

# Emphasizing the Importance of Naproxen Prophylaxis May Decrease the Rate of Heterotopic Ossification After Hip Arthroscopy



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**Purpose:** To investigate the incidence of heterotopic ossification (HO) in patients prescribed prophylactic nonsteroidal anti-inflammatory drugs (NSAIDs), both before and after the introduction of a standardized education protocol. **Methods:** A retrospective review was conducted using a database of hip arthroscopy patients treated by a single surgeon at an academic hospital from 2015 to 2023. The inclusion criteria were (1) primary hip arthroscopy for the treatment of femoroacetabular impingement, (2) completion of a 2-week course of prophylactic postoperative NSAIDs (500 mg of naproxen twice daily), and (3) availability of follow-up radiographs at the 6-month postoperative visit. The control cohort was merely prescribed the postoperative prophylactic NSAIDs, whereas the intervention cohort also received dedicated in-person education, emphasizing the importance of NSAID adherence. The presence of HO was determined through review of follow-up radiographs. Standard descriptive statistics were used to describe the findings. **Results:** Both the control and intervention groups consisted of 200 continuous hip arthroscopy patients, with the control group treated from 2015 to 2017 and the intervention group treated from 2020 to 2023. Within the control group, 10 cases of HO (5%) were detected. Within the intervention group, 2 cases of HO (1%) were found. The Pearson  $\chi^2$  test with Yates continuity correction produced a value of 4.21, with a *P* value of .04. **Conclusions:** In this study, we found a significantly lower incidence rate of HO in patients who received standardized education on the importance of NSAID compliance versus those who did not. This finding suggests that patient education may play a contributory role in reducing the incidence of HO after hip arthroscopy. **Level of Evidence:** Level III, comparative cohort study.

Heterotopic ossification (HO) is a known complication after hip arthroscopy and has been a focus of research and reporting in recent years.<sup>1-5</sup> HO is defined by the extraskelatal formation of histologically normal lamellar bone.<sup>3,6</sup> The underlying pathophysiology of this condition entails a complex inflammatory signaling cascade, predominately mediated by mesenchymal precursor cells and the bone morphogenetic protein signaling pathway, ultimately resulting in seeding and ossification of surrounding soft tissues.<sup>7</sup> HO can range from small, asymptomatic islands of bone to large,

ankylosing lesions and can occur virtually anywhere in the body.<sup>4,8</sup> Generally, these lesions develop within 6 weeks of surgical intervention.<sup>9-11</sup> The Brooker classification has become the standard of classification,<sup>8</sup> although the ensuing effects of HO vary and ultimately depend on location. If nonobstructive, these lesions are often asymptomatic and identified incidentally on follow-up imaging.<sup>3,4</sup> However, if they are found near articular surfaces, pain and profound functional impairment can develop, requiring revision surgery for excision of the ectopic bone (Fig 1).<sup>4</sup> HO has been well described in multiple tissue types, after spinal cord or traumatic brain injuries, after thermal and blast injuries, and as a postsurgical complication.<sup>4</sup> In patients undergoing hip arthroscopy, male sex, mixed femoroacetabular impingement, volume of cam resection, and unrepaired capsulotomy have all been shown to predispose them to the development of HO postoperatively.<sup>12</sup>

A variety of prophylactic treatments have been described to address the inflammatory markers that stimulate the aberrant osteoblastic activity and reduce the risk of HO development.<sup>2,5,13</sup> Historically, high-dose

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**Fig 1.** Case of heterotopic ossification identified on follow-up radiograph after right hip arthroscopy.

postoperative radiation therapy has been used.<sup>13</sup> However, given the innate risks introduced by radiotherapy, many providers have since transitioned to less carcinogenic practices, more specifically a prophylactic course of nonsteroidal anti-inflammatory drugs (NSAIDs).<sup>2,5,14-20</sup> One review has even suggested that NSAIDs are potentially more efficacious than radiotherapy in reducing HO after total hip arthroplasty.<sup>16</sup> Both selective and nonselective NSAIDs, including naproxen, celecoxib, indomethacin, and so on, have proved efficacious in reducing the incidence of postoperative HO.<sup>5,15,18,19,21</sup> In hip arthroscopy, the recent literature has shown that naproxen, taken anywhere from 1 to 6 weeks postoperatively, consistently reduces the incidence of postoperative HO.<sup>2,5,17,21-23</sup> However, the reported ranges of the HO incidence with NSAID use vary widely, with reports of anywhere from 0% to 44%, likely as a result of differences in treatment practices of surgeons.<sup>15</sup>

Existing research has consistently established the efficacy of NSAIDs in preventing HO postoperatively. There remains significant variation in reported incidence rates of HO, which may be attributed to differences in institutional practices, or patient adherence to their postoperative medications. The purpose of this study was to investigate the incidence of HO in patients prescribed prophylactic NSAIDs, both before and after the introduction of a standardized education protocol. Our hypothesis was that the incidence of HO would be decreased after the implementation of the patient education protocol.

## Methods

### Patient Selection

After receiving institutional review board approval (No. 00055341), we performed a retrospective review of all patients who underwent hip arthroscopy at a single, high-volume academic institution performed by the senior author (S.K.A.) from 2015 to 2017, when no verbal patient education was provided, and from 2020 to 2023, once the verbal education protocol was consistently used in all patients. Patients in both groups were included if they met the following inclusion criteria: (1) primary hip arthroscopy with cam lesion resection and either an interportal or periportal capsulotomy; (2) documented HO prophylaxis with naproxen for 2 weeks; and (3) follow-up imaging at the 6-month postoperative appointment. Patients were excluded if they (1) underwent revision arthroscopy or previous hip surgery, (2) underwent bilateral hip arthroscopy, (3) had absent or inadequate follow-up imaging, and (4) underwent other procedures at the time of primary hip arthroscopy. The patients in the control group did not receive any formal verbal education, and their only guidance to take their medication was listed directly on their postoperative naproxen prescription bottle, which stated, "Take as scheduled for 2 weeks for heterotopic ossification prophylaxis, then as needed for pain." On the other hand, the education protocol was implemented consistently as standard of care by the senior author in January 2020. This included a verbal explanation of why naproxen was being prescribed for HO prophylaxis and indicated that adherence to the regimen was imperative for minimizing the risk of HO development. The discussion was performed preoperatively with the patient just prior to the surgical procedure in the preoperative holding area. The discussion stressed that there was only 1 medication (naproxen) that was required to be taken after the operation and the main reason for taking the naproxen was to prevent unwanted bone from forming in areas around the hip. The discussion stressed the importance of taking the medication twice a day for 2 weeks. No supplemental written materials were provided to the verbal education group.

### Surgical Technique

Hip arthroscopy was performed in a consistent fashion throughout the study period. The capsule was incised using either an interportal or periportal capsulotomy, each of which involved the formation of 2 portals, which were either connected via an incision (interportal) or not connected (periportal).<sup>24</sup> With the joint space made accessible, the labrum was repaired, if damaged, and resection of the cam lesion was performed in all patients. Once completed, the joint space was irrigated, and the capsulotomy was repaired using

the same figure-of-8 suture technique. The postoperative rehabilitation protocol was consistent in both groups, including recommendations for physical therapy starting at 2 weeks after surgery.

### Radiographic Analysis

Demographic data were collected from the institution's electronic medical record software (Epic Systems, Verona, WI). Plain-film radiographs were assessed, and radiology reports were analyzed by a single, trained reviewer (A.Z.K.) using the institution's picture archiving and communication system (IntelliSpace; Philips, Amsterdam, The Netherlands). HO was determined to be present if any detached, nonphysiological radiopaque structure was visually appreciated within or around the tissues surrounding the hip joint on follow-up radiographic imaging and was not appreciated on preoperative imaging. The standard hip radiographic series reviewed consisted of a pelvic anteroposterior radiograph, as well as false-profile lateral, modified Dunn lateral, and frog-leg lateral views. HO was deemed present if identifiable on at least 2 views and was classified according to the Brooker criteria.<sup>8</sup> Grade 1 represents isolated bony islands within the soft tissues; grade 2, bone spurs between the femur and pelvis with greater than 1 cm between the bone surfaces; grade 3, bone spurs reducing the space to less than 1 cm; and grade 4, complete ankylosis between the pelvis and femur. The 2-dimensional maximal HO length was measured on both anteroposterior and lateral views and averaged.

### Statistical Analysis

All calculations and statistical analyses were performed using Microsoft Excel (version 16.54; Redmond, WA) and the R package (2023 version; R Foundation for Statistical Computing, Vienna, Austria). Statistical analyses were performed using standard descriptive statistics, including mean age at surgery and mean time to follow-up imaging. To compare significance between cohorts, the Pearson  $\chi^2$  test with Yates continuity correction was performed, with  $P < .05$  showing statistical significance.

## Results

In the control group, 200 continuous primary hip arthroscopy patients met the inclusion criteria out of 486 hip arthroscopy cases performed between January 2015 and August 2017. We excluded 95 cases because they were revisions, 114 because they were bilateral cases, and 77 because of lack of adequate follow-up. In the experimental group, 200 continuous primary hip arthroscopy patients met the inclusion criteria out of 489 cases performed between July 2020 and May 2023. We excluded 86 cases because they were revisions, 93 because they were bilateral cases, and 110 because of lack of adequate follow-up. The mean age in the control group was  $33.3 \pm 13.2$  years and the mean follow-up

**Table 1.** Demographic Characteristics of Control and Education Groups

Characteristic	Control Group (2015-2017)	Education Group (2020-2023)	P Value
Age, yr	$33.3 \pm 13.2$	$31.6 \pm 13.2$	.104
Follow-up, mo	$12.8 \pm 8.8$	$8.3 \pm 5.0$	.000157*
Laterality			.306
Left	85	75	
Right	115	125	
Sex			.376
Male	62	54	
Female	138	146	
Capsulotomy type			
Interportal	200 (100)	71 (35.5)	
Periportal		129 (64.5)	

NOTE. Data are presented as mean  $\pm$  standard deviation or number (percentage).

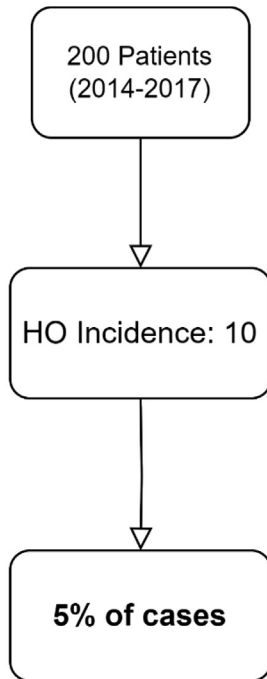
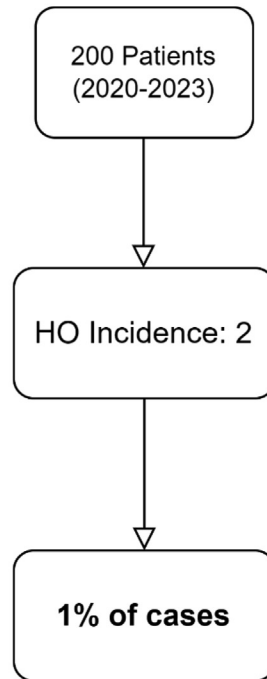
\*Statistically significant (defined as  $P < .05$ ).

period was  $12.8 \pm 8.8$  months, with 138 female and 62 male patients (Table 1). This group included 115 right- and 85 left-sided procedures. In the education group, the mean age was  $31.6 \pm 13.2$  years, with a mean follow-up period of  $8.3 \pm 5.0$  months. This group included 125 right- and 75 left-sided procedures, with 146 female and 54 male patients. Within the control group, 10 patients (5%) were found to have radiographic evidence of HO on at least 2 views (Fig 2). All 10 cases were deemed Brooker grade 1, with a mean maximal length of  $10.64 \pm 5.26$  mm. Within the education group, 2 patients (1%) were found to have evidence of HO on at least 2 views. Both cases were Brooker grade 1, with a mean length of  $10.60 \pm 5.21$  mm. The Pearson  $\chi^2$  test with Yates continuity correction produced a value of 4.21, with a  $P$  value of .04.

## Discussion

Our findings revealed a statistically significant decrease in the HO incidence among patients having received dedicated in-person education on postoperative naproxen use versus those who did not receive dedicated education. This finding suggests that patient education may play an important role in medication adherence and, ultimately, desired outcomes.

It is evident that various NSAIDs have a proven beneficial effect against the development of HO.<sup>2,5,14,15,21,25,26</sup> Considering the alternative therapy of high-dose radiation, this option provides comparable, and potentially superior, prophylaxis with a lower carcinogenic risk.<sup>16</sup> A review by Shapira et al.<sup>16</sup> found that high-risk patients receiving postoperative radiation therapy versus those taking a course of NSAIDs, either selective or nonselective, had reduced rates of mild and severe HO formation. When navigating the wide range of available NSAIDs, the literature has consistently revealed no significant differences in the HO incidence

**Without Dedicated Education****With Dedicated Education**

$\text{Chi}^2 = 4.21$   
 $\text{p-value} = 0.04$

**Fig 2.** Incidence rates of heterotopic ossification (HO) and Pearson  $\chi^2$  test results in control group versus education group.

between selective and nonselective variants.<sup>5,15</sup> A systematic review by Zhang et al.<sup>2</sup> found that, among 45 studies on NSAID prophylaxis, 4 randomized controlled trials (RCTs) used a regimen of oral naproxen (taken at least twice daily) for 1 to 6 weeks postoperatively. Among these RCTs, the reported incidence rates of HO at 12 months postoperatively were 30.8%, 4.6%, 11%, and 14.8%. Considering that the same pharmacologic processes are occurring in all these cohorts, there is much confusion as to why these rates show considerable variation.<sup>2</sup> One of the most plausible differences is whether these patients are truly adhering to the prescribed postoperative medication regimen.

In our practice, we have been routinely prescribing naproxen for HO prophylaxis since 2010. The use of naproxen as HO prophylaxis dates back to the 1990s in the hip arthroplasty literature.<sup>22,23</sup> This regimen was further proved efficacious in hip arthroscopy procedures by a 2015 double-blinded RCT in which the control group received a placebo whereas the intervention group received a 3-week course of 500 mg of naproxen twice daily.<sup>17</sup> The results of this study showed a stark difference in the HO incidence, with the placebo group incurring a 44% incidence rate whereas only 4.6% of patients in the intervention group had HO at 3 months'

follow-up.<sup>17</sup> Since the integration of the education protocol, the authors noted that the incidence of HO seemed quite rare, which inspired our investigation.

Patient education and adherence to medication have been a center of investigation in many other fields of medicine. In the wake of the opioid epidemic, much research has been conducted on the efficacy of patient education regarding the risks of habitual prescription use, as a precursor for the development of substance use disorder. A 2019 study by Yajnik et al.<sup>27</sup> found that, after total knee arthroplasty, postoperative opioid use decreased by nearly half after implementation of a simple information card, with no differences in reported pain scores.

A 2021 review by Simon et al.<sup>28</sup> investigated the various contributing factors to medication non-adherence, which is estimated to account for 10% of all hospitalizations, and an annual health care burden of \$100 to \$500 billion in the United States alone. Within the education-based literature, in a review of multiple large-cohort RCTs with in-person education protocols, provided by physicians, nurses, and even pharmacists, all studies showed significant improvements in medication adherence in the treatment of cardiovascular pathologies.<sup>28</sup> Similarly, our study found



significant improvements in outcomes among patients receiving education, further supporting the benefits of patient education protocols. Of note, this is particularly useful in our patient cohort because NSAIDs are generally perceived as and taken as a pain-relief medication, rather than a prophylactic medication. Given the continually improving, minimally invasive nature of hip arthroscopy, most patients generally feel better after a few days and may choose to discontinue taking this medication, thinking that it is only prescribed for postoperative pain. This rationale is further justified by the non-negligible rate of reported adverse events with naproxen use, specifically gastrointestinal side effects.<sup>29</sup> This further highlights the importance and utility of proper patient education to optimize desired outcomes.

“Patient empowerment” has become a globally popular term in health care, striving to create an involved environment of patient-informed decision making and intrinsic motivation. This holistic concept aims to create an improved, mutualistic relation between the patient and provider through self-efficacy.<sup>30</sup> Many factors contribute to this process. A 2018 study found that the 2 largest contributors to patient empowerment were patient education and patient satisfaction scores.<sup>31</sup> To combat existing distrust in the health care system, education creates a sense of autonomy and self-determination that leads to informed decision making. The results of our study contribute to this school of thought, and we intend to continue to investigate the efficacious benefits of informed and shared decision making to patient outcomes.

### Limitations

This study has several limitations. First, we investigated 2 cohorts of patients between 2015 and 2017 and between 2020 and 2023. We did not analyze hip arthroscopy patients in the transition period between 2017 and 2020. Although education was provided during the period of 2017 to 2020, it was not until January 2020 that we began making patient education standard of care for all patients. We chose to omit this period with inconsistent education and, rather, analyze 2 populations in which either all patients received education or all patients did not. Second, there were slight differences in surgical technique for capsular repair, along with mean follow-up time, between the cohorts. In the control group, all hip capsule incisions were made using the interportal technique. In contrast, the experimental group comprised 71 interportal capsulotomies (35.5%) and 129 periportal capsulotomies (64.5%). For all patients included in this study, the intraoperative processes of cam impingement takedown, reshaping, washout, and closure were consistently performed and were virtually identical between the cohorts. In theory, variations in capsular management may introduce a risk of performance bias. However, we believe

this risk to be minimal concerning HO formation, as the majority of surgical steps, particularly those involved in osteoplasty, were nearly identical between the groups. In addition, the mean time to follow-up imaging differed between the 2 groups, with mean values of  $12.8 \pm 8.8$  months in the control group versus  $8.3 \pm 5.0$  months in the education group. The historical literature has consistently revealed that the vast majority of HO cases present within 6 weeks of surgery.<sup>1,3,9,14</sup> Although our ranges for both cohorts were far greater than this period, there is a theoretical risk of very late-onset HO, which—although highly improbable—creates a potential risk of detection bias. Third, reviewed radiographs were obtained from both our institution and outside institutions. Slight differences in imaging protocols and radiograph quality could theoretically affect the rate of HO identification; however, given its radiopaque nature, HO would be very difficult to conceal. Fourth, medication adherence was not evaluated. Regarding our investigated patient population in which HO developed, we did not specifically reach out to these individuals to confirm whether they adhered to the NSAID regimen, nor did we have them return to our institution to perform functionality tests. Given the retrospective nature of this study, contacting patients regarding their medication adherence years after the fact would create a significant risk of recall bias. We relied on HO incidence as a proxy for adherence given that the literature has consistently shown decreased rates of HO with NSAID adherence.<sup>2,5,15,17,20</sup> Nonetheless, additional investigation is warranted to further evaluate rates of adherence. Fifth, we chose not to include patient-reported outcome data in our analysis, due to transitions in institutional protocols during our study period, ultimately resulting in a low collection rate (about 20% in both cohorts). That said, among the scantily available data (Patient-Reported Outcomes Measurement Information System – Physical Function and Visual Analog Scale – pain scores), there were no appreciable differences when comparing the two cohorts. Among the patients with HO, patient-reported outcome scores were generally lower, consistent with the historical literature. Given the sub-optimal collection rate, we were not in the position to confidently report on outcome measures.

### Conclusions

In this study, we found a significantly lower incidence rate of HO in patients who received standardized education on the importance of NSAID compliance versus those who did not. This finding suggests that patient education may play a contributory role in reducing the incidence of HO after hip arthroscopy.

### Disclosures

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: S.K.A. reports a

consulting or advisory relationship with Stryker. All other authors (A.Z.K., N.E.M., J.F., A.K.M., D.C.L.) declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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