Incidence of Heterotopic Ossification and Effects of Various Prophylactic Methods After Hip Resurfacing

Michel J. Le Duff, M.A., Kohtaroh B. Takamura, B.S., and Harlan C. Amstutz, M.D.

Abstract

A retrospective analysis of 1000 hips in 838 patients was conducted to determine the efficacy of alterations made throughout the series to the prophylactic protocol used to minimize the incidence of heterotopic ossification (HO) after hip resurfacing.

Materials and Methods: Four groups were determined following the initiation of these changes. Initially, the patients received indomethacin and 1000 milliliters of both saline and duobiotic (group 1). In group 2, a single pre-operative 700 cGy radiotherapy session was added for males undergoing one-stage bilateral procedures or the second stage of a two-stage procedure when HO had formed on the first hip. In group 3, the volume of saline used to clean the wound after implantation was increased from 1000 to 2000 milliliters, while the 1000 milliliters of duobiotic remained throughout the series. Finally, the use of a plastic drape was added to collect bone debris during the reaming of the femoral head in group 4. Chi-square analyses were conducted between groups to identify significant decreases in the prevalence of HO.

Results: Group 3 showed a reduction in incidence of all HO grades combined, and severe HO only compared with group 2 (p = 0.003 and p = 0.007, respectively). A decrease in severe HO incidence was observed between group 1 and group 2 in males who underwent bilateral surgery (p = 0.048). In addition, there was a significant decrease in the incidence of both all HO grades (p = 0.0001) and severe HO (p = 0.029) between groups 1 and 4.

In contrast to most studies that have assessed the individual effect of prophylactic methods in a single protocol, the present study confirmed the effectiveness of combining indomethacin and radiation therapy in high-risk patients, as well as copious pulse lavage of the wound in reducing the incidence of HO. The use of the plastic drape did not confer any additional gain.

Heterotopic ossification (HO) is a common complication characterized by abnormal bone formation within muscle and connective tissue following surgical trauma, often observed after total hip arthroplasty. It has been reported that the incidence of HO ranged from 15% to 90%, with 1% to 27% of patients reporting clinically important pain and reduced hip motion. Generally, the incidence of HO is higher in males with osteoarthritis than females, and patients who receive bilateral and repeated procedures are also at high risk for HO.

The pathogenesis of HO formation is unknown; however, HO formation may be associated with bone dust and appreciable bleeding that occur during total hip arthroplasty. As for the molecular mechanism of HO, previous investigations inferred that undifferentiated mesenchymal cells migrate to the site of surgery and differentiate into osteoblasts to secrete osteoid, which is then mineralized into bone. Furthermore, osteoblasts causing ectopic bone formation over express BMP-2 and BMP-4. In contrast, a few studies have suggested that the osteogenic precursor cells arise from local soft tissues that undergo stretching and surgical trauma, rather than from bone debris. In comparison with conventional total hip replacement, hip resurfacing is likely to generate much more bone debris during the reaming of the femoral head. Also, additional stretching of the soft tissues surrounding the hip should be expected during the reaming of the acetabulum and the implantation of the acetabular component because of the need to keep the femoral head and neck out of the way. These two reasons make hip resurfacing
a procedure thought to be more prone to the development of HO than conventional total hip arthroplasty.

Many prophylactic methods have been integrated into protocols to prevent the occurrence of HO. Modern surgical protocols include the use of saline lavage and a plastic drape for removal of bone debris and reamings, as a general precaution in total hip arthroplasty. Radiation therapy after surgery has been proven to be effective in reducing the incidence of HO; however, further studies confirmed that a reduction to 700 cGy in a single dose was as effective and further reduces the risk of sarcoma. In addition, nonsteroidal antiinflammatory agents (NSAIAs), such as indomethacin, are used to prevent mesenchymal cells from differentiating into osteoblasts. Similarly, diphosphonates have been used to inhibit calcification of the osteoid matrix but have not demonstrated a clear advantage. The purpose of the present study was to assess the effectiveness of a combination of prophylactic methods on the incidence of HO after hip resurfacing.

**Materials and Methods**

From the senior surgeon’s (HCA) database, the first 1000 hips in 838 patients implanted with Conserve Plus hip resurfacing devices (Wright Medical technology, Inc., Arlington, Tennessee) were retrospectively reviewed. The surgeries were performed between November 1996 and September 2006. The patients were followed radiographically at 4 months and then yearly during postoperative visits. Patients coming from out of state were either followed in one of 20 annual satellite clinics sites organized by the senior investigator or by radiographs forwarded to our center after follow-up visits with their local orthopaedist. Only anteroposterior radiographs were evaluated for this review, using the Brooker grading system to categorize the magnitude of HO. The clinical results of this cohort have previously been reported. However, no mention of the prevalence of HO was made in that report. The surgical technique used was also previously described. All hips were operated on through a posterior approach except three, for which a trochanteric lateral approach was used.

At the onset of the series, the only prophylactic prevention of HO was the use of indomethacin (50 milligrams given pre-operatively and postoperatively, then 25 milligrams given three-times a day for 5 days. This use of indomethacin remained the same for all patients throughout the series. After the first patient of the series operated using a one-stage bilateral procedure (hips Nos. 58 and 59) developed high grades of HO of both hips, a change in the prophylactic protocol was implemented, and all male patients undergoing simultaneous bilateral surgery were given a single dose of 700 cGy of radiation preoperatively, starting with hip No. 116. Male patients undergoing the second stage of a two-stage bilateral procedure followed the same protocol if any HO had formed on the first hip. Further alterations were made progressively to this protocol throughout the series, including an increase in the amount of saline from 1000 to 2000 milliliters used with powered jet lavage to clean the wound after implantation of the components, while 1000 milliliters were utilized throughout the procedure using a bulb syringe. This change was effective by hip no. 450. In addition, the use of a plastic drape to collect bone debris from femoral head reamings was implemented at the onset hip number 700 (Fig. 1).

Of the 1000 hips analyzed, 744 of the hips (74%) were in males and 256 (26%) were in females. The mean age of the patients was 50 years (range, 14 to 78 years), the mean weight was 83 kg, and the mean body mass index was 26.9. We elected to review only the hips with 2-years minimum of follow-up to ensure that HO formation, if any, was complete at the time of review. Sixteen hips did not have a postoperative radiograph with 2-year follow-up or beyond, leaving 984 hips for the review.

The effect of each modification of the HO prevention protocol was studied by comparing the occurrence of HO in the different treatment groups determined by the chronological introduction of these modifications. Chi-square analysis was performed using two different remarkable events: presence of HO regardless of the Brooker grade (all HO) and presence of HO Brooker grade III or IV only (severe HO), which can have clinical implications. The grouping of the hips and the corresponding HO protocols are described in Table 1. The four groups were comparable in terms of male-female ratios. However, there was a slight increase in the proportion of hips operated for osteoarthritis in groups 3 and 4 as compared with groups 1 and 2 (Table 2).

**Results**

The prevalence of HO of any grade for the whole series was 211 cases in 984 hips (21.4%), and the prevalence of severe HO (Brooker grades III and IV) was 39 cases in 984 hips (4.0%). From these 39 hips, only one was symptomatic, with a UCLA pain score of 7. This patient presented with the most...
severe limitation of motion in this cohort, a flexion arc of 75°, and a rotation arc of 20°. Nine other patients had some limitation of motion (nine Brooker grade III and one Brooker grade IV), including two who had undergone simultaneous bilateral resurfacing, despite having pre-operative radiation therapy. The flexion arc for these 10 hips ranged between 80° and 95°, while three had rotation arcs of 20° to 30°. All other hips had greater than 100° of flexion, with rotation arcs

<table>
<thead>
<tr>
<th>Group</th>
<th>Hips</th>
<th>Number of Radiograph</th>
<th>Radiograph Reviewed</th>
<th>HO Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>115</td>
<td>4</td>
<td>111</td>
<td>Indomethacin – 1000 ml saline jet lavage plus 1000 ml duobiotic (bacitracin 100,000 units + polymixin 500,000 units)</td>
</tr>
<tr>
<td>2</td>
<td>334</td>
<td>2</td>
<td>332</td>
<td>Indomethacin – 700 cGy for bilateral males 1000 ml saline jet lavage plus 1000 ml duobiotic</td>
</tr>
<tr>
<td>3</td>
<td>251</td>
<td>4</td>
<td>247</td>
<td>Indomethacin – 700 cGy for bilateral males 2000 ml saline jet lavage plus 1000 ml duobiotic</td>
</tr>
<tr>
<td>4</td>
<td>300</td>
<td>6</td>
<td>294</td>
<td>Indomethacin – 700 cGy for bilateral males 2000 ml saline jet lavage plus 1000 ml duobiotic Use of plastic drape to collect bone debris from femoral reaming</td>
</tr>
</tbody>
</table>

Table 1 Grouping and Corresponding HO Protocol

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of Hips Reviewed</th>
<th>Group 1 (hips 1-115)</th>
<th>Group 2 (hips 116-449)</th>
<th>Group 3 (hips 450-700)</th>
<th>Group 4 (hips 701-1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>111</td>
<td>332</td>
<td>247</td>
<td>294</td>
<td></td>
</tr>
<tr>
<td>Male hips</td>
<td>79 (71%)</td>
<td>248 (75%)</td>
<td>192 (78%)</td>
<td>212 (72%)</td>
<td></td>
</tr>
<tr>
<td>Female hips</td>
<td>32 (29%)</td>
<td>84 (25%)</td>
<td>55 (22%)</td>
<td>82 (28%)</td>
<td></td>
</tr>
<tr>
<td>Idiopathic OA</td>
<td>73 (66%)</td>
<td>203 (61%)</td>
<td>187 (76%)</td>
<td>221 (75%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 Gender and Etiologic Distributions Between Groups

Figure 2 A. Anteroposterior radiograph of the pelvis of a 43-year-old male who is an avid cyclist and has bilateral osteoarthritis. The radiograph was performed 8 months after resurfacing of the right hip. The patient developed Brooker grade III HO, which restricted his range of motion in flexion (flexion 65°, with 10° flexion contracture) and prevented him from participating in recreational activities. B. Prior to left-side surgery, radiation therapy was performed. Heterotopic bone was surgically removed from the superolateral aspect of the right femur at the same time hip resurfacing was performed on the left side. The bone medial to the lesser trochanter was not removed. C. The 5-year radiograph shows no recurrence of HO on the right side and a clear film on the left side. The patient’s current flexion arcs are 125° on the right and 130° on the left, with no flexion contracture. His UCLA scores are pain 10, walking 10, function 10, and activity 10. He cycles 1 to 2 hours more than three-times a week.
Three hips with range-of-motion limitation underwent surgical removal of HO, including one for which HO removal was performed at the same time a resurfacing was performed on the contralateral hip that received pre-operative radiation therapy (Fig. 2). The comparative HO incidence rates between groups are shown in Figure 3 for all grades and in Figure 4 for Brooker grades III and IV.

The prevalence of HO of any grade was 37/111 (33.3%) for group 1, 89/332 (26.8%) for group 2, 37/247 (15.0%) for group 3, and 48/294 (16.3%) for group 4. The difference was significant between group 2 and group 3 (p = 0.003), but not between groups 1 and 2 (p = 0.264) or between groups 3 and 4 (p = 0.455). The prevalence of HO of Brooker grade III or IV was 6/111 (5.4%) for group 1, 23/332 (6.9%) for group 2, 5/247 (2.0%) for group 3, and 5/294 (1.7%) for group 4. Similarly, the difference was significant between group 2 and group 3 (p = 0.007) but not between group 1 and 2 (p = 0.587) or between group 3 and 4 (p = 0.783).

Due to the fact that the first protocol change only affected the hips from male patients undergoing simultaneous bilateral procedures and the second hip of male patients undergoing staged bilateral procedures when the first hip had developed HO, we elected to test the effectiveness of radiation therapy on this subset of patients. There was no difference between group 1 and the other three groups combined for HO of all grades (p = 0.691). However, the prevalence of severe HO was significantly reduced (p = 0.011). The comparative analysis between group 1 and group 4 yielded a drop in the prevalence of both HO of all grades (p = 0.0001) and severe HO only (p = 0.029).

Discussion

Most studies that assess the efficacy of prophylactic methods to reduce the incidence of HO focus on the effects of just
one method or treatment in comparison with the results of a control group receiving no treatment. In the present study, we assessed the effect of multiple methods used in combination as this represented the experience of the senior investigator throughout his series of metal-on-metal hip resurfacing. Therefore, the results of the present study might differ from the findings of other studies using each method in isolation, because the effect of one method can be attenuated by the effect of another. However, the value of this study resides in the possibility that a combination of methods might enhance the overall protection against the development of HO. One limitation of this study resides in that we were not able to factor in the learning curve of the surgeon. This is especially true with regard to debulking and mobilizing the femoral head and placing it under the abductor muscles to allow the preparation of the acetabulum and implantation of the socket. It is our belief that the procedure has been progressively performed with less stretching of the muscles, a factor that could have also reduced the incidence of HO.9,10

The first result that can be highlighted from this study is that hip resurfacing performed with adequate prophylactic methods does not appear to lead to an excessive incidence of HO, as compared with reports of conventional THR.6,17,28,29 We did not find a significant reduction in HO incidence between group 1 and group 2, because the prophylactic modification involved only a small portion of the group of patients. However, the application of radiotherapy to high-risk patients (males undergoing simultaneous bilateral procedures or second hip surgery in male patients who developed HO on the first side) showed effectiveness in reducing the incidence of severe HO in this group of patients (Fig. 4); this result is consistent with the findings of Healy and colleagues.24

The greatest improvement in the protocol against HO came from the increase from 1000 to 2000 milliliters of the saline used to clean-up the wound after component implantation. This change showed great efficacy, in addition to the use of indomethacin and radiation therapy for high-risk patients. This result suggests that bone debris remaining in the tissues surrounding the hip are a cause for HO formation and is in contrast with the findings of Sneath and coworkers.10

The addition of a plastic drape used during the reaming of the femoral head to collect bone debris did not lead to any significant improvement in the incidence of HO, whether mild or severe. This result differs from the findings of Shields and associates,11 who showed the effectiveness of this intra-operative technique for hip resurfacing. However, they reported incidence levels of 32% using the plastic sheet versus 58% without, which are levels substantially greater than those observed in our study. Their patients did not receive any other form of prophylactic treatment for HO. It is likely that the effect of indomethacin and the copious pulse lavage administered to our patients offset the effect of collecting the bone debris during reaming, making this additional precaution unnecessary.

Conclusion

Overall, our study showed incremental progress with the combination of several prophylactic methods against HO formation, as reflected by the drop in incidence from 33% in group 1 to 15% in group 3 and 16% in group 4, with less than 2% of severe HO cases. This result compares favorably with most reports of HO incidence in conventional total hip arthroplasty,6 particularly because the patient population seeking hip resurfacing is typically dominated by male patients with osteoarthritis, who are considered to be at high risk for the development of HO.3,4

Disclosure Statement

None of the authors have a financial or proprietary interest in the subject matter or materials discussed, including, but not limited to, employment, consultancies, stock ownership, honoraria, and paid expert testimony. Funding for this study was provided by Saint Vincent Medical Center, Los Angeles, and Wright Medical Technologies Inc.

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