femoral nailing [17, 23, 30], but to our knowledge, not specifically after operatively treated acetabular fractures.

The purpose of this study is to evaluate a large series of patients with acetabular fractures treated through the Kocher-Langenbeck approach without routine postoperative prophylaxis to determine whether there are risk factors for the development of severe (Brooker Class III or IV) HO that are specific to this approach and what the frequency of development of severe HO is after this approach to acetabular fracture surgery.

Patients and Methods

The orthopaedic trauma database at a Level I trauma center was queried to identify all patients who underwent open surgical treatment for diagnosis of acetabular fracture between January 2000 and January 2010. Approval was obtained from the institutional review board for review of the medical records and relevant radiological examinations pertaining to these patients. A total of 508 patients were treated by one surgeon (MR) through an isolated Kocher-Langenbeck approach during this time. Radiation and indomethacin prophylaxis measures were not used routinely based on the results of Rath et al. [26], which displayed the value of necrotic gluteus minimus muscle débridement caudal to the superior gluteal neurovascular bundle in preventing HO. However, during the study period, the senior author used indomethacin for HO prophylaxis in patients who had ipsilateral femur fracture treated with antegrade reamed medullary nailing or severe local soft tissue injury. A total of 49 (10%) of the patients he treated with the Kocher-Langenbeck approach received indomethacin for this indication, and they were excluded from this study, leaving a total of 459 patients who met inclusion criteria. Of those, 147 (29%) were lost to followup or did not have radiographs both before and at a minimum of 6 weeks (median, 1 week; range, 0–3 weeks), leaving 312 (61% of the patients treated with the Kocher-Langenbeck approach during this time) available for this analysis. Exclusion criteria included nonoperative treatment, percutaneous treatment, or open treatment using an ilioinguinal, extended iliofemoral, or double sequential or double-staged approach (ie, Kocher-Langenbeck and ilioinguinal approaches). Patients treated with surgery by the senior author (MR) through an isolated Kocher-Langenbeck approach were included in the study population with additional exclusion of patients with less than 6 weeks of followup and those who received postoperative indomethacin for prophylaxis against formation of HO (Fig. 1).

Medical records and initial radiographic evaluations (radiographs and CT) were reviewed. Data collection included demographics, details pertaining to the injury, fracture-related details (type of fracture based on the Letournel classification, presence of associated dislocation, clinical and radiographic findings including comminution, nerve injury, intraarticular debris, femoral head injury, and local degloving injury), treatment interventions (number of trips to the operating room, need for and duration of mechanical ventilation, complications), and associated injuries (head Abbreviated Injury Score [AIS], chest AIS, number of fractures, ISS). A standard prone Kocher-Langenbeck approach was performed in all patients. The iliotibial band was split longitudinally and the gluteus maximus was split in line with its fibers. The gluteus

Fig. 1 Exclusion diagram is shown for 1159 patients with acetabular fractures over a 10-year period. ORIF = open reduction and internal fixation.

medius was retracted cephalad and the piriformis and obturator internus were tenotomized and tagged for later repair. Superior and inferior gemelli were débrided as was the caudal aspect of the gluteus minimus, which was routinely noted to be contused and obstructing the area of planned implant application [26]. The sciatic nerve was gently retracted while the knee was held in 90° of flexion. Intraarticular debris, when present, was débrided from the joint and the joint was irrigated. Areas of impaction were reduced and grafted with either local autograft obtained from the greater trochanter or morsellized cancellous allograft chips. Major fracture fragments were reduced and fixation generally consisted of one or two appropriately contoured 3.5-mm pelvic reconstruction plates. Additional fixation, if necessary, consisted of percutaneous insertion of a 3.5-mm anterior column screws and/or modified 1/3 tubular plates applied as spring hooks. Wounds were irrigated with 1 to 3 L of sterile saline through pulsatile lavage. Piriformis and obturator internus tendons were repaired. The iliotibial band and skin were closed over deep and subcutaneous hemovac drains.

All patients received routine perioperative antibiotics. Additional postoperative treatment included prophylaxis for deep venous thrombosis with compression stockings and sequential compression devices in addition to either subcutaneous heparin or enoxaparin. All patients were restricted to toe-touch weightbearing unless they had contralateral lower extremity injuries or upper extremity injuries, which prevented the use of a walker or crutches in which case the patients were restricted to bed-to-chair transfers only. These precautions were maintained for 6 weeks. At 6 weeks postoperatively, radiographs were obtained and the patients were started on a progressive

Table 1. Mechanisms of injury

Mechanism	Number
Automobile crash	203 (65%)
Motorcycle crash	40 (13%)
Fall	32 (10%)
Automobile versus pedestrian	9 (3%)
Bicycle crash	9 (3%)
Sports injury	8 (3%)
Crush injury	8 (3%)
Plane crash	1 (0.3%)
Parachute mishap	1 (0.3%)
Blast injury	1 (0.3%)

weightbearing program advancing to full weightbearing over 4 to 6 weeks and back and abdominal exercises were instituted to work on core stabilization.

Postoperative radiographs were evaluated at 6 weeks postoperatively and at final followup (in those patients who had later radiographs) to determine the modified Brooker classification [22]. Radiographs were evaluated by two of the authors (TJO, AS) and in cases in which no agreement could be made, a third person (RF) was involved to make a decision. No inter- or intraobserver reliability was performed. Patients were separated into two groups termed “not severe” (Brooker Class 0, I, or II) and “severe” (Brooker Class III or IV) [3, 7]. For patients with severe HO, the presence of symptoms and/or the need for surgical excision were noted. Logistic regression was performed to identify the significant predictors of development of severe ectopic bone. Potential predictor variables tested in our model included: ISS, sex, presence of comminution, femoral head impaction, dislocation, degloving injury, debris in the joint, number of other fractures, head and chest AIS > 2, and prolonged ventilation.

Injuries were typically the result of high-energy mechanisms (Table 1). The majority of fracture patterns were either transverse with an associated posterior wall or isolated posterior wall (fracture types presented in Table 2). Dislocation and comminution was the most common associated fracture characteristic (associated characteristics in Table 3). Time to reduction was assessed but as a result of lack of documentation and/or poor documentation, it is not reported.

Average patient age was 41 years (range, 7–84 years). Seventy-two percent of the patients were male (223 of 312). Minimum followup was 40 days (average, 256 days; range, 40–2061 days). Medical comorbidities existed in 209 patients (tobacco or heavy alcohol use, diabetes mellitus, asthma, hypertension, liver disease), whereas 103 patients had no known medical problems. Seventy-five patients were initially evaluated at our institution, whereas 237 patients were transferred from outside institutions.

Table 2. Fracture types by Letournel classification

Fracture type	Number
Elementary patterns	
Posterior wall	118 (38%)
Transverse	6 (2%)
Posterior column	3 (1%)
Associated patterns	
Transverse with posterior wall	126 (40%)
Posterior column with posterior wall	21 (7%)
T-type	13 (4%)
Associated both-column	1 (0.3%)
Other	
T-type with posterior wall	24 (8%)

Table 3. Associated fracture characteristics

Presence of	Number
Documented dislocation	252 (81%)
Comminution	254 (81%)
Intraarticular debris	214 (69%)
Impaction of acetabulum	116 (37%)
Femoral head injury (impaction/fracture)	77 (25%)
Nerve injury (sciatic/peroneal)	54 (17%)
Local degloving injury	11 (4.0%)

Patients had between one and 11 general anesthetics (average of two) with 100 patients having only a single general anesthetic at which time their acetabular fracture was treated along with any other injuries requiring surgery. Complications were noted in 118 patients (22%). These included thromboembolic events in 34 patients (30 patients with deep vein thrombosis, four patients with pulmonary embolism), pulmonary complications (pneumonia, respiratory failure, acute respiratory distress syndrome) in 25 patients (8%), and local complications (hematoma, wound dehiscence, infection) in eight patients (3%). The acetabular fracture was an isolated orthopaedic injury in 181 patients. The other 131 patients had one to six additional fractures. Mean ISS was 15 (range, 4–57). ISS was > 16 in 118 patients. Chest injury (AIS > 2) was noted in 63% of patients and head injury (AIS > 2) in 9% of patients. Mechanical ventilation was required for > 72 hours in 19% of patients. These 56 patients were categorized as requiring “prolonged mechanical ventilation.”

Results

The only factor we identified that was associated with the development of severe HO was prolonged intubation (characterized as 0, 1, or 2 days versus 3 or more days).

The overall R^2 for this equation was 0.168. The odds ratio for each additional day of intubation was 7.1 (95% confidence interval, 2.9–17.3). The other 10 variables assessed were not found to be associated with the development of heterotopic ossification (Table 4).

A total of 38 patients (12%) developed severe HO (Table 5). Patients in this group often had no complaints but occasionally did report pain, mass, stiffness, or numbness/weakness related to sciatic nerve compression. Five of these patients (13%) underwent excision of the ectopic bone. No patient with Grade 0 HO had clinical signs of sciatic nerve dysfunction or required surgical excision of the ectopic bone. Progression of HO was only noted in two patients when comparing 6-week postoperative radiographs and final radiographs. One patient progressed from Class I to Class II and one patient progressed from Class III to Class IV; no patients progressed from Class II to Class III.

Discussion

HO is a common postoperative complication in the treatment of acetabular fractures with a reported incidence of 7% to 100% [1, 2, 5–8, 10–16, 18, 21, 24, 25, 27, 29, 31, 33]. The exact pathogenesis is unknown. Excessive HO around the hip can cause severe limitations in ROM leading to decreased function. Although many studies have sought to evaluate risk factors [5, 7, 14, 33], there also are areas of disagreement among these studies [5, 7, 9, 14], which call for further evaluation. Accordingly, this study was designed to determine the specific risk factors that place patients at high risk for developing severe HO. Prophylaxis could then be used for patients who are found to be at high risk. We identified prolonged mechanical ventilation as a risk factor for developing severe HO, but interestingly, the chest injury score did not correlate. This could be attributable to the fact that not all patients who remain intubated for extended periods of time have chest injuries.

Our study has several weaknesses in addition to inherent weaknesses with retrospective studies. First, although our final study population was treated with a standard protocol by a single surgeon, we did have 49 patients who were excluded because they were given prophylaxis. This represents 10% (49 of 508) of the population treated by the senior surgeon. Reasons for prophylaxis included ipsilateral femur fracture treated with antegrade reamed medullary nailing or severe local soft tissue injury. Because of this, one cannot conclude from our study that the severity soft tissue injury does not increase rates of severe HO, because in this study, patients with the most severe soft tissue/degloving injuries received prophylaxis and were excluded.

Table 4. Logistic regression analysis results

Variable	β	SE	Wald	df	p value	Exp(B)	95% CI for EXP(B)	
							Lower	Upper
Sex	0.178	0.515	0.120	1	0.729	1.195	0.436	3.277
Comminution	0.230	0.698	0.108	1	0.742	1.258	0.321	4.939
Femoral head injury	−0.484	0.507	0.913	1	0.339	0.616	0.228	1.664
Dislocation	1.136	0.951	1.427	1	0.232	3.114	0.483	20.078
Degloving/soft tissue injury	20.348	12325.664	0.000	1	0.999	686997613.932	0.000	.
Intubation (3 or more days)	2.215	0.677	10.718	1	0.001	9.164	2.433	34.520
ISS > 16	1.444	0.772	3.504	1	0.061	4.239	0.934	19.234
Chest AIS > 2	−1.346	0.752	3.202	1	0.074	0.260	0.060	1.137
Head AIS > 2	−0.666	0.696	0.917	1	0.338	0.514	0.131	2.008
Number of other fractures	−0.001	0.178	0.000	1	0.997	0.999	0.705	1.415
Debris in joint	0.034	0.526	0.004	1	0.949	1.034	0.369	2.897
Constant	−44.064	24651.327	0.000	1	0.999	0.000		

CI = confidence interval; EXP(B) = exponent of beta; ISS = Injury Severity Score; AIS = Abbreviated Injury Score.

Table 5. Final modified Brooker classification

Brooker classification	Number
“Not severe”	
Class 0	212 (68%)
Class I	16 (5%)
Class II	46 (15%)
“Severe”	
Class III	19 (6%)
Class IV	19 (6%)

Lack of patient followup and use of 6 weeks as a minimum followup duration is another weakness of our study. One hundred thirty-nine of 508 (27%) patients were excluded as a result of lack of followup. This is typical with our high-volume institution that treats patients from multiple states. Over 76% of these patients were transfer patients and 45% were from out of state. Loss to followup of this magnitude may result in our study underreporting the frequency of severe or symptomatic HO and may have caused our study to fail to identify important risk factors because of insufficient study power. ISS > 16 is one such factor; larger numbers might have resulted in the identification of the ISS as a meaningful factor associated with the development of HO. Our minimum followup of 6 weeks seems quite short; however, in our series, Brooker class at 6 weeks did not change significantly over time, which confirms our own anecdotal observations that ectopic bone forms within the first 6 weeks, and additional time leads to progressive ossification rather than spread or increased volume. Additionally, outcome measurement instruments were not used during the study period and ROM recordings were inconsistent during chart review.

We identified prolonged mechanical ventilation as a risk factor for the development of HO after acetabular fracture surgery using an isolated Kocher-Langenbeck approach. Interestingly, prolonged mechanical ventilation has been demonstrated as a risk factor for HO in other studies assessing hips without a fracture of the acetabulum, around uninjured joints, or around the hip after femoral nailing [17, 23, 30]. Pape et al. [23] demonstrated an increased frequency of HO around uninjured joints in polytraumatized patients without head trauma compared with patients with head trauma suggesting that other pathways are involved. This is consistent with our findings in that we did not find a correlation between head AIS and HO.

Studies have demonstrated that the formation of ectopic bone after surgical treatment of acetabular fractures is related to the surgical approach. Of the three classic exposures to the hip, the Kocher-Langenbeck approach is associated with intermediate risk [12]. Ghaleb et al. [7] retrospectively evaluated a population of 236 patients with 237 acetabular fractures to determine risk factors for the development of severe HO. These patients were treated surgically through one of the three classic approaches described by Letournel [16]. They showed that risk factors for development of Brooker Class III or IV ectopic bone included use of the iliofemoral approach, T-type fractures, associated abdominal/chest injuries, and presence of multiple operative findings suggestive of severe local injury (ie, femoral head damage, sciatic nerve damage, intra-articular bone fragments, impaction). They also demonstrated that the development of severe ectopic bone was associated with poor clinical results at 1-year followup. Other risk factors have been suggested such as craniocerebral trauma, time delay to surgery, concurrent trochanteric osteotomy, and ipsilateral femur fractures [4,

5, 14, 33]. However, these studies have not evaluated patient populations treated in a uniform surgical fashion by one surgeon, and risk factors were not consistent among those studies.

In this retrospective study, which evaluated a relatively homogeneous patient population, and which excluded a number of patients who were identified in advance as being at high risk (and so who received prophylaxis with indomethacin), we showed rates of HO comparable to previous studies [9, 28, 32] and we identified prolonged mechanical ventilation as a risk factor for the development of severe HO. Although we cannot recommend for or against routine prophylaxis, patients who are expected to be ventilated for a prolonged period may benefit from prophylaxis. Basic science research is still needed to identify the pathogenesis of this condition, and a prospective study would be helpful to confirm risk factors as well to determine outcomes of patients with HO.

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