A Review Paper

Heterotopic Ossification After Total Hip Arthroplasty

Randy M. Cohn, MD, Ran Schwarzkopf, MD, and Fredrick Jaffe, MD

Abstract

Heterotopic ossification (HO), the development of bone outside its normal location in the skeleton, can compromise outcomes of total hip arthroplasty (THA). The etiopathogenesis of HO, though incompletely understood, involves genetic abnormalities, neurologic injury, and musculoskeletal trauma. Several systems are used to classify severity of HO after THA. Numerous risk factors for HO, including patient factors and surgical techniques, have been described. Prophylaxis against HO traditionally has involved radiation therapy or use of nonsteroidal anti-inflammatory drugs. Once formed, heterotopic bone can be managed only with surgical excision.

Heterotopic ossification (HO) is the development of bone outside its normal location in the skeleton. Formation of bone in soft-tissue structures results from disruptions in normal skeletogenesis. These disruptions have a variety of causes, such as surgery, neurologic injury, arthropathies, and genetic disorders. The consequences of HO can range from clinically insignificant ones to complete joint ankylosis with significant loss of motion and severe pain.[1]

HO is a concern in joint arthroplasty, particularly hip arthroplasty. Reported rates of HO after hip arthroplasty have been as low as 2% and as high as 90%, with rates of severe HO ranging from 3% to 55% depending on the population studied, risk factors involved, prophylactic measures taken, and surgical technique used.[1]

In this review, we examine the literature to determine which surgical approaches and techniques for hip arthroplasty have the lowest incidence of HO. We also evaluate the prophylactic measures and patient risk factors to determine the likelihood of HO.

Histopathology and Etiopathogenesis

The etiopathogenesis of HO is complex and incompletely understood. HO requires inductive signaling, inducible osteoprogenitor cells, and an environment conducive to bone growth.[2] There are 3 broad pathways to HO: genetic abnormalities, neurologic injury, and musculoskeletal trauma.[3] Traumatized muscle-derived mesenchymal progenitor cells can function as osteoprogenitor cells in HO.[4] However, HO is not limited to cells of mesenchymal lineage. As recently shown, circulating, hematopoietically derived cells with osteogeneic potential can settle in inflammatory sites and initiate HO.[5]

Classification and Diagnosis

The most widely used classification system for HO after total hip arthroplasty (THA), developed by Brooker and colleagues,[6] is based on an anteroposterior radiograph of the pelvis. According to the Brooker system, there are 4 classes of HO: class 1 (islands of bone within soft tissue of any size), class 2 (bone spurs from pelvis or femur with at least 1 cm between opposing bone surfaces), class 3 (bone spurs from pelvis and femur reducing space between opposing bone surfaces to less than 1 cm), and class 4 (complete ankylosis of hip) (Figures 1–4).[6,7] Several authors have called into question the reliability and validity of the Brooker system.[7]

Della Valle and colleagues[7] proposed a modified system consisting of 3 grades: grade A (hips without HO and hips with islands of bone 1 cm or less in length [Brooker class 1]), grade B (hips with at least 1 island of bone more than 1 cm in length or hips with spurs from femur or pelvis with at least 1 cm between oppos-

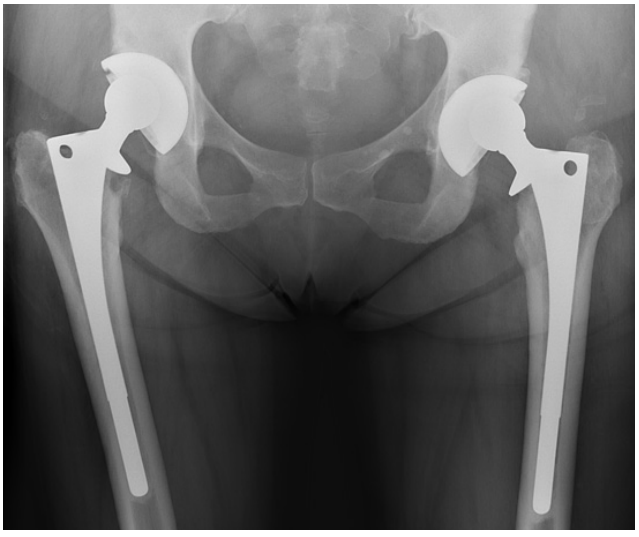

Figure 1. Woman (age 61) with total hip arthroplasties. Right hip has no heterotopic ossification. Left hip has islands of bone within soft tissue (Brooker stage 1).

Dr. Cohn and Dr. Schwarzkopf are Residents, and Dr. Jaffe is Chief, Division of Adult Reconstruction, and Clinical Professor, Orthopaedic Surgery, Department of Orthopaedic Surgery, New York University Hospital for Joint Diseases, New York, New York.

Address correspondence to: Randy M. Cohn, MD, Department of Orthopaedic Surgery, New York University Hospital for Joint Diseases, 301 E 17th St, Suite 1400, New York, NY 10003 (tel, 212-598-6000; fax, 212-598-6793; e-mail, randy.cohn@nyumc.org).

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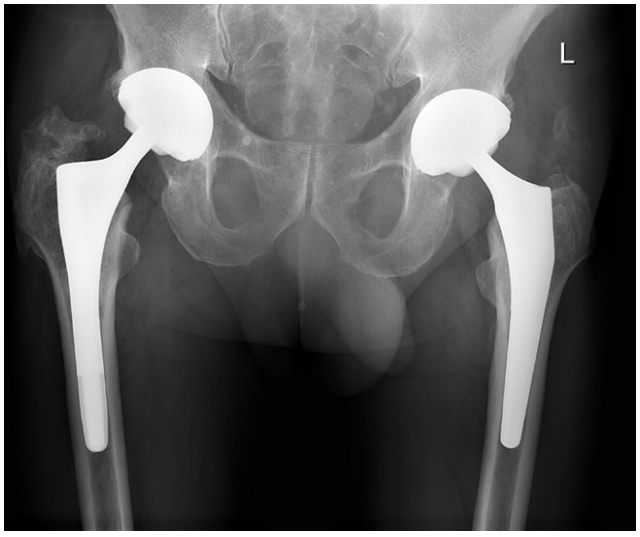

Figure 2. Man (age 65) 3.5 years after right total hip arthroplasty (THA) and 1.5 years after left THA. Right hip has bone spur originating from femur with more than 1 cm between opposing bone surfaces (heterotopic ossification, Brooker stage 2). Left hip has islands of bone within soft tissue (Brooker stage 1).

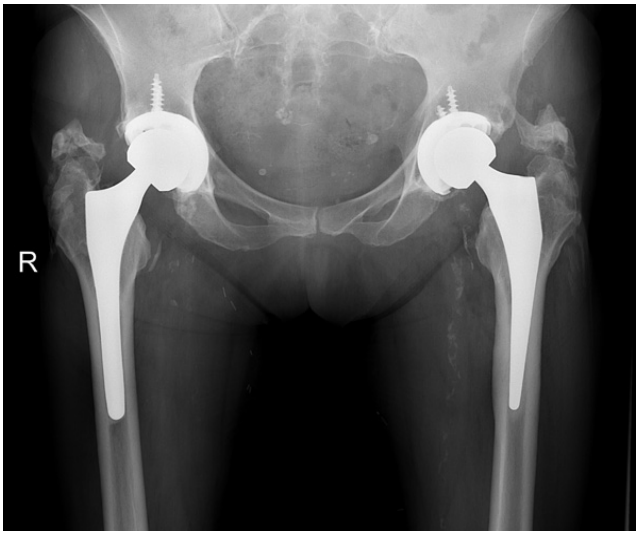

Figure 3. Woman (age 79) 2 years after right total hip arthroplasty (THA) and 1 year after left THA. Right hip has bone spur originating from femur with more than 1 cm between opposing bone surfaces (heterotopic ossification, Brooker stage 2). Left hip has bone spurs on pelvic and femoral sides with less than 1 cm between opposing bone surfaces (Brooker stage 3).

ing bone surfaces [Brooker class 2]), and grade C (hips with spurs and less than 1 cm between femur and pelvis [Brooker class 3] or apparent ankylosis of hip [Brooker class 4]).

Arcq[8] developed a system that is widely used by authors writing in German but seldom by those writing in English. This system has 3 classes: class I (isolated or marginal ossifications that "bridge" the opposing bone surfaces), class II (bone bridging on 1 side of implant), and class III (bone bridging on both sides).

A less commonly used system, developed by DeLee and colleagues,[9] takes into account severity and location of HO.

Toom and colleagues[10] found that interobserver reliability was lower for the Brooker system than for the Della Valle, Arcq, and DeLee classification system. Toom proposed a combined classification system attempting to provide easier clinical assessment and improved interobserver reliability. Despite its weaknesses, the Brooker system remains the most widely used in the English literature.

Risk Factors

Authors have reported numerous risk factors for HO, including sex, age, body mass index (BMI), blood type, osteoarthritis (OA) type, operative time, surgical approach, blood transfusion, anesthesia (spinal, epidural), prosthetic design, and preoperative function.[1,9,11]

Patient Demographics

In a study of 124 consecutive patients, Ahrengart and Lindgren[12] found a higher incidence of HO in males (84%) than in females (67%) and a larger mean surface area of HO in males (24.7 cm^2) than in females (0.69 cm^2). Male sex as a risk factor for HO after THA has been confirmed by several authors.[13-15]

Older age also has been associated with increased risk for HO in several series,[12] although this finding has been refuted by several authors.[13]

Handel and colleagues[14] found that frequency and severity of HO were statistically significantly higher in patients with very high BMI than in patients with low BMI. Eggli and Woo,[13] however, found that height and weight independently had no effect on HO.

In a retrospective study of 178 THAs, Toom and colleagues[15] found a 3-fold decrease in incidence of HO in patients with type O blood compared with patients with blood other than type O (type A, B, or AB). This correlation has not been confirmed elsewhere.

Osteoarthritis Type

Morphologic characteristics of OA have been found to affect risk for HO.[9] Bombelli[16] used radiographic appearance to define 3 morphologic types of OA of the hip: atrophic OA (hips with no or few femoral and acetabular osteophytes), normotrophic OA (hips with moderate number of osteophytes), and hypertrophic OA (hips with multiple large osteophytes).[16,17] In several series, patients with hypertrophic OA were found to be at increased risk for HO after THA.[17]

Surgical Approach

Development of HO is influenced by the surgical approach used in THA. Few investigators have compared the association between different surgical approaches and incidence of HO. In a study of 507 consecutive patients with OA or avascular necrosis, Morrey and colleagues[11] found that incidence of severe HO was lower with a posterior

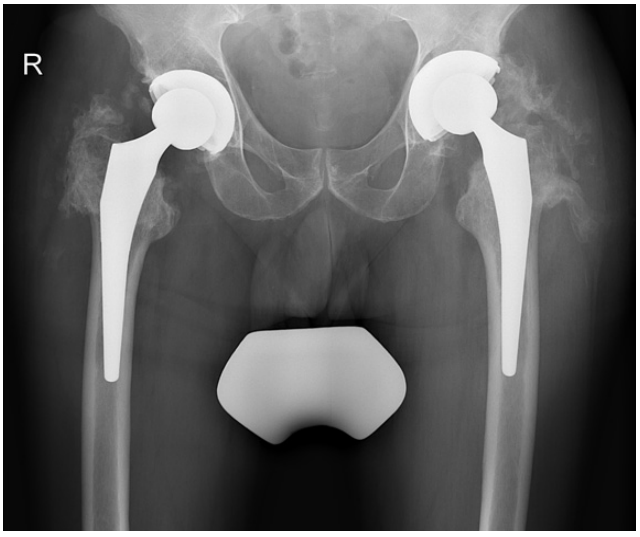

Figure 4. Man (age 54) 6 months after total hip arthroplasties. Right hip has bone spurs originating from femur and pelvis with less than 1 cm between opposing bone surfaces (heterotopic ossification, Brooker stage 3). Left hip is completely ankylosed (Brooker stage 4).

approach (22%) than with an anterolateral (29%) or a transtrochanteric (28%) approach. In a study of 1420 consecutive THAs using the direct lateral approach, Harwin[18] found a 27% overall incidence of HO, with HO occurring around the greater trochanter in 15% of hips. These findings were confirmed by Eggli and Woo,[13] who found that incidence of HO was 8.1% higher with an anterior or anterolateral approach than with a posterior approach, and that incidence was 15.1% higher when a trochanteric osteotomy was performed. Pai[19] retrospectively compared various lateral approaches and found a 5-fold increased risk for HO with the Liverpool method compared with the Hardinge or transtrochanteric approach. Authors of a study of the minimally invasive, 2-incision approach found the incidence of HO to be 26.5%.[20] Other authors have found no effect of surgical approach on HO.[21]

Operative Time, Blood Loss, Anesthesia

Findings regarding the role of operative time and blood loss in development of HO are contradictory. In a retrospective study of 178 cases, Toom and colleagues[15] found a 1.9 times higher incidence of HO after longer THAs (operative time, >100 minutes) than after shorter THAs. However, they also found no relationship between incidence of HO and amount of blood transfused and type of anesthesia. Fransen and colleagues[22] found increased risk for moderate to severe HO after THA in patients who received a blood transfusion, or in patients who received spinal or epidural anesthesia along with general anesthesia.

Cemented Versus Cementless Implants

The effect of cemented arthroplasty on development of HO is controversial. In a retrospective review of 135 THAs using cementless or hybrid implants (cemented femoral component, cementless acetabular component), Maloney and colleagues[23] found statistically significant higher incidence and severity of HO in the group with an uncemented femoral component.

This finding has been refuted by several authors.[24] A prospective randomized clinical trial of 226 lateral-approach THAs found no statistically significant difference in incidence of HO between cemented and cementless implants.[25] In their review of 134 cementless hydroxyapatite-coated primary THAs, Kasetti and colleagues[24] found a 67.2% incidence of HO but concluded that hydroxyapatite coated (uncemented) THAs did not increase the incidence or severity of HO, and that the fear of HO should not impact surgical decision making with regards to femoral fixation.

THA Versus Surface Replacement Arthroplasty

In recent studies on development of HO after surface replacement arthroplasty (SRA), incidence ranged from 26% to 60%.[26] A randomized clinical trial comparing SRA and THA found a 6-fold increase in severe HO with SRA,[27] though the overall incidence of HO was not statistically significant (44% for SRA, 31% for THA; $P = .057$).

Prophylaxis

Prophylaxis against HO traditionally has involved radiation therapy or use of nonsteroidal anti-inflammatory drugs (NSAIDs).

Several series have found that single-dose perioperative irradiation (600-1000 cGy) reduced incidence of HO after THA.[28]

A review of 17 studies (>4700 patients) found that numerous NSAID regimens, in medium to high doses, have been effective in reducing risk for HO, including ibuprofen 1200 mg/d, naproxen 750 mg/d, indomethacin 75 mg/d, and diclofenac 150 mg/d.[29]

Use of aspirin in HO prevention is controversial.[29,30] One randomized controlled trial of 2649 patients who received low-dose aspirin (162 mg/d, 35 days) found no significant benefit in HO prevention. High-dose aspirin (650 mg twice daily, 2 weeks to 6 weeks) was effective in reducing HO after THA.[29] In several series, medium-dose aspirin (325 mg twice daily for 4 weeks to 6 weeks) also reduced incidence of HO.[30,31]

Radiation therapy combined with NSAID use has been studied. In a study of 60 consecutive high-risk patients with hypertrophic OA, Pakos and colleagues[32] found a 20.4% incidence of HO with combined therapy: radiation (700 cGy) administered by postoperative day 3 and indomethacin 75 mg/d administered the first 15 postoperative days.

Surgical Management

Once HO-related symptoms have developed, the only treatment is surgical excision.[1] In their review of 53 patients with HO, Cobb and colleagues[33] found a statisti-

cally significant increase in range of motion after surgical excision. However, in no patient who underwent excision solely because of pain were symptoms completely alleviated. Warren and Brooker[34] found increased range of motion in all 12 patients who underwent HO excision and improved pain in 11 of the 12. All 12 patients underwent radiation therapy after excision, and HO recurred in 2 of the 12.

As patients who develop HO are at risk for recurrence after excision, it is recommended that prophylaxis (radiation, NSAIDs, or both) be used after HO excision.

Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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